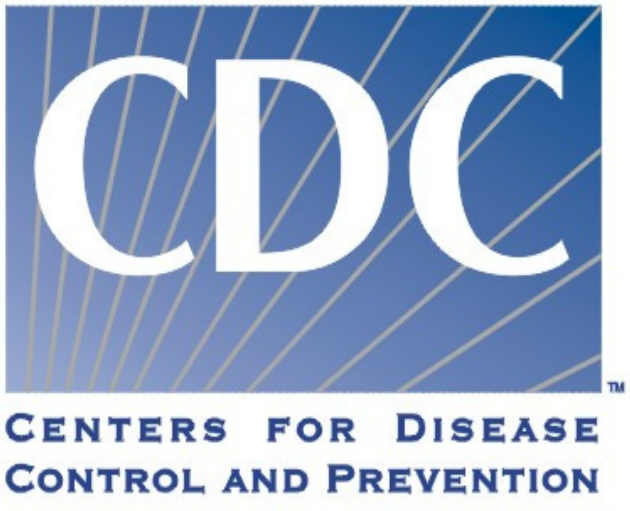
DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Division of Tuberculosis Elimination



Advisory Council for the Elimination of Tuberculosis
October 7-8, 2008
Atlanta, Georgia

Record of the Proceedings

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List of Participants

ACET Members

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

Designated Federal Official

Dr. Hazel Dean

***Ex-Officio* and Liaison Members**

Dr. Naomi Aronson (Department of Defense)
Dr. William Baine (Agency for Healthcare Research and Quality)
Dr. Robert Benjamin (National Association of County and City Health Officials)
Dr. Edward Desmond (Association of Public Health Laboratories)
Dr. Fred Gordin (American Thoracic Society)
Mr. Phillip Griffin (National Tuberculosis Controllers Association)
Dr. Michael Leonard, Jr. (Infectious Disease Society of America)
Ms. Susan Perez (Treatment Action Group)
Dr. Gary Roselle (Department of Veteran Affairs)
Dr. Diana Schneider (Department of Homeland Security)
Ms. Rachel Stricof (Association for Professionals in Infection Control and Epidemiology)
Dr. Litjen Tan (American Medical Association)
Dr. Lornel Tompkins (National Medical Association)
Dr. Charles Wallace (International Union Against Tuberculosis and Lung Disease-North American Region)
Dr. Theresa Watkins-Bryant (Health Resources and Services Administration)

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Dr. Mitesh Desai
Ms. Heather Duncan
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Dr. Denise Garrett
Ms. Judy Gibson
Dr. Richard Goodman
Ms. Natalie Greene (CDC Contractor)
Mr. Andrew Heetderks
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Dr. Tanya Sharpe
Dr. Thomas Shinnick
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Dr. Angela Starks
Mr. Phillip Talboy
Ms. Lisa Tombley
Dr. Andrew Vernon

Dr. Elisa Villarino
Dr. Wanda Walton
Dr. Carla Winston

Guest Presenters and
Members of the Public
Ms. Nuala Moore (American Thoracic Society)
Ms. Carol Poszik (National Tuberculosis Controllers Association)
Mr. Carl Schieffelbein (Public)
Mr. John Seggerson (STOP TB USA)
Ms. Kelly Wroblewski (Association of Public Health Laboratories)

ATTACHMENT 2

Acronyms Used In These Meeting Minutes

AAs	—	African Americans
ACET	—	Advisory Council for the Elimination of Tuberculosis
ACIP	—	Advisory Committee on Immunization Practices
AFB	—	Acid Fast Bacilli
APHL	—	Association of Public Health Laboratories
APIC	—	Association for Professionals in Infection Control and Epidemiology
ATS	—	American Thoracic Society
BCG	—	Bacille Calmette-Guerin
BSC	—	Board of Scientific Counselors
CAP	—	College of American Pathologists
CBP	—	U.S. Customs and Border Protection
CCID	—	Coordinating Center for Infectious Diseases
CDC	—	Centers for Disease Control and Prevention
CLIA	—	Clinical Laboratory Improvement Amendments
CMS	—	Centers for Medicare and Medicaid Services
DFO	—	Designated Federal Official
DGMQ	—	Division of Global Migration and Quarantine
DHAP	—	Division of HIV/AIDS Prevention
DHS	—	Department of Homeland Security
DNB	—	Do Not Board
DOI	—	U.S. Department of Interior
DOPT	—	Directly Observed Preventive Therapy
DOS	—	U.S. Department of State
DOT	—	Directly Observed Therapy
DST	—	Drug Susceptibility Testing
DTBE	—	Division of Tuberculosis Elimination
EDN	—	Electronic Disease Notification
FBPs	—	Foreign-Born Populations/Persons
FDA	—	Food and Drug Administration
FSM	—	Federated States of Micronesia
GAO	—	Government Accountability Office
GRA	—	Georgia Research Alliance
GSA	—	General Services Administration
HCV	—	Hepatitis C Virus
HCWs	—	Healthcare Workers
HHS	—	Department of Health and Human Services
HRSA	—	Health Resources and Services Administration
HSC	—	Homeland Security Council
ICE	—	U.S. Immigration and Customs Enforcement
IDSA	—	Infectious Disease Society of America
IFR	—	Interim Final Rule
IGRAs	—	Interferon Gamma Release Assays

LTBI	—	Latent TB Infection
MASO	—	Management Analysis and Services Office
MDR-TB	—	Multi-Drug Resistant TB
MIRU	—	Mycobacterial Interspersed Repetitive Unit
MMWR	—	*Morbidity and Mortality Weekly Report*
MSM	—	Men Who Have Sex With Men
M.tb	—	*Mycobacterium Tuberculosis*
NAATs	—	Nucleic Acid Amplification Tests
NACCHO	—	National Association of County and City Health Officials
NCHHSTP	—	National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
NEDSS	—	National Electronic Disease Surveillance System
NIAID	—	National Institute of Allergy and Infectious Diseases
NIH	—	National Institutes of Health
NTCA	—	National Tuberculosis Controllers Association
NTGS	—	National TB Genotyping Service
NTM	—	Non-Tuberculous Mycobacteria
PCSI	—	Program Collaboration and Service Integration
PITCA	—	Pacific Island TB Controllers Association
PPD	—	Purified Protein Derivative
PPM	—	Provider-Performed Microscopy
QFT-G	—	QuantiFERON®-Gold
QFT-GIT	—	QuantiFERON®-Gold In Tube
RTMCC	—	Regional Training and Medical Consultation Center
RVCT	—	Report Verified Case of TB
SGEs	—	Special Government Employees
SPWG	—	Strategic Planning Workgroup
TBESC	—	TB Epidemiologic Studies Consortium
TB-GIMS	—	TB Genotyping Management System
TBTC	—	TB Trials Consortium
TBTIs	—	TB Technical Instructions
TST	—	Tuberculin Skin Testing
WHO	—	World Health Organization
XDR-TB	—	Extensively Drug-Resistant TB

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ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
October 7-8, 2008
Atlanta, Georgia

Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention (NCHHSTP) Division of Tuberculosis Elimination (DTBE) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on October 7-8, 2008 in Building 8 of CDC's Corporate Square Offices, Conference Room A/B/C in Atlanta, Georgia.

Opening Session

Dr. Hazel Dean, Deputy Director of NCHHSTP and Designated Federal Official (DFO) of ACET, called the meeting to order at 8:37 a.m. on October 7, 2008. She welcomed the attendees to the proceedings and particularly recognized the new members and alternate liaisons. She opened the floor for introductions. The list of participants is appended to the minutes as Attachment 1.

Dr. Dean announced that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. She emphasized that ACET members should be mindful of potential conflicts of interest identified by the CDC Committee Management Office and recuse themselves from participating in discussions or voting on issues in which they have a real or perceived conflict.

NCHHSTP Director's Report

Dr. Dean presented the update on behalf of Dr. Kevin Fenton, Director of NCHHSTP, who was unable to attend the meeting. CDC is continuing to develop its new "Healthiest Nation

Initiative." This activity reinforces and builds on CDC's health protection goals and strategic imperatives and also provides a road map for CDC's contribution to creating the healthiest nation.

The strategic intent of the Healthiest Nation Initiative is to catalyze a self-sustaining, primarily externally resourced, and broad-based U.S. movement to accelerate health protection, improve equity and strengthen the value of health investments. The Healthiest Nation Initiative was created with six key strategies. The "vision will be expanded" in collaboration with partners, organizations and other stakeholders at federal, state, local and private-sector levels to create a clear and compelling vision that motivates individuals and groups to support a true health system.

"Leaders will be empowered" by convening and collaborating with current and new partners to assist in leading and aligning support. "Persons will be energized" by generating excitement among employees and other individuals. "Health will be enacted in all policies" by creating opportunities to integrate health considerations into societal policies across sectors at all levels.

"Health protection goals will be executed" to achieve greater health impact by focusing on the priorities of CDC's health protection goal portfolio and addressing the priorities and needs identified in CDC's goal action plans. "Health will be evaluated" by defining and measuring health and health value for individuals, families, communities, organizations, states and the nation.

CDC established the Healthiest Nation Coordinating Council to guide its overall direction, support and participation in the Healthiest Nation Alliance. The Healthiest Nation Alliance is a partnership among CDC, the Association of State and Territorial Health Officials, and the National Association of County and City Health Officials (NACCHO). However, partners from public health, medicine, third-party payers, business, policy, government and academia are engaged in this effort as well.

CDC convened a "Leaders-to-Leaders Conference" in July 2008 to obtain input on potential strategies and goals for the Healthiest Nation Initiative. The conference participants were charged with achieving several outcomes. Policies with the greatest likelihood of improving the health of Americans would be identified. Specific actions that will be needed to actually implement these policies would be explored.

Actionable ideas would be generated to encourage Americans to take steps in preventing disease. Specific mechanisms would be determined to continue to share information and collaborate with local, state, regional and national efforts to transform the health system through policy development and implementation. CDC invites employees, contractors and all other persons to join the Healthiest Nation Alliance at www.healthiestnation.org.

CDC implemented an internal "Go Green, Get Healthy" initiative to promote a greener and healthier agency; make healthy and environmentally sound workplace choices easier for all staff; and showcase CDC as a workplace model for health promotion, environmental responsibility and quality of work life programs. Activities to support this initiative include a

green vendor fair, green purchasing training, enhanced recycling, and green tips on the Intranet. "Go Green, Get Healthy" is aligned with the Healthiest Nation Initiative and dovetails with CDC's health protection goals, particularly Healthy Communities, Healthy Homes and Healthy Workplaces. The initiative also complements CDC's efforts to design and build healthy places to increase accessibility and address gentrification related to land use.

CDC is operating under a continuing resolution that provides continued funding for all agencies and activities at FY'08 levels. The President signed the continuing resolution on September 30, 2008 to extend government operations through March 6, 2009 or until enactment of regular appropriations bills.

Dr. Julie Gerberding, Director of CDC, testified before the House Oversight and Government Reform Committee in September 2008 on "a look forward and a look back" of HIV/AIDS in the United States. The hearing assessed the impact of HIV prevention programs, research and policies in the United States and also explored changes that are needed to turn the tide of HIV infections.

Dr. Gerberding's testimony included information on CDC's new HIV incidence estimates that were published in the *Journal of the American Medical Association* in August 2008. To arrive at these estimates, CDC used new technologies and methodologies that more directly measure the number of new HIV infections in the United States.

The estimate of 56,300 new HIV infections in 2006 was substantially higher than the previous estimate of 40,000 new infections annually. The new estimate of HIV incidence does not represent an actual increase in the number of infections, but reflects a more accurate approach to measure new infections. CDC's new historical trend analysis suggests that the previous annual estimate of new HIV infections was never as low as 40,000 and has been roughly stable since the late 1990s.

Of 56,300 new HIV infections estimated for 2006 by transmission category, men who have sex with men (MSM) accounted for 53%, heterosexual contact accounted for 31%, injection drug users accounted for 12%, and MSM who inject drugs accounted for 4%. By race/ethnicity, the number of new infections among African Americans (AAs) peaked in the late 1980s and has exceeded the number of infections in whites since that time. New infections among Hispanics historically have been lower than for both AAs and whites. New infections among whites slightly increased during the late 1990s and have remained stable since 2000. Asians/Pacific Islanders and American Indians/Alaska Natives accounted for ~2% and ~1%, respectively, of new infections in 2006.

As part of its Program Collaboration and Service Integration (PCSI) strategic imperative, NCHHSTP released the first annual disease profile in a series of profiles that will be published each year. The disease profiles combine annual surveillance data that are separately reported by each NCHHSTP division. The 2006 disease profile includes a special focus on AA men to illustrate that overlapping factors influence an excess burden of HIV/AIDS, viral hepatitis, STDs and TB in certain populations.

Dr. Fenton launched a new online blog on the CDC/NCHHSTP web site to facilitate the exchange of ideas on HIV/AIDS, viral hepatitis, STD and TB prevention. Ms. Susan DeLisle, the NCHHSTP Associate Director for Program Integration, retired from CDC in September 2008.

NCHHSTP is extremely pleased that the Georgia Research Alliance (GRA) awarded an FY'09 Collaboration Planning Grant to a joint proposal submitted by DTBE and Emory University entitled "Development of new generation mucosal subunit vaccine against tuberculosis." GRA grants reflect a partnership among CDC scientists, local academic investigators and the CDC Foundation. Each grantee was awarded $100,000 to advance GRA's new $10 million research initiative, "Next Generation Vaccines and Therapeutics."

DTBE Director's Report

Dr. Kenneth Castro covered the following areas in his update. Between January 2007-August 2008, DTBE responded to 11 requests for technical assistance to evaluate TB clusters. The clusters occurred in various settings in states throughout the country. Due to declining TB trends, many programs were not sufficiently prepared to respond to new clusters of TB cases.

As of September 2008, ~40,000 isolates were genotyped under the National TB Genotyping Service (NTGS). DTBE is now covering the cost for all states to ship isolates to two contract laboratories for genotyping. DTBE successfully renewed contracts with California and Michigan laboratories for genotyping of isolates. To provide greater specificity that will be more useful in identifying chains of transmission, DTBE plans to increase mycobacterial interspersed repetitive unit (MIRU) loci from 12 to 24.

DTBE will take several actions to apply NTGS into new program practice. Capacity will be enhanced for local health departments to detect aberrations and validate algorithms of TB clusters. Onsite consultations will be held with TB controllers to prioritize investigations of clusters at the local level. The TB Epidemiologic Studies Consortium (TBESC) Task Order 26 will be used to improve the utilization and integration of TB genotyping into routine TB program practice.

The TB Genotyping Management System (TB-GIMS) is being developed as a web-based genotype data management system. Information technology program requirements for the system are being finalized at this time. The TB-GIMS fact sheet is available on the CDC web site. Usability and pilot testing of the beta version of the system will be launched in spring 2009.

TB controllers applied lessons learned from Hurricane Katrina for advanced preparedness of Hurricanes Gustav and Ike in August and September 2008. Patients in Louisiana and Houston were provided with either a one-month or two-week supply of TB medications and a card with contact information for TB staff. The National TB Controllers Association (NTCA) was given the list of TB patients for broader distribution to other states. DTBE reestablished its command center and had daily communications with local TB controllers, NTCA and the CDC Director's

Emergency Operations Center. Public health advisors and other staff were ready to be deployed to impacted areas.

All 111 TB patients who were evacuated from Louisiana were located and placed on directly observed therapy (DOT). One TB suspect was triaged in Mississippi before entering a shelter. The Louisiana plan was re-implemented in Houston in preparation for Hurricane Ike. Houston TB patients were located and monitored.

State and local staff in Houston assisted with treating and monitoring 48 TB patients from the coastal region and performing active case finding in shelters throughout the city. Local staff continued to provide these services while challenged by personal and environmental obstacles. DTBE and NTCA plan to memorialize the preparedness and response activities in Louisiana and Houston by publishing a joint article in the *Morbidity and Mortality Weekly Report* (*MMWR*).

CDC released a funding opportunity announcement to expand and integrate HIV testing for populations disproportionately affected by HIV, primarily AAs. The funding announcement included a component for HIV testing of TB patients. The Division of HIV/AIDS Prevention (DHAP) awarded $23 million to 23 grantees in 19 states and four cities. The goal of this initiative is to test 1.5 million persons for HIV over three years and identify 20,000 new persons with HIV/AIDS.

Of 23 grantees, seven collaborated with local TB programs to improve HIV testing of TB patients. A portion of the funding will be allocated to support several activities in the seven TB programs, including appropriate HIV counseling and testing, community awareness of risk factors associated with HIV/TB co-infection, and prevention messages. A DTBE liaison attended the grantee orientation and DTBE and DHAP program consultants conducted joint site visits to review activities.

CDC and the Health Resources and Services Administration (HRSA) are partners in a new initiative to improve minority health and reduce health disparities. The overarching purpose of this effort is to improve outcomes for clients with TB and hepatitis C virus (HCV) and also to implement coordinated health care between HRSA health centers and local health departments for optimal outcomes.

HRSA's $200,000 investment through its Primary Care Associations will be allocated to TB and hepatitis programs in South Carolina, Maryland and New Jersey. Under this initiative, vulnerable populations will be targeted, primarily AAs who are at risk for TB and HCV. A Vanguard meeting will be held in November 2008 to enhance program services. Findings from the project will be evaluated and reported. Lessons learned will be shared with programs that report high TB or HCV caseloads.

Several jurisdictions are exercising transition options for TB surveillance. As of October 3, 2008, ten of 54 jurisdictions were using the electronic revised report of verified case of TB (RVCT), 15 were using a system based on the National Electronic Disease Surveillance System (NEDSS), 12 were using commercial systems, and 17 were using state-developed surveillance systems. DTBE has made a commitment to collaborate with these jurisdictions to ensure that

capacity to monitor TB trends is not jeopardized during the transition from the Tuberculosis Information Management System to NEDSS.

DTBE is continuing its TB training and education efforts. Culturally and linguistically appropriate TB patient education materials were developed in partnership with the Northeastern Regional Training and Medical Consultation Center (RTMCC) and are available in low-literacy English, Spanish and Tagalog. TB disease, tuberculin skin testing (TST), contact investigations, TB infection, TB/HIV co-infection and TB medication are described in each language.

Self-study TB modules 1-5 were updated in 2008 to provide basic TB information in a self-study format for healthcare workers (HCWs). The five updated modules cover transmission and pathogenesis; epidemiology; targeted testing and diagnosis of latent TB infection (LTBI) and TB disease; treatment of LTBI and TB disease; and infectiousness and infection control. New TB fact sheets were developed on a variety of topics: RVCT, TB-GIMS, basic information on TB genotyping, the National TB Indicators Project, and recommendations for HIV screening in TB clinics. The fact sheets can be downloaded from the CDC/DTBE web site.

The theme of the TB Education and Training Network Eighth Annual Conference was "TB Education and Training: Going for the Gold." Over 100 participants attended the event in August 2008. The goal of the TB Education and Training Network is to convene TB professionals to network, share resources, and build education and training skills. The current membership of 750 persons represents TB programs, correctional facilities, hospitals, nursing homes, federal agencies, academic institutions, American Lung Associations, RTMCCs, and other U.S. and international organizations.

ACET commended DTBE, NTCA, and state and local health department personnel for developing and implementing an effective preparedness and response plan to assure continued care and treatment to TB patients who were evacuated from Louisiana and Texas as a result of recent hurricanes. However, several members emphasized the need for DTBE and NTCA to encourage TB controllers throughout the country to educate local shelters about the infection control implications and other public health issues associated with crowding hurricane evacuees into small spaces.

Update on TB Legislation

Ms. Nuala Moore, of the American Thoracic Society (ATS), was pleased to announce that both the Senate and House unanimously passed the Comprehensive TB Elimination Act legislation in September 2008. The new legislation reauthorizes national TB control programs and is expected to be signed into law by the President within the next week.

In terms of funding, the new law authorizes $200 million to DTBE in FY'09. This funding level represents a 43% increase over DTBE's FY'08 budget of $140.3 million. The new law also authorizes 5% increases each year from 2010-2013 for a total TB budget of $243.1 million in 2013. Although annual Congressional appropriations and overall budgets will determine the

actual allocation to DTBE, ATS is optimistic that the FY'09 TB budget will be close to the $200 million authorized in the new law.

Additional language in the new law is highlighted as follows. CDC is authorized to expand research on TB diagnostic, treatment and prevention tools. Targeted efforts can be intensified to prevent, detect and treat TB among U.S-born AAs and other minorities, foreign-born persons (FBPs) and residents along the U.S.-Mexico Border. The HHS Secretary must provide Congress with an evaluation and recommendations regarding challenges to containment of TB and other diseases by federal and state public health agencies.

The ACET statute is updated and the Federal TB Task Force is codified along with its mission to advise the HHS Secretary on the Comprehensive Plan for New Tools Development. The National Institutes of Health (NIH) has new authority to expand TB research with an emphasis on basic and clinical research, particularly the relationship between HIV/AIDS and TB. Ms. Moore thanked NTCA for providing ATS with outstanding technical expertise and invaluable information on state TB control programs throughout the entire legislative process.

Dr. Castro added that DTBE would allocate a portion of the FY'09 appropriation to strengthening interagency coordination and collaboration with NIH on TB research. He confirmed that NIH would be invited to a future ACET meeting to discuss its role in this effort.

ACET applauded the diligent efforts of ATS, NTCA and other groups in tirelessly leveraging Congressional support and providing strong advocacy over the past seven years for authorization of the Comprehensive TB Elimination Act. ACET thanked Ms. Moore for providing an update on this historic event.

Overview of the Federal Advisory Committee Act (FACA)

Ms. Renee Ross, of the CDC Management Analysis and Services Office (MASO), explained that FACA provides a legal foundation for establishing and managing all federal advisory committees. Congress created FACA with a number of guiding principles. New advisory committees are to be established only when these groups are determined to be essential. Advisory committees are to be formed to provide guidance that is relevant, objective, free of undue influence and open to the public.

Standards and uniform procedures must govern the establishment, operation, administration and duration of all advisory committees. All persons must have knowledge of the purpose, membership, activities and costs of advisory committees. Each advisory committee must be terminated after its purpose is fulfilled.

The General Services Administration (GSA) is responsible for FACA oversight, management and compliance. Agency heads establish uniform procedures and administrative guidelines for advisory committees and also designate Committee Management Officers to exercise control and supervision of establishment procedures and accomplishments of all advisory committee.

Federal advisory committees can be established by mandate or at the discretion of an agency. Mandated committees are authorized by statute or the President through an Executive Order. Discretionary committees are established when an agency determines the need for advice and recommendations from an advisory committee, consults with GSA, and provides notice to the public of its intent.

The purpose of each advisory committee is determined and memorialized in its charter. The agency assigns a DFO to serve as the Executive Secretary, approve meeting agendas, ensure the publication of meetings in the *Federal Register*, and attend all meetings. The President or agency head appoints committee members and designates a chair.

The role of a federal advisory committee is to provide federal officials and the nation access to information and advice on a broad range of issues that affect federal policies and programs. Advisory committees allow the public to actively participate in the federal government decision-making process. The membership of an advisory committee must be fairly balanced to the fullest extent possible in terms of its function and points of view represented.

Advisory committees can be established with three categories of members. Special government employees (SGEs) are private citizens who are appointed based on their expertise and are subject to the "Standards of Ethical Conduct for Employees of the Executive Branch." *Ex-officio* members are representatives of federal agencies who provide subject matter expertise on behalf of their respective agencies. Liaison members represent special interest groups, organizations or affected populations.

FACA outlines specific requirements for advisory committees to convene meetings. A notice announcing the meeting must be published in the *Federal Register* with a description of the purpose of the meeting and a summary of the agenda with the time, location and contact information. The notice must be published not less than 15 days prior to the meeting. The DFO must approve the agenda and attend all meetings.

Any member of the public must be given an opportunity to speak or file a written statement. Detailed minutes must be developed and made available to the public. Any official records generated by or for an advisory committee must be retained for its duration. The records will be transferred to the National Archives and Records Administration upon the termination of the advisory committee.

Advisory committees can form subcommittees or workgroups to perform special tasks. A subcommittee must be represented by at least one member of the parent committee and report directly to the parent committee. Although subcommittees are not subject to FACA, CDC policy requires compliance with these provisions. The parent committee must deliberate the subcommittee's recommendations.

Workgroups are formed to conduct research, gather information, and analyze issues and facts. Workgroups must be represented by at least two members of the parent committee or

subcommittee and report directly to the parent committee or subcommittee. Workgroups are not subject to FACA and cannot formulate advice or recommendations.

After an advisory committee deliberates and votes on issues, the recommendations can be forwarded to the Director of CDC, Secretary of HHS, GSA, the President or Congress. Overall, FACA ensures that advice rendered to the Executive Branch by advisory committees, task forces, boards and commissions is objective and accessible to the public.

Ms. Cathy Ramadei, of MASO, informed ACET of FACA requirements regarding financial disclosure and conflicts of interest. The Ethics Reform Act of 1989 requires SGEs to provide financial disclosure upon appointment and each year of their terms thereafter. Agencies use financial disclosure reports of SGEs to ensure that advice and recommendations are free from conflicts of interest.

Financial disclosure reports also allow agencies to determine appropriate actions to take if a conflict arises with an SGE. MASO, the DFO and the CDC Office of General Counsel review financial disclosure reports to identify any potential conflicts of interest or problematic issues with an SGE.

The primary conflict of interest statute prohibits SGEs from participating in any specific matter that would specifically and directly affect their financial interests. The bribery statute prohibits SGEs from seeking or accepting any item of value in return for being influenced in relation to performing their official duties. Two representation statutes prohibit SGEs from receiving compensation for representing an individual or an issue before an agency in a particular matter involving specific parties where an SGE has acted in an official capacity.

The post-employment statute imposes a lifetime ban in which former SGEs cannot represent another individual or entity to the government in any matter involving a specific party if the SGE was involved in that matter as a federal advisory committee member. The foreign activities statute prohibits any SGE from receiving any present, emolument, office or title from a foreign state without the consent of Congress. SGEs cannot act as an agent or lobbyist on behalf of a foreign entity under the Foreign Agents Registration Act.

Dr. Dean, as the DFO for ACET, should serve as the first point of contact if members have any questions or concerns regarding potential conflicts of interest that might arise during their respective terms. Ms. Ramadei concluded the overview of FACA by presenting “The Ethical Choice” video.

Update on TBESC

Dr. Denise Garrett, of DTBE, explained that the new ten-year cycle for TBESC will be dedicated to accomplishing the single overarching research focus. New TBESC members will be selected based on their national representation of TB epidemiology and ability to address the overarching

goal. All TBESC members will participate in core scientific activities to achieve the overarching goal.

DTBE created a four-step process to select the research focus for the new TBESC. A list of broad research concepts was developed with broad input from the entire TB community in the United States. The research concepts were discussed and ranked for development into research proposals. The best research proposals will be selected and developed into research plans. A report with recommendations will be submitted to Dr. Castro for his final decision on the new research focus for TBESC.

DTBE formed the Strategic Planning Workgroup (SPWG) to assist with the re-competition process and selection of the new research focus for TBESC. SPWG members include scientists with a wide range of expertise in the public health and scientific aspects of TB research from both domestic and global perspectives. However, none of the SPWG members are eligible to compete for the new TBESC. The 12 broad research concepts that were submitted covered a variety of topics, including contact and outbreak investigations, LTBI screening, TB diagnostics and treatment.

SPWG ranked the 12 broad research concepts based on the following criteria: feasibility, cost, impact, sustainability, and the unique role of the project to CDC. The initial list of research concepts were ranked as "red" for low priority, "yellow" for further discussion needed and "green" for high priority. There was consensus towards the concepts related to LTBI. If this research focus is selected, the best LTBI interventions will be determined, such as screening of high-risk populations, targeted testing and treatment, contact and outbreak investigations, TB treatment, diagnostics and adherence.

SPWG is currently developing the broad research concepts into proposals and will convene a meeting in January 2009 to select research proposals for development into research plans. The new research focus for TBESC will be selected by the end of 2009. In March 2010, CDC will release a request for applications for new TBESC sites. CDC expects to select and fund the new TBESC sites by September 2010. In 2011, old TBESC sites will continue to be funded for the completion of projects in the current ten-year cycle.

Dr. Garrett provided additional information on the re-competition of TBESC in response to specific questions posed by the ACET members. The inclusion of international sites in the new TBESC will depend on the selection of the new research focus. Efforts to develop a partnership between TBESC and the TB Trials Consortium (TBTC) would be difficult because data collection and other research activities of the two Consortia are different.

Due to the long ten-year project period of TBESC, DTBE will attempt to strike a balance between one research focus and flexibility to modify the topic in response to changing TB trends or priorities over time. For example, DTBE will reserve a portion of the TBESC budget to address new or emerging TB trends that might arise during the ten-year project period.

Dr. Castro added that DTBE's reorganization of TBESC for the new ten-year cycle responds to recommendations by an external peer review panel. The reviewers informed DTBE that

multiple small studies in the current TBESC did not collectively show a significant impact in decreasing TB rates in the United States. The reviewers advised DTBE to decrease the number of research activities in the new TBESC and adopt TBTC's effective model of single protocol/multi-site studies.

A number of ACET members fully supported SPWG's suggestion for LTBI to be a specific goal and the target of TBESC's epidemiologic studies in the new ten-year cycle. The members made two key suggestions for DTBE to consider in the ongoing re-competition process. First, efforts should be made in the new TBESC to address aspects of TB control that are unique to certain settings, such as low-incidence versus high-incidence areas and geographic variations. Second, DTBE should make stronger efforts to showcase and more widely publicize research findings, new tools and other important outcomes of the current ten-year cycle of TBESC.

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

Dr. Drew Posey, of DGMQ, reported on DGMQ's ongoing activities related to the TB Technical Instructions (TBTIs), Electronic Disease Notification (EDN), and the Interim Final Rule (IFR) for medical examination of aliens. In terms of the TBTIs, all immigrants and refugees who apply for U.S. immigration are required to undergo TB screening. The 1991 TBTIs only relied on sputum smears, were inadequate to detect all applicants with TB disease, and missed smear-negative/ culture-positive persons.

To address these issues, DGMQ and a wide range of partners developed and distributed updated TBTIs in 2007 that required TST for applicants 2-14 years of age in areas where the World Health Organization (WHO) estimated the TB rate to be $\geq$20/100,000. Other requirements of the 2007 TBTIs include sputum cultures for all applicants suspected of having TB; drug susceptibility testing (DST) on positive isolates; treatment according to ATS/CDC/ Infectious Disease Society of America (IDSA) guidelines; and treatment delivered as DOT.

Implementation of the new TBTIs began in April 2007 with Burmese refugees who were screened in Thailand. As of October 1, 2008, populations from 14 countries on three continents were being screened according to the 2007 TBTIs. These countries include Mexico, Southern Africa, Turkey, Vietnam, the Philippines, Kenya, Nepal and Thailand. Based on 2007 population data, 28% of immigrants and 40%-50% of refugees are now being screened with the new TBTIs. Efforts are underway to implement the 2007 TBTIs in China, East Africa, the Middle East, India, Australia, Dominican Republic, Haiti, and additional countries in Latin America.

TB indicators in Mexico showed that 75,671 persons were screened from October 1, 2007-July 31, 2008. Of 44 persons identified with pulmonary TB disease, 16% were smear-positive/ culture-positive based on the 1991 TBTIs. The number of smear-negative/culture-positive cases increased to 36 based on implementation of the 2007 TBTIs in Mexico. Of 43 culture-positive pulmonary TB cases, 32 were pan-susceptible, three had drug resistance, and eight have pending DST results.

Panel physicians are currently attempting to expand DOT sites in Mexico to address the problem of applicants who do not wish to remain in Ciudad Juarez while receiving TB treatment. Most notably, a physician was hired in Tijuana to manage DOT patients and plans are underway to build a TB laboratory with culture capability. Moreover, negotiations are ongoing for Tijuana to take over the treatment of TB patients for Project Puentes.

DGMQ is taking several actions to refine and more broadly implement the 2007 TBTIs. To assure consistency with the 2007 TBTIs, DGMQ and the Department of State are continuing to revise DS forms that panel physicians are required to complete. DGMQ will update its TBTI document for consistency with the revised DS forms. Recommendations made by reviewers during the Philippines site visit will be incorporated into the updated TBTI document. The TBTI Workgroup will discuss these recommendations.

In terms of EDN, DGMQ has regulatory responsibility to provide information to receiving health departments of arriving aliens with notifiable health conditions. DGMQ developed EDN to fulfill its mandate. EDN replaced the paper-based Immigrant and Migrant Populations System on October 1, 2008 to provide health departments with access to recorded information from DS forms and all DS forms scanned overseas. EDN also provides health departments with an electronic system to record and evaluate outcomes of domestic follow-up evaluations.

DGMQ and DTBE will jointly convene an EDN Summit in November 2008 with representatives from NTCA, the EDN Workgroup, and lead EDN users from priority states based on TB notifications and immigrant and refugee arrivals. The goal of the summit will be for the participants to engage in substantive dialogue on the challenges and other aspects of EDN; focus on the long-term effectiveness of the TBTIs based on full utilization of EDN by states, and reach consensus on advancing EDN.

In terms of the IFR, DGMQ has regulatory responsibility to administer regulations for the medical examination of aliens. The 1991 regulations defined “communicable diseases of public health significance” as active TB, infectious syphilis, gonorrhea, infectious leprosy, chancroid, lymphogranuloma venerum, granuloma inguinale and HIV infection. The IFR was published in the *Federal Register* on October 6, 2008 with revisions to the 1991 medical screening process of aliens. The updated regulations will provide DGMQ with greater opportunities to respond to important and new emerging infectious diseases.

Key changes between the 1991 regulations and the IFR are highlighted as follows. The IFR has the same definition of “communicable diseases of public health significance,” but the following quarantinable diseases specified by Presidential Executive Orders were added: pandemic influenza, severe acute respiratory syndrome, viral hemorrhagic fevers, cholera, diphtheria, infectious TB, plague, smallpox and yellow fever. The updated definition will not require refugee programs in the United States to provide broader screening.

The IFR specifies the following communicable diseases that are a public health emergency of international concern and must be reported to WHO: smallpox, poliomyelitis due to wild-type poliovirus, cholera, viral hemorrhagic fevers and others. The IFR outlines a risk-based approach for medical screening and testing based on medical and epidemiologic factors.

The IFR supports TBTIs that use medical knowledge and practice, including flexibility in making future changes to the TBTIs; no firm age restrictions for chest radiographs; and the ability to incorporate new diagnostic tests as they become available. The TBTI Workgroup will discuss these regulatory changes during its next conference call. Additional information on the IFR will be posted on the CDC/DGMQ web site in the near future.

The ACET members made a number of comments and suggestions for DGMQ to consider regarding the EDN Summit. DGMQ will convene the EDN Summit on November 20-21, 2008, but has not yet distributed invitations. Insufficient notification will not provide NTCA with adequate time to inform states of this event. Moreover, DGMQ's plan to invite "lead EDN users from priority states" to the EDN Summit will not provide an opportunity for small states and low-incidence areas to give input during this event. DGMQ should ensure that the EDN Summit has equal representation and diverse feedback from a variety of sources.

Update on Travel Restrictions for TB Patients

Dr. Francisco Averhoff, of DGMQ, announced that the 3rd edition of the *WHO TB and Air Travel Guidelines* was published in 2008 and will be valid until 2013. The revised guidelines provide an updated framework and reference for action and also encourage countries to follow their national guidelines if these are consistent with WHO.

The major changes between the 2nd and 3rd editions of the guidelines include updated case definitions; revised guidance restricting commercial air travel based on the case definitions; elimination of cabin crews as contacts except in special circumstances; and clarification of the roles and responsibilities of international public health authorities when exposure to TB is suspected.

The 2008 WHO guidelines contain the following case definitions and actions. "Infectious TB" is defined as all cases of respiratory TB, including pulmonary or laryngeal TB, that are both sputum- and culture-positive if cultures are available. The recommended action for infectious TB is to initiate contact investigations with consideration given to national policies.

"Potentially infectious TB" is defined as all cases of respiratory TB that are sputum-negative/ culture-positive, including persons with susceptible disease, multidrug-resistant TB (MDR-TB), or extensively drug-resistant TB (XDR-TB). The recommended action for potentially infectious TB is to request additional information and conduct a risk assessment to determine the need for a contact investigation. "Non-infectious TB" is defined as all cases of respiratory TB that have two consecutive negative sputum smears and negative cultures if culture is available. No further action is recommended for non-infectious TB.

In terms of TB contact investigations, 83 were conducted in 2007 and 85 were conducted in January-June 2008. DGMQ attributes the increase to greater awareness of TB in the public health community and the new strategy of conducting contact investigations for both inbound

flights to and outbound flights from the United States. Federal air travel restrictions for public health purposes were published in the September 19, 2008 edition of the *MMWR*. From May 2007-September 26, 2008, 47 persons were added to and 27 persons were removed from the Do Not Board (DNB) list. Of 47 DNB and Lookout requests, 20 cases are active and 27 were removed.

For three cases in which Lookouts were requested, the individual would be identified upon arrival at a port of entry to ensure receipt of follow-up care. These persons posed a risk for land border crossings only. For 12 telephone calls that did not result in placement on the DNB or Lookout list, the requesting health department decided to take further action at the local level, confirmed the patient's compliance, or determined that the case did not meet DNB criteria.

Data from quarantine stations showed that California and Texas requested DNB placements most frequently, but Canada, the Guatemalan Embassy, Mexico and Guam used this tool as well. By country of citizenship, the United States, Vietnam, India, Mexico and the Philippines accounted for most of the cases placed on the DNB list. Of 47 cases, 26 were susceptible to first-line anti-TB medications; 10 had MDR-TB or XDR-TB; four were smear-positive and are awaiting results; four were smear-positive and have unknown or uncollected results; and three did not have TB.

The length of stay for the 27 cases that were removed from the DNB list as of September 26, 2008 was a mean of 45 days, a median of 24 days, and a range of 2-191 days. On average, 10 hours are required to place an individual on the DNB list and 12 hours are needed to remove a case. The following case reports illustrate effective approaches and ongoing challenges to identifying and placing persons on the DNB and Lookout lists.

Case 1 was a Vietnamese citizen with TB overseas who was placed on the DNB and Lookout lists on April 5, 2008 and arrived in the United States on April 17, 2008. The U.S. Customs and Border Protection (CBP) identified the individual at the port of entry and paroled the individual into the United States due to visa violations. The quarantine station and DGMQ were notified of the case. The quarantine station and local health department jointly transported the individual to a local hospital for isolation and CBP provided law enforcement. Local authorities asked CDC or the Department of Homeland Security (DHS) to cover the cost of isolation and treatment for the period of time the individual was not in DHS custody.

CBP's identification of the individual from the Lookout list was effective, but case 1 emphasized several opportunities for improvement. The individual was allowed to board the flight. Some persons may use different names or variations of names to obtain identification documents. Discussions should be held with leadership of the following federal agencies before admitting a non-U.S. citizen to the country: DHS/Immigration and Customs Enforcement (ICE), DGMQ, CBP and the Office of Health Affairs. Agencies that will provide transportation, law enforcement and funding for treatment as soon as the individual is taken into custody should be clearly identified.

Case 2 was a Japanese citizen with TB overseas who was placed on the DNB and Lookout Lists on February 9, 2008 and arrived in the United States on May 29, 2008. CBP identified the

individual at the port of entry and refused admission into the country due to visa violations. The individual was placed in ICE custody, isolated, and eventually deported after non-infectiousness was determined.

Effective approaches in case 2 included collaboration with ICE from the beginning to facilitate treatment; refusal to admit the individual into the country; and clearly defined roles and responsibilities for paying for treatment and providing law enforcement. Similar to case 1, however, case 2 also was allowed to board the flight.

Case 3 was a Canadian citizen with TB who entered the United States by land border from Canada and might have exposed 27 bus passengers to TB. The local health department requested DNB and Lookout actions because the individual was unable to be located. The individual was placed on the DNB and Lookout lists on August 19, 2008 and was identified on the bus manifest by CPB on August 31, 2008 prior to arrival into the United States.

The individual was traveling with children who were U.S. citizens and was allowed entry into the United States until acceptance by the Canadian Public Health Department. The individual was transported to a local hospital for isolation, placed under the care of local and state health departments, and remained in CBP custody until deportation to Canada the following day.

Effective approaches in case 3 included CBP's advanced identification of the individual and solid communication between CDC and DHS. However, case 3 emphasized a number of areas that need improvement, such as clearly defined responsibilities for isolation costs, law enforcement issues, increased difficulty in monitoring land borders, criteria for executing federal isolation orders, and persons traveling with minors who are U.S. citizens.

DGMQ acknowledges that several ongoing issues still need to be addressed related to TB travel restrictions, including barriers to execution of the DNB list; determination of whether the DNB list is a public health or criminal/legal issue; unclear roles and responsibilities of federal, state and local agencies for TB care, enforcement and payment; the need for better domestic and international coordination; and the actual public health impact of the DNB list.

Several actions have been taken in an effort to address these issues. DGMQ established the Travel Restriction and Intervention Team to strengthen coordination between federal agencies and among federal, state, local and international agencies. CDC, the Homeland Security Council (HSC) and Government Accountability Office (GAO) responded to recommendations in after-action reviews. CDC is exploring the possibility of sending a certified letter to any patient who is placed on the DNB list.

An interagency meeting was held in September 2008 to discuss payment and custody issues at the federal level; operational issues regarding international notification and communication; and repatriation of U.S. citizens. The federal agencies also used the meeting as an opportunity to discuss next steps to reach consensus at the federal level and engage state and local public health agencies.

ACET and DTBE commended DGMQ on its diligent efforts in balancing difficult situations in which an individual's rights must be protected while protecting the public from an individual with infectious TB. Several ACET members described successful experiences in which DGMQ rapidly provided technical assistance and guidance to local programs for TB patients who planned to travel on commercial airlines.

The ACET members made two key suggestions for DGMQ to consider in its ongoing efforts to more clearly define TB travel restrictions. First, DGMQ should educate all quarantine stations about ICE's routine process of paying for care when persons are taken into custody and hospitalized.

Second, DGMQ should clarify language for public health travel restrictions used at the federal level to minimize confusion at state and local levels. For example, some TB programs and epidemiologists interpret "DNB," "Do Not Fly" and "Be on the Lookout" lists as the same action rather than three different actions. DGMQ should develop and provide health departments with a table of public health travel restriction definitions, examples of each specific action, and guidance to access these tools.

Update on Nucleic Acid Amplification Tests (NAATs)

Dr. Thomas Shinnick, of DTBE, announced that CDC convened an expert consultation to obtain guidance on the use of NAATs for the diagnosis of TB. Members of the expert panel included clinicians, laboratorians, and TB controllers from low- and high-incidence states. The expert panel was charged with evaluating the need for changes to the current guidelines; reviewing the available science base to support any potential revisions and recommendations; and identifying action steps to implement the recommendations.

The expert panel took two key actions to fulfill its charge. First, the expert panel thoroughly reviewed the NAAT guidelines that were published in the *MMWR* in 2000. The guidelines state that based on available information, the following algorithm is a reasonable approach to NAA testing of respiratory specimens from patients with signs or symptoms of active pulmonary TB for whom a presumed diagnosis has not been established.

Second, the expert panel considered a number of factors to guide the evaluation. Optimum patient care and public health must be cornerstones of the recommendations. Many TB suspects are initially seen by less experienced clinicians who may delay specific treatment until laboratory results confirm the diagnosis. The expert panel reviewed data from a San Francisco study that demonstrated this outcome.

The laboratory will play an increasingly critical role in reducing delays in the initiation of TB treatment, particularly as TB is treated more in the hospital setting rather than in the public health setting. The expert panel reviewed data from a study published in 2005 that showed results from NAATs and acid fast bacilli (AFB) smear microscopy were available at nearly the same time frame, but NAATs identified ~33%-50% more cases. The study also showed that the

period of time to receive confirmation from culture or solid media was significantly longer than NAATs.

The expert panel further noted that NAATs have significant potential added value for clinicians and TB control officials, such as a reduced period of infectiousness and improved outcomes due to earlier initiation of treatment; earlier notification of TB cases; earlier respiratory isolation decisions; and the elimination of unnecessary contact investigations due to earlier identification of smear-positive specimens containing non-tuberculosis mycobacteria (NTM).

Based on these factors and the literature review, the expert panel proposed three revisions to the NAAT guidelines. All U.S. clinicians and public health TB programs should have access to molecular tests to aid in the diagnosis of TB. NAATs for the diagnosis of TB should become standard practice for TB suspects. NAATs should be performed on at least one respiratory specimen from each patient with signs and symptoms of active pulmonary TB for whom a diagnosis of TB is being considered (*i.e.*, a TB suspect), but has not been established.

The expert panel issued its guidance to CDC with a number of caveats. NAA testing should not replace culture or smear testing. All current guidelines or recommendations on the use of culture and smear testing should remain in effect, particularly with regard to the recommended turnaround times for DST. A single positive NAAT result can support the diagnosis of TB in a patient with a reasonably high index of suspicion of TB. This result should trigger reporting to public health officials, initiating treatment and intensifying efforts to recover an isolate for DST. A single positive NAAT result should be viewed with suspicion in a patient with little suspicion of active TB and also should be interpreted in the same manner as a single culture-positive result. A single negative NAAT result should never be used as the definitive test to exclude TB.

The expert panel made several recommendations to ACET and CDC to assist in implementing the updated guidelines. ACET should review and discuss adopting the expert panel's guidance and recommendations. ACET and CDC should urge the College of American Pathologists (CAP) to add a checklist of questions to its surveys regarding the provision of NAATs for the diagnosis of TB by laboratories. ACET should develop and promote a research agenda for NAATs for the diagnosis of TB.

ACET and CDC should develop guidance on the use of molecular tests for the detection of drug-resistant TB in the United States. ACET and CDC should assist in the development of more sources of NAATs for the diagnosis of TB that are approved by the Food and Drug Administration (FDA). ACET and CDC should explore strategies to encourage manufacturers to develop new or improve existing NAATs and also should discuss with FDA potential approaches to streamlining the approval process for NAATs for the diagnosis of TB.

The expert panel also formulated guidance specifically to CDC. Leadership should be provided on disseminating the expert panel's recommendations. Priority should be given to assisting TB programs in gaining access to NAATs for the diagnosis of TB. For example, language in the TB cooperative agreement could be modified and additional resources could be provided to TB programs and laboratories for NAA testing. Consideration should be given to establishing Centers of Excellence to provide access to molecular tests.

Assistance should be provided in ensuring the availability of proficiency testing for NAATs for the diagnosis of TB. Collaborations should be established with partners to develop an education program on the appropriate use and interpretation of NAATs. The education program should be targeted to laboratorians, healthcare providers and TB control authorities. CDC should play a role in regulatory quality trials to assist manufacturers in sampling new NAATs.

CDC's next steps in updating the NAAT guidelines will be to harmonize the expert panel's recommendations with the proposed revised ATS Diagnostic Statement. The updated NAAT guidelines will be published in the *MMWR*. The expert panel's report will be posted on the CDC web site and published in journals that target laboratorians, clinicians and TB control officials. The report will be tailored for each of these audiences. The expert panel's draft report was distributed to ACET for review.

Dr. Shinnick concluded his update with a request for ACET's input on the expert panel's three proposed revisions to the NAAT guidelines. He emphasized that ACET's formal resolution on these changes would allow CDC to move forward in publishing the *MMWR* article.
The ACET members made a number of comments and suggestions on the expert panel's draft report on updating the current NAAT guidelines.

- CDC should post "interim" guidance on its web site as quickly as possible. Most notably, clearance of the *MMWR* article and harmonization between the revised NAAT guidelines and the ATS Diagnostic Statement will require some time. However, interim guidance from CDC would assist programs in more rapidly approving and endorsing a change in practice at the national level.
- Problems with the packaging of NAAT kits should be addressed in the updated guidelines to increase the number of laboratories that would perform testing.
- The expert panel's caveats regarding the "imperfection" of NAATs should be prominently highlighted in the updated guidelines. For example, previous specificity data on NAAT showed that the rate of false-positive results for persons who were smear-negative was substantial and the rate of false-negative results for persons who were smear-positive was ~10%. As a result, the recommendation for CDC to develop an education program on the appropriate use and interpretation of NAATs also should be strongly emphasized in the updated guidelines.
- The updated guidelines should include language on the current cost of NAATs, including a fair comparison between NAATs and direct and concentrated smear testing as well as the amount of time required for laboratory technicians to perform NAATs. A statement on both the positive and negative predictive values of NAATs, particularly in low-incidence areas, would help to support the updated guidelines.
- The updated guidelines should provide specific guidance on implementing NAATs, particularly since workloads will increase if NAATs become the national standard of practice for all TB suspects.
- The updated guidelines should clearly define "TB suspects" with the following statement: "A NAAT should be ordered each time an AFB smear and culture are ordered."
- The updated guidelines should include a "package" of two new recommendations. CAP should establish a maximum number of NAATs that laboratories perform each year.

Laboratories should perform rapid drug resistance testing on all positive results. The package of recommendations might achieve two important goals. First, the number of false-positive and false-negative results associated with the volume of NAATs performed by laboratories would be reduced. Second, TB controllers would be much more likely to endorse and implement the updated guidelines because the guidance would allow more rapid diagnoses and assessments of high-risk drug resistance.

Dr. Michael Fleenor, Chair of ACET, was aware that some ACET members did not agree with all three of the revisions to the current NAAT guidelines proposed by the expert panel. During the discussion, several ACET members noted that "TB suspects" was not clearly defined; issues regarding the availability and cost of NAATs were not adequately addressed; and no specific guidance was given on actual implementation of the recommendations.

Dr. Fleenor proposed the following process to respond to Dr. Shinnick's request for ACET's input. ACET would thoroughly review the expert panel's draft report overnight and particularly focus on the three revisions proposed by the expert panel. Dr. Shinnick would be available during the business session on the following day to clarify any outstanding issues or answer any additional questions. Dr. Fleenor would entertain a motion on the expert panel's three proposed revisions to the current NAAT guidelines to determine whether ACET wished to take formal action or table the matter for a future meeting.

In preparation of the business session, Dr. Castro pointed out that the cost of NAATs should not serve as barrier to ACET's formal approval of the three revisions proposed by the expert panel. He explained that if NAATs become the standard of practice nationally, Medicaid, Medicare and other types of insurance would cover the tests as a billable diagnostic procedure. He also noted that Medicaid and Medicaid reimburse the current FDA-approved NAATs.

Update on Interferon Gamma Release Assays (IGRAs)

Dr. Andrew Vernon, of DTBE, explained that a first-generation IGRA used purified protein derivative (PPD) and avian PPD antigens. FDA preliminarily approved the first-generation IGRA in December 2001 and CDC published guidelines for the test in the *MMWR* in January 2003.

A second-generation IGRA, QuantiFERON®-TB Gold (QFT-G), used two more specific antigens. FDA preliminarily approved QFT-G in December 2004 and CDC published guidelines for the test in the *MMWR* in December 2005 with two key recommendations. QFT-G may be used in all circumstances in which TST is currently used. Further research is needed regarding the use of QFT-G in multiple clinical circumstances. The guidelines also provided specific cautions for interpreting negative QFT-G results in persons from selected populations. A third-generation IGRA, QFT-G In Tube (QFT-GIT), received preliminary FDA approval in October 2007. FDA recently approved the first IGRA assay with an approved ELISPOT format, called T spot TB.

CDC has considered six key issues in evaluating IGRAs. One, a "gold standard" for TB infection is lacking. Although this data gap has been firmly established as a challenge, no solution has been

developed to date. Two, the sensitivity of IGRAs has been assessed based on a comparison to culture results. Comparisons between IGRAs and skin tests have been similar overall, but the T-SPOT TB test has been slightly more sensitive in identifying culture-positive TB disease than QFT-GIT.

Three, the specificity of IGRAs has been assessed based on a comparison of results in persons believed to be at low risk for LTBI. A number of evaluations have shown that the specificity of QFT-GIT was slightly higher than the T-SPOT TB test. IGRAs have a greater advantage in terms of specificity due to the elimination of cross-reactivity in the Bacille Calmette-Guerin (BCG) vaccine and most NTM.

Four, agreement with positive or negative TST results has been assessed, but this evaluation has been increasingly challenging due to the presence of every type of discordance. Poor agreement between IGRAs and TST might be a solid outcome to eliminate a large number of false-positive results, but agreement widely varies. Discordance between positive TST and negative IGRA results has been associated with BCG use, substantial exposure to NTM, TB prevalence and sensitivity to a TST cutoff. Discordance between negative TST and positive IGRA results is less frequent and somewhat random.

Five, evidence has increasingly shown that the association of positive IGRA results with exposure was similar to or stronger than the association of positive TST results with documented exposure. Six, the ability of IGRAs to predict TB disease has been assessed, but more research is needed to add to only three studies that have been conducted on this issue to date.

Study 1 followed ~200 household TB contacts in Ethiopia and demonstrated that the ELISPOT format was predictive of the occurrence of disease two years after follow-up. Study 2 followed 601 TB contacts in Germany. Of the entire study population, 11% were positive based on QFT-GIT results and 40% were positive based on TST results. QFT-GIT predicted all six persons who developed TB and TST predicted five of the six persons who developed TB.

Study 3 followed 2,348 TB household contacts in Gambia. Of 25 cases that were tested at recruitment and later diagnosed as secondary cases, 56% were Mantoux-positive. Of 21 secondary cases that were initially tested, 52% were ELISPOT-positive and 71% were positive by one of the two tests. Agreement in the secondary cases of the two tests at recruitment was 61.9%. Of nine index and secondary case pairs that had cultured isolates available for molecular genotyping, six pairs were concordant and three were discordant. Of six contacts who had concordant isolates with their respective index cases, 67% were Mantoux-positive at recruitment; 50% were ELISPOT-positive; and 83% were positive by one of the two tests.

CDC acknowledges that several outstanding questions must be answered in its ongoing effort to revise the 2005 IGRA guidelines. (1) What is the sensitivity of IGRAs in LTBI, particularly in vulnerable populations? (2) What is the risk of TB associated with a positive IGRA result or when TST and IGRA results are discordant? (3) What is the definition and proper interpretation of “IGRA conversion?” (4) What actions can be taken to address issues related to assay performance, such as gray zones, appropriate cut points, weighted interpretation of results or “odd” results? (5) Should the United States adopt the international model of sequential

strategies in which IGRAs are used to confirm positive skin test results or negative results in vulnerable populations? (6) What is the cost-effectiveness of IGRAs?

CDC identified major differences between IGRAs and TST. On the one hand, IGRA is an *in vitro* test that contains TB-specific antigens, does not require boosting, and can be stimulated within 12-16 hours. IGRA can be completed in one patient visit and test results can be obtained in one day. The risk for TB based on a positive IGRA result is uncertain. On the other hand, TST is an *in vivo* test that contains less specific PPD, requires boosting, and can be read in 48-72 hours. TST can be completed in two patient visits and test results can be obtained in 2-3 days. The risk for TB based on a positive TST result is increased.

To fill these data gaps while revising the 2005 IGRA guidelines, CDC convened an expert panel that included 26 basic scientists, clinical researchers, clinicians, and public health officials from both inside and outside the United States. To guide the evaluation, CDC provided the expert panel with a number of publications in the literature and placed several items on the agenda of the expert consultation that was held in August 2008 with >80 persons in attendance.

Manufacturers of both FDA-approved IGRAs presented data. New York City and San Francisco have widely adopted IGRA testing over the past 2-3 years. Public health officials from these two cities made presentations on their local experiences with the implementation of IGRAs. The expert panel and other researchers in the field reviewed studies regarding the performance of both FDA-approved IGRAs.

CDC is currently updating the 2005 IGRA guidelines based on the expert panel's written report of its opinions. Efforts are being made to harmonize the updated IGRA guidelines with the ATS Diagnostic Statement. CDC plans to review the updated guidelines over the next 2-4 weeks and aims to submit the document to the *MMWR* in December 2008.

Dr. Masahiro Narita represented ACET on the IGRA expert panel. He noted that the expert panel agreed IGRA is a more specific test than TST. He raised the possibility of ACET making a recommendation for Medicaid, Medicare and other health insurance companies to reimburse the cost of IGRAs nationally because reimbursement varies among states.

Dr. Fleenor pointed out that the expert panel's draft report on updating the IGRA guidelines was not distributed to ACET for review and substantive input. CDC plans to submit the updated guidelines to the *MMWR* in December 2008, but this date will be before ACET's next meeting in 2009. Dr. Fleenor conveyed that the absence of the expert panel's draft report might preclude ACET from taking formal action on the updated IGRA guidelines during the business session on the following day.

Overview of Direct Specimen Microscopy Regulations

Dr. Beverly Metchock, of DTBE, explained that a variety of laboratories perform TB testing and mycobacteriology in the United States, including hospital and medical center laboratories in

which mycobacteriology is generally a part of the microbiology laboratory; clinic, commercial and reference laboratories; and state, county and city public health laboratories. Data from a 1999 training needs assessment showed that 35.5% of laboratories performed AFB smear microscopy only, 46.5% performed microscopy and culture without identification, 10.3% performed culture with identification, and 7.7% performed DST.

These data demonstrated that mycobacteriology laboratories services are often dispersed and piecemeal with specimens or isolates being referred from one laboratory to another. Communication between laboratories and between caregivers and TB programs is problematic, particularly when testing becomes further removed from the originating laboratory or specimen collection site.

The two types of acid-fast microscopy methods are described as follows. The Fuchsin-based method is performed with a Brightfield microscope that examines smears using oil immersion magnified 1,000 times. Specimens can be characterized as smear-negative after examining ~300 fields of Kinyoun or Ziehl-Neelsen stains.

The Fluorochrome method is performed with a fluorescence microscope that magnifies smears 250 times or 450 times for confirmation of AFB. Specimens can be characterized as smear-negative after examining 30 fields. The Fluorochrome method is the recommended staining procedure for direct specimen microscopy because the screening process is easier and more rapid, practical and sensitive.

The sensitivity of AFB microscopy is 50%-70% for pulmonary TB, but the rate is much less for extrapulmonary TB. The amount of organisms correlates with disease infectiousness and severity. For a positive smear, 5,000-10,000 organisms/ml of a specimen would be needed, while 10-100 organisms/ml of a specimen would be needed for a positive culture.

AFB microscopy is not specific for *Mycobacterium tuberculosis* (*M.tb*) and its positive predictive value depends on the prevalence of NTM in the population. The value of AFB microscopy for TB includes an inexpensive and relatively quick method, provision of the first bacteriologic evidence of TB, detection of infectious patients because AFB in smear is quantified, and a determination on the need for additional testing, such as NAAT.

In terms of direct specimen microscopy regulations, the Centers for Medicare and Medicaid Services (CMS) administers the Clinical Laboratory Improvement Amendments (CLIA). Congress enacted CLIA in 1988 to ensure the accuracy and reliability of all laboratory testing performed in hospital, public health, clinic, independent, commercial, physician office and all other types of laboratories in the United States. CLIA oversight extends to testing of patients who are neither Medicare beneficiaries nor Medicaid recipients.

CLIA regulations are arranged to match the path of patient specimens throughout the entire laboratory testing process, including the pre-analytic, analytic and post-analytic phases. CLIA clearly defines requirements for testing staff, laboratory directors and all other laboratory personnel; quality control/quality assurance requirements; and requirements for procedures, competency testing of personnel, equipment maintenance, proficiency testing and test method

verification. CMS has a regulatory function to inspect laboratories. Each specific laboratory test system, assay and examination is characterized as “waived,” “moderate complexity” or “high complexity.”

Criteria to categorize the complexity of CLIA tests include knowledge; training and experience; reagents and materials preparation; characteristics of operational steps; calibration, quality control and proficiency testing materials; test system troubleshooting and equipment maintenance; and interpretation and judgment. Each of the seven criteria is scored from “1” for a minimal need for CLIA requirement to “3” for highly complex. The criteria are added for scores of “$\leq$12” for moderately complex or “$\geq$12” for highly complex. CLIA categorizations of “moderately complex” for direct acid-fast smear and “highly complex” for concentrated acid-fast smear became effective on July 26, 1994.

The Clinical and Laboratory Standards Institute recently published recommendations in 2008 on mycobacteriology testing in laboratories. Microscopists should read a minimum of 15 smears per week to maintain proficiency. Confirmation of all positive smears is good practice. Smears are best prepared from sediments of specimens that have been liquefied, decontaminated and concentrated by centrifugation. Positive and negative control slides should be ran with each run.

CLIA outlines a number of provider-performed microscopy (PPM) requirements. Physicians or mid-level practitioners under the supervision of a physician must personally examine specimens obtained from their patients or patients of a group medical practice in which the physician is a member or employee. The procedure must be categorized as “moderately complex” and performed as bright-field or phase-contrast microscopy. The specimen must be labile or a delay in performing the test could compromise the accuracy of the test result. Control materials generally are not required to monitor the entire testing process. Limited handling or processing of specimens is required.

The Clinical Laboratory Improvement Advisory Committee conducts reviews of specific testing algorithms, products or staining methods at the request of HHS and provides HHS with recommendations on revising the criteria for categorization of procedures. HHS determines whether the procedure meets PPM criteria. Procedures that have been given CLIA approval for PPM include all direct wet mount preparations to detect the presence or absence of bacteria, fungi, parasites and human cellular elements, potassium hydroxide preparations, pinworm examinations, and fecal leukocyte examinations.

Update by the Rapid Drug Resistance Assay Workgroup

Dr. Shinnick reported that a workgroup is being formed to respond to ACET's previous resolution on the use of molecular DST in the United States. ACET advised the Director of CDC to fund and expedite implementation of currently available rapid drug resistance assays in select qualified reference laboratories to quickly identify drug-resistant TB, reduce transmission, and prevent further acquired resistance for laboratories to be able to provide this assay for optimal patient care by the end of 2008.

The workgroup members will include representatives from ACET, DTBE, the Association of Public Health Laboratories (APHL), state and local public health departments, and NTCA members from big cities and high-, medium- and low-incidence states. The workgroup will address a number of programmatic issues to fulfill its charge, including specific patients who would be tested, the number of tests to perform each year, entities that would submit specimens, performance indicators, and logistical, reporting and funding issues.

The workgroup also will address several laboratory issues, including organization of molecular DST in every laboratory or regional laboratories only, guidance on accessioning and testing protocols, requirements to implement and validate rapid molecular testing, the potential use of non-FDA-approved tests, and compliance with CLIA and FDA regulations.

From October 2008-February 2009, the workgroup will convene conference calls, hold a face-to-face meeting, and deliver its report to the DTBE Office of the Director. The workgroup's report will contain recommendations regarding TB patients or suspects who would be eligible for molecular DST, the submission of specimens, laboratory organization, protocols, methods and turnaround times, and funding for programs. In addition to obtaining guidance from the workgroup, DTBE also will convene an expert consultation on the use of molecular DST in the United States.

ACET advised the workgroup to consider military personnel as one of the populations that would be eligible for molecular DST. This recommendation would address the problem of the two- to three-month period of time that is required to obtain test results of U.S. military personnel who are deployed overseas and exposed to persons with likely MDR-TB.

Update on the State TB Cooperative Agreement and Laboratory Funding Formula

Drs. Kashef Ijaz and Angela Starks, of DTBE, presented recommendations from the NTCA FY'10 Formula Workgroup. An excess of 52,100 TB cases was reported in the United States in 1985-1992 due to a deficiency in the TB control infrastructure, the HIV epidemic, MDR-TB, and immigration of FBPs. In 1982-2007, 13,929 TB cases were reported in the United States for an overall case rate of 4.4/100,000.

Based on the resurgence of TB and the emergence of MDR-TB, federal funding for TB prevention and control activities was increased in 1992. The majority of this funding was allocated to New York City, Los Angeles, San Diego, Houston, the District of Columbia and five other big cities. The epidemiology of TB in the United States has evolved over the past 15 years, but funding amounts have remained relatively static. However, the Biomedical Research and Development Pricing Index showed a decrease in federal TB funds in 1990-2006. Overall, TB cooperative agreement funds have decreased by 14% since 2001 due to inflation.

DTBE and its partners developed and incorporated a model into the FY'05 TB cooperative agreement to redistribute funds that would more closely reflect the changing epidemiology of TB in the United States. The formula resulted in redistributing 20% of funds annually through FY'07 based on a five-year average of selected factors. The funding amounts was increased to 35% in FY'08.

The 35% redistribution formula was weighted based on data reported to CDC in 2001-2005 for specific occurrences of TB cases in various subpopulations. The formula also relied on a five-year average of 40% of incident cases, 15% of U.S.-born minorities, 15% of FBPs, 10% of Class A/B1/B2 TB, 5% of HIV co-infection, 5% of MDR-TB, 5% of the substance abuse population, and 5% of the homeless population.

To re-compete the TB cooperative agreement with the redistribution formula, DTBE and NTCA formed the FY'10 Formula Workgroup with representatives from NTCA, DTBE, ACET, big cities, laboratories, and high-, medium- and low-incidence states. The workgroup was charged with achieving three key objectives in evaluating the redistribution formula and submitting a draft report to the CDC clearance process by October 2008.

Existing formulas for prevention/control and laboratory components were reviewed and recommendations for the new proposed formula were both made for the FY'10 TB cooperative agreement funding allocations. Criteria for direct TB cooperative agreement funding to big cities in the future were assessed. The distribution of funds to hold-harmless states that receive $\leq$$255,000 for TB were evaluated.

To ensure transparency throughout the evaluation, DTBE distributed "Dear Colleague" letters. NTCA updated its website with the workgroup's meeting minutes; information on the workgroup members; a description of the purpose, goals and objectives of the workgroup; and the workgroup's background materials and timeline. The NTCA website also provided an opportunity for TB controllers to provide input on the workgroup's process of updating the TB redistribution formula.

The workgroup used the following methods to evaluate the prevention/control component of the TB cooperative agreement funding redistribution formula. The current formula was reviewed to determine any necessary additions, deletions or drastic changes to the variables, weights or entire formula. Data previously reported to CDC through existing surveillance systems were considered to justify all revisions and ensure the variables and weights would be measurable.

The advantages and disadvantages associated with existing formula variables were discussed based on epidemiologic data, workload, level of effort, cost, and input from workgroup members and TB controllers in a Delphi process. Epidemiologic data were reviewed, including six different scenarios that illustrated the cost per case distribution. Breakdowns were developed for funding that is currently allocated to big cities and hold-harmless states. Data from nationally representative samples of big cities and high-, medium- and low-incidence states were analyzed and included measures of centrality in terms of means, medians and standard deviations.

A list of new variables was created based on the possibility and feasibility of inclusion in the redistribution formula. These factors included incarceration at diagnosis, smear-positive pulmonary cases, confirmed cases not counted, co-morbidity with diabetes, reactivated cases and immigration status. Because the last four variables were not included in the old RVCT and have no historical data at this time, the workgroup raised the possibility of applying 2015 rather than 2010 objectives to measure progress on these variables.

The workgroup proposed and reached consensus on the following language for the redistribution formula for the FY'10 TB cooperative agreement. The 45% redistribution formula should be based on data reported to CDC in 2004-2008 to determine specific occurrences of TB cases in various subpopulations. The formula also should rely on the following five-year average: 30% of incident cases, 35% of U.S.-born minorities and FBPs, 5% of HIV co-infection, 5% of MDR-TB, 5% of the substance abuse population, 5% of the homeless population, and 15% of smear-positive pulmonary TB patients.

The workgroup did not reach consensus on direct funding to big cities, but the following four options were proposed: 1) The currently funded cities should remain the same; 2) A new group of the top nine cities and the District of Columbia should be funded based on an analysis of five-year data for cites listed in Table 45 of the "CDC Surveillance Report" and use of the current formula without Class A/B1/B2 TB; 3) A baseline threshold should be established and direct funding should be discontinued to cities that fall below this threshold; 4) Direct funding should not be allocated to any cities with the exception of the District of Columbia; instead, funding should be allocated to states with the stipulation that states must develop funding formulas in collaboration with their respective cities and counties.

The workgroup acknowledged the inequity among hold-harmless states that receive $\leq$\$255,000 for TB because funding in these states has not been realigned or redistributed as part of the changing epidemiology since 2005. The workgroup proposed three options to CDC: 1) The currently funded hold-harmless states should remain the same. 2) A pot with a minimum amount of funds should be created and distributed to hold-harmless states only. 3) The current funding pot assigned to hold-harmless states should be redistributed, but U.S.-affiliated islands and territories should be excluded from this funding source.

CDC identified both advantages and disadvantages with the workgroup's recommendations on direct funding to big cities. On the one hand, making no changes would be easy. Funding of the new top nine cities and the District of Columbia would reflect the change in TB epidemiology in the United States. Establishing a baseline threshold or providing no direct funding to cities

with the exception of the District of Columbia would consolidate funding, simplify budgets, and encourage integration and collaboration among cities and states.

On the other hand, making no changes would be difficult to justify because the current group of big cities does not reflect the change in TB epidemiology in the United States. Funding of the new top nine cities and the District of Columbia, establishing a baseline threshold, or providing no direct funding to cities with the exception of the District of Columbia would have political implications. Applying the current TB distribution formula would lead to a close difference between directly and non-directly funded cities.

In terms of the laboratory component of the TB cooperative agreement funding redistribution formula, the workgroup noted that funds were allocated using a formula based on the number of TB cases for which the laboratory provided results. In FY'05-FY'07, 80% of funds were distributed based on prior funding and 20% of funds were distributed based on workload. In FY'08-FY'09, 65% of funds would be distributed based on prior funding and 35% of funds would be distributed based on workload.

A TB Laboratory Formula Workgroup was formed to review the existing formula and recommend modifications for the FY'10-FY'14 allocations. The workgroup members included representatives from DTBE, NTCA, APHL, and laboratories in low-, medium- and high-incidence states with low, medium and high testing volumes.

The workgroup developed and ranked a broad list of 12 potential elements according to their impact on laboratory workload, ease of acquiring data, and appropriateness based on the intent of upgrading the laboratory component of the TB cooperative agreement. The workgroup agreed that data provided by laboratories would be used to determine funding amounts for each element and amounts for each element would be added to determine the formula-based portion of the award.

The six elements that the workgroup selected to calculate the formula-based funding amount for laboratories and the proposed weight for each element are outlined below:

1. The total number of clinical specimens processed and cultured in the laboratory. [5% weight]
2. The number of individual patients for whom a clinical specimen was processed and a TB culture was inoculated. [15% weight]
3. The number of individual patients for whom a reference isolate or reference culture was received by the public health laboratory to rule out or confirm the identification of *M.tb* complex. [15% weight]
4. The number of individual patients for whom *M.tb* DST was performed for first-line drugs, including both in-house and referral testing. [25% weight]
5. The number of individual patients for whom a clinical specimen was directly tested with NAAT, including both in-house and referral testing. [25% weight]
6. Development of an integrated laboratory system, but funds for this element would be distributed on a per program basis or an equal amount to each laboratory. [15% weight]

The workgroup reached consensus on selecting the element weights by analyzing the impact of each element on workloads and its contribution to TB control. The element weights were selected after analyses of ~10 different funding scenarios that were calculated based on data provided by seven laboratories represented on the workgroup.

The workgroup's proposed funding plan and timeline for the laboratory component of the TB cooperative agreement are summarized as follows. In FY'10, the current distribution formula of 55% base funding/45% formula funding would be followed to allow data reporting to catch up to averages of the six proposed elements. In FY'11 and FY'12, the 55%/45% distribution would remain the same, but the six proposed elements would be implemented with an incentive for using NAAT. In FY'13 and FY'14, the 55%/45% distribution would change to 40% base funding/ 60% formula funding with no incentive for using NAAT.

CDC has taken a number of actions to broadly solicit input from stakeholders on the proposed redistribution formula for the laboratory component of the TB cooperative agreement. During the "5th National Conference on the Laboratory Aspects of Tuberculosis" in August 2008, CDC held a post-conference workshop for participants to provide feedback on the formula. APHL collaborated with CDC to send a letter and a slide set of the draft formula to laboratory directors in September 2008. CDC and APHL convened a 50-state conference call in September 2008 with 66 participants to discuss the laboratory formula elements and weights.

The workgroup has reviewed comments from the post-conference workshop and is waiting to review feedback from the 50-state conference call. In conjunction with the release of the funding opportunity announcement for the TB cooperative agreement, CDC will send a letter to stakeholders in the spring of 2009 to highlight key points of the laboratory component of the redistribution formula. CDC is engaging in preliminary discussions to hold an information session on the laboratory component of the redistribution formula during the APHL conference in May 2009.

For both the prevention/control and laboratory components of the redistribution formula of the TB cooperative agreement, a presentation has been made to ACET and briefings will be given over the next few weeks to NCHHSTP Division Directors, the NCHHSTP Issues Management and Communication Team, and leadership of the Coordinating Center for Infectious Diseases (CCID). The focus will then be placed on developing a process summary document, an issues management and communication strategy, a list of frequently asked questions, and a document to justify the workgroup's recommendations.

Dr. Castro added that ACET's input would be most helpful to DTBE on the four options the workgroup proposed for direct funding to big cities. He confirmed that DTBE would collaborate with TB controllers and other groups to provide guidance to ensure the recommendations are not viewed as "discretionary" TB dollars at the state level.

ACET commended CDC, NTCA and APHL for providing leadership in formulating guidance on the redistribution formula for the FY'10 TB cooperative agreement. The members recognized the difficulty of this effort due to vast differences among TB programs and laboratories in terms of needs, interests, perspectives, levels of capacity, geographic locations and other factors.

ACET was particularly pleased with the quality improvement component of the funding formula as well as the performance indicators for TB programs and laboratories. However, a number of members emphasized the need for more active involvement by CDC program staff to interact with and hold state grantees accountable to the stipulations in the funding formula, particularly the requirement for states to closely collaborate with big cities to ensure proper distribution of funds to the local level.

ACET urged CDC to ensure that the funding formula addresses public health needs and does not respond to political issues. The members made two key suggestions for CDC to consider in finalizing the redistribution formula of the TB cooperative agreement. First, CDC should explore the possibility of placing a cap on the indirect rate for states in the funding formula.

Second, CDC should ensure that the redistribution formula and RVCT reflect major differences between MDR-TB and XDR-TB in terms of costs, personnel time and other resources expended by local health jurisdictions. The funding formula and RVCT also should consider other local challenges, such as tremendous workloads based on the emergence of drug intolerance among older TB patients, non-compliant TB patients, and Class 5 cases that are at least 3-4 times greater than reportable TB cases.

Overview of the MDR-TB Investigation in Chuuk, Micronesia

Dr. Mitesh Desai and Mr. Andrew Heetderks, of DTBE, described the outcomes of CDC's recent investigation of MDR-TB. In May 2008, the Secretary of Health of the Federated States of Micronesia (FSM) requested CDC's assistance on four laboratory-confirmed cases of MDR-TB that were reported from Chuuk, Micronesia. Of the four cases, three resulted in death and one was a child two years of age who had MDR-TB and evidence of recent transmission of *M.tb*.

FSM is an independent country with >600 islands and >200 islands and atolls in Chuuk alone. Since 1986, the United States has awarded grants of ~$80 million per year to FSM under the Compact of Free Association. Of the total population of ~111,000 persons in FSM and ~55,000 persons in Chuuk, ~27% is below the poverty level. The estimated TB case rate in FSM is 100-199/100,000. Of 70 TB cases reported in Chuuk in 2007, 7% resulted in deaths for an overall case rate of 127/100,000.

Chuuk performs sputum smear microscopy and has routinely performed DST since January 2006. However, Hawaii performs culture and first-line DST for Chuuk, while California performs second-line DST and universal genotyping. Of at least 15 non-MDR drug-resistant cases reported from Chuuk by July 2008, 27% resulted in deaths.

FSM's annual budget is ~$170,000 and its workforce of one part-time physician and two staff is insufficient for contact investigations or DOT. Self-administered therapy is primarily used because clinics and laboratory facilities are remotely located. Chuuk's TB control infrastructure includes one hospital, one x-ray machine and no second-line drugs.

The objectives of CDC's Epi-Aid were to describe the epidemiology of MDR-TB in Chuuk; identify and prioritize contacts of MDR-TB cases for evaluation and treatment; and determine next steps to prevent further transmission of MDR-TB. During the investigation, CDC identified two distinct and simultaneous MDR-TB outbreaks in which four of five laboratory-confirmed MDR-TB cases resulted in deaths due to the absence of adequate second-line drugs. The investigation also confirmed extensive and ongoing transmission among household contacts and detected 13 new suspect MDR-TB cases. Of 195 contacts who were identified for the five cases, 148 started evaluation. Of 88 contacts who completed evaluation, 51% had LTBI.

CDC hypothesized that the emergence of MDR-TB in Chuuk with outbreak 1 was associated with acquired three-drug resistance due to inadequate therapy and an underlying pool of two-drug resistance with ongoing transmission. CDC further hypothesized that outbreak 2 with five-drug resistance was associated with possible importation of TB by the index case and limited availability of genotyping and DST data. CDC concluded that the MDR-TB outbreaks in Chuuk were driven by multiple diagnostic, therapeutic and programmatic challenges, including delayed diagnoses of MDR-TB, the lack of second-line drugs, and limited resources for DOT and contact investigations.

CDC determined that several actions would need to be taken after the Epi-Aid Team left Chuuk in July 2008. To stop ongoing transmission of TB and MDR-TB, Chuuk would need to complete contact evaluations; isolate and treat confirmed TB cases with DOT and monitor laboratory results; monitor TB suspects for confirmation of active TB disease; and seek consultation to treat the contacts of MDR-TB cases and initiate directly observed preventive therapy (DOPT).

CDC identified a number of existing resources that most likely would contribute to Chuuk's success in stopping ongoing transmission of TB and MDR-TB, including the cooperative agreement between FSM and the United States; availability of diagnostic laboratory services in Hawaii and mycobacterial laboratory testing in California; onsite and repeated technical assistance by CDC and WHO, and medical consultations by an RTMCC. PCSI in FSM with the Pacific Island TB Controllers Association (PITCA) was an additional resource that led to a rapid response to a public health emergency with local and regional implications and collaborations with partners to pool resources and maximize impact.

The PCSI partners in the MDR-TB investigation in Chuuk included DTBE, PITCA, WHO, HHS, the U.S. Department of Interior (DOI), U.S. Department of State (DOS), Secretariat of the Pacific Community, a TB program official from the Commonwealth of the Northern Marianas Islands, an RTMCC, regional reference laboratories, FSM national and state TB programs, and a U.S. Naval ship. The PCSI partnership resulted in DOI, DOS and HHS approving >$2 million for lifesaving second-line drugs in Chuuk.

The new funding allowed the five key components of the WHO DOT short-course strategy to be adapted for MDR-TB in Chuuk. These strategies include government commitment to TB control, adequate antimicrobial DST for TB case identification, individualized therapy under DOT, a secure supply of quality second-line drugs, and case registry, monitoring and evaluation.

A number of programmatic successes were achieved after the MDR-TB investigation in Chuuk to strengthen the public health impact. The FSM government committed to controlling the TB outbreak and declared a state of emergency in Chuuk. Second-line drugs were procured. An isolation ward was opened in the Chuuk hospital for inpatient DOT. TB cases and suspects are currently on appropriate second-line treatment regimens and have good prognoses.

The regional reference laboratories in California and Hawaii are continuing to be utilized. Clinical consultations with MDR-TB experts from CDC, an RTMCC and the Pacific region were expanded. The majority of the TB contact investigation has been completed. Funds were identified to hire and train DOT workers in Chuuk. CDC and its partners provided onsite training and education for contact investigations and DOT.

The next step in stopping ongoing transmission of TB and MDR-TB in Chuuk will be to target outpatient DOT with appropriate case management to three groups: pan-susceptible and other drug-resistant TB patients, patients on DOPT and MDR-TB patients. Moreover, TB program management will be improved by assigning responsibility, conducting a systematic regular review and developing plans to address barriers to adherence.

CDC and its partners learned several important lessons during the MDR-TB investigation in Chuuk. A TB control infrastructure, including regional reference laboratories, should be maintained. Political will should be established with cooperative agreement recipients, all other stakeholders and the general population. All partners should be held accountable to the goals, objectives, methods, activities and evaluation measures of the investigation. Responsible parties should be clearly identified at the outset of the investigation to monitor and oversee outcomes.

Patience should guide the TB investigation because implementation of recommendations requires time and procurement of drugs through the Green Light Committee can take up to one year. Nurses, DOT workers and laboratorians should be repeatedly trained in TB interventions. PCSI should be utilized to promote synergy among all partners.

Efforts to build capacity in DOT, DOPT, contact investigations and other areas of TB should be made in incremental steps. The tremendous expense related to poor TB control should be used as an opportunity to practice prevention. CDC plans to collaborate with its partners to apply lessons learned in the Chuuk MDR-TB investigation to other Micronesian Islands.

Update on CDC's Public Health Law and TB Control Activities

Dr. Richard Goodman, of the CDC Public Health Law Program, explained that the overarching aim of CDC's TB legal preparedness activities is to improve understanding of the status and sufficiency of state laws for TB control and prevention among practitioners and other groups in the setting of progressively emergent drug-resistant TB.

CDC and the Centers for Law and the Public's Health conducted five activities to build on ACET's 1993 recommendations on TB control laws in the United States. The description and current status of these five activities are outlined below.

1. *Activity*: Express laws for TB control within selected states and local jurisdictions would be reviewed and characterized.
   Status: The penultimate draft report of this review was submitted to CDC on October 3, 2008 for the final clearance review. CDC submitted its final comments to the Centers for Law and the Public's Health and expects to receive the final version in the very near future. CDC is requesting ACET's input on strategies to widely disseminate the report.

2. *Activity*: A scenario-based assessment would be conducted to better understand the sufficiency of TB control laws in selected states.
   Status: The scenario-based assessment of TB control laws was conducted in Kansas and Florida in May 2008. Implementation guidance will be developed for any jurisdiction that anticipates using the scenario. Additional guidance is needed from ACET and NTCA on implementing ACET's previous recommendation for jurisdictions to use the scenario-based assessment before implementing the model TB control act.

3. *Activity*: Selected tribal laws for TB control would be reviewed and characterized to inform the development of the TB control model act
   Status: This activity was completed and no new developments have occurred since CDC's update during the June 2008 ACET meeting. However, the review demonstrated the paucity of tribal laws for TB control.

4. *Activity*: A "model act" on state TB control would be developed based on data collected from the review of state laws and implementation of the scenario-based assessment.
   Status: The development of the model act on state TB control is underway. In November-December 2008, several iterations of the draft model act will be revised based on expert input from CDC, ACET, NTCA and other partners. The document will be finalized in January 2009.

5. *Activity*: A TB control law handbook for state TB control practitioners and a companion instructional slide set would be developed and disseminated to improve competency and understanding in applying these laws among local, state and tribal public health practitioners and their legal counsel.
   Status: Penultimate drafts of these documents were submitted to CDC on October 3, 2008 for the final clearance review. CDC expects to receive the final versions in the very near future. Additional guidance is needed from ACET and NTCA regarding strategies to disseminate the handbook and companion instructional slide set.

Dr. Goodman provided ACET with the penultimate draft of the handbook: *A Framework for Improving Cross-Sector Coordination for Emergency Preparedness and Response: Action Steps for Public Health, Law Enforcement, the Judiciary and Corrections*. He explained that the

handbook provides a strategic rationale and describes resources to improve cross-sector coordination during preparedness efforts.

The handbook also lists >50 action options under four broad categories: organizing to implement opportunities for action; identifying roles and responsibilities; communicating and sharing information; and providing training, education and exercises. Dr. Goodman concluded his update by presenting the draft companion instructional slide set to the handbook that can be used for training or continuing education purposes.

ACET commended CDC and its partners for undertaking the important effort of developing and disseminating materials on public health law and TB control activities. The members noted that strong, cogent and reasonable guidance is particularly important to justify legal actions on TB control at the local level.

ACET pointed out that after CDC's meeting on November 3, 2008 for key partners to provide input on the initial draft of the TB model act, comments would be due by November 30, 2008. Due to DTBE's requests for external input on other projects during this same time period, TB controllers would be unable to provide CDC with adequate and thoughtful feedback by the deadline. ACET asked CDC to extend the deadline for the submission of comments on the TB model act from November 30 to mid-December 2008.

Dr. Fleenor confirmed that CDC's request for ACET's recommendations on dissemination of the TB legal preparedness materials would be discussed during the business session on the following day.

With no further discussion or business brought before ACET, Dr. Fleenor recessed the meeting at 5:26 p.m. on October 7, 2008.

Update by STOP TB USA

Dr. Fleenor reconvened the ACET meeting at 8:34 a.m. on October 8, 2008 and yielded the floor to the first presenter.

Mr. John Seggerson, of STOP TB USA, informed ACET of ongoing efforts to update the "Plan for Elimination of TB in the United States." The draft Plan is ready to be distributed to partners for review and comment of the seven sections: an executive summary, background and overall progress in eliminating TB in the United States, TB among U.S.-born populations, TB among FBPs, TB in low-incidence areas, new tools for TB, and mobilization of partners in the fight against TB. Key points of the draft Plan are highlighted below.

The executive summary outlines recent trends that have prompted reevaluation of national plans and efforts for eliminating TB in the United States. Most notably, TB remains a serious and persistent threat to the health of communities throughout the country. The emergence of XDR-TB threatens TB elimination in the United States and around the world. Interim targets for

TB elimination have not been met. The rate of decrease in TB incidence is slowing rather than accelerating. TB elimination in the United States will require nearly 100 years if the current trends continue.

The executive summary also points out that in response to these trends and the threat to TB elimination around the world due to the emergence of XDR-TB, STOP TB USA established a TB Elimination Plan Committee. The Committee was charged with assessing the status of the U.S. TB elimination effort over the past eight years since the release of the Institute of Medicine report and formulating recommendations to update the Plan. The Committee established a number of goals for the updated Plan.

The Plan will provide a realistic appraisal of the current status of the overall U.S. TB elimination effort. The Plan will provide the following general recommendations to overcome challenges to TB elimination in the United States. Stakeholders and partners should join with STOP TB USA in maintaining public awareness of the threat of TB and the importance of TB elimination. The commitment to TB elimination in the United States, including adequate funding and other resources, should be renewed or expanded. The full complement of stakeholders and partners should assure that all U.S. citizens are provided with timely access to lifesaving services for the diagnosis, treatment and prevention of TB.

The Plan will provide specific recommendations to call for the development of new tools and address persistent challenges to TB elimination that are unique to certain populations: (1) FBPs, (2) U.S.-born minority populations with continued TB disparities; (3) high-risk groups defined by socioeconomic constraints; and (4) persons living in low-incidence areas where the provision of timely and effective TB medical and public health services remains a challenge, but must be addressed to achieve TB elimination. The Plan will assess the challenges and progress in the development and implementation of TB diagnostics, drugs, vaccines and other new tools. The Plan will identify partners who will need to be engaged to successfully achieve TB elimination in three segments of the U.S. population.

The Plan will provide the following guidance on advocacy, mobilization and partnerships. Responsibility for planning and implementing TB control cannot exclusively stay within the public health sector. TB elimination in the United States requires complex interventions in groups with different cultural approaches to health care and varying socioeconomic contexts that affect their access to health care. Advocacy is one of the most important tools available to confront the need to change existing attitudes and conditions concerning the prevention and control of TB.

Mobilization of community partners and public health organizations is required to build a framework for TB advocacy. Advocacy builds awareness of TB and supports patient-centered activities by maximizing resources and services for persons with TB. Advocacy efforts should include educating healthcare providers about TB and its associated health disparities. Efforts to raise public awareness of health disparities, daily domestic outbreaks and ongoing transmission in U.S.-born populations among local, state and national lawmakers are important. Partnerships with key community members are necessary to mobilize communities affected by TB to plan and implement interventions for TB education, prevention and control.

The Committee has scheduled several activities through December 2008 to launch the updated Plan. The document will be distributed to consultants for review and written comments. The consultants will convene conference calls to discuss the revised draft Plan and also will develop a summary document of their feedback. The consultant summary document will be distributed for review and input and incorporated into the final updated Plan.

Mr. Seggerson acknowledged the TB experts, consultants, partners and advocates throughout the country who volunteered their valuable time and expertise to write various sections of the updated Plan and review the document. Dr. Castro also thanked the TB community for launching a national grassroots movement to update the Plan. ACET offered to provide guidance to the Committee on disseminating the updated Plan. Most notably, consideration should be given to launching the Plan during World TB Day in 2009.

Overview of CDC's External Peer Review of Research and Scientific Programs

Dr. Philip LoBue, Associate Director for Science of DTBE, defined a number of terms related to CDC's peer review policy. "External peer review" is an independent assessment of research and scientific programs by experts external to CDC. These reviews address the quality, mission relevance, impact and direction of a program or research activity. A "scientific program" includes intramural and extramural research and non-research, such as public health practice and core support services.

"Research" is a systematic investigation that is designed to develop or contribute to generalizable knowledge. "Extramural research" includes activities that are funded through a grant, cooperative agreement or other assistance mechanism. "Intramural research" includes activities that are directed by CDC or funded through a contract or other acquisition mechanism.

"Non-research public health practice" includes surveillance, specialized investigations, public health programs, services and responses, and program evaluation. "Non-research support activities" include initiatives that serve the needs of research or public health practice and are subject to accreditation, audit or performance review. For non-research programs, funding recipients conduct extramural research, while DTBE provides management and oversight of intramural research.

CDC policy requires all research and scientific programs conducted or funded by CDC to undergo periodic external peer review. All extramural research applications submitted to CDC are required to undergo external peer review by a federal advisory committee, but this policy is not relevant to DTBE at this time. All intramural research conducted by CDC, such as TBESC and TBTC, must be externally peer reviewed for scientific and technical quality at least once every five years.

Non-research scientific programs conducted or funded by CDC, such as surveillance, outbreak investigations and program evaluations, are subject to external peer review at least once every

five years, but a flexible approach is encouraged. For example, a review of non-research scientific programs might include the total portfolio, individual projects, organizational structure or cross-cutting topics.

The CCID Board of Scientific Counselors (BSC) administers both intramural research peer reviews and non-research scientific programs, but this role is not clearly defined. Although results of peer reviews should be regularly reported to the BSC for review and comment, the expectation for the BSC to conduct all peer review activities is not feasible due to the large number of divisions and individual programs within CCID. During the next BSC meeting in December 2008, NCHHSTP will present its future peer review strategy.

Dr. LoBue presented a proposal for ACET to serve as a peer reviewer of DTBE's intramural program and research activities. ACET's role in this effort primarily would be limited to non-research and less technically complex programs and projects. ACET would conduct peer reviews of DTBE's surveillance, outbreak response activities, program evaluation, and the intramural components of RTMCCs and prevention and control support to state and local programs. For example, ACET would continue to review the RVCT, National TB Indicators Project and TB cooperative agreement. Ad hoc expert panels, with input from ACET, would conduct reviews of TBTC, TBESC, the research component of the Mycobacteriology Laboratory and other complex research activities.

The proposed process for ACET to systematically peer review DTBE's intramural program and research is summarized as follows. DTBE would propose a topic to be peer reviewed to the ACET Chair. The Chair would determine whether the proposed topic is appropriate for ACET to peer review. The topic would be placed on the ACET agenda and identified as a peer review activity.

DTBE would provide ACET with background materials well in advance of the meeting, make a presentation to ACET on the topic during the meeting, and pose specific questions that should be answered during the peer review. ACET would discuss the information and make formal recommendations to DTBE during the business session. DTBE would formally respond to ACET's comments or recommendations during a subsequent meeting. DTBE does not expect more than one peer review topic to be placed on a specific meeting agenda or ACET's peer review reports to exceed one page.

The proposed process for non-ACET peer reviews is summarized as follows. External experts would be identified to serve on an ad hoc panel. The members would include an ACET member and external subject matter experts designated by ACET. After the review, the ad hoc expert panel would report to ACET and DTBE would provide a formal response to both ACET and the BSC. The non-ACET peer review process would be used for TBTC and TBESC.

Dr. Fleenor confirmed that Dr. LoBue's proposal for ACET to serve as a peer reviewer of DTBE's intramural program and research activities would be revisited during the business session for formal action. If ACET voted to undertake this effort, DTBE agreed with the suggestion to designate an ACET member as the primary reviewer for each specific topic.

Update on TBTC

Dr. Vernon explained that TBTC is an investigator-driven consortium with 27 clinical sites worldwide. TBTC performs clinical trials and other studies related to TB therapy and diagnostics. In its 13-year history, TBTC has enrolled 10,274 patients and an additional 1,250 patients in pharmacokinetics and other sub-studies in its seminal trials in TB therapy. TBTC trials also have made significant contributions to current TB therapy or drug development.

TBTC underwent an internal review of its scientific agenda by the TBTC Core Science Group; an external review of the scientific agenda by 13 internationally recognized experts; and a peer review of the TBTC Intramural Research Program as required by CDC's peer review policy. The review panel identified TBTC's two highest priorities.

For LTBI treatment, enrollment in Study 26 with a 12-dose/3-month regimen of isoniazid and rifapentine should be completed. Adequate enrollment of young children and HIV-positive persons in Study 26 should be assured. For active TB, efforts should be made to rapidly advance from a very promising treatment-shortening regimen in a Phase II trial to definitive evaluation in a Phase III trial.

The review panel provided guidance on other potential TBTC trials. MDR-TB trials should be conducted only with increased funding and after consultation with other experts in the field. Involvement in HIV/TB co-morbidity trials should be continued to evaluate important questions. Pediatric TB trials should be conducted only after new regimens have been evaluated in adults. Diagnostic trials should be conducted only in conjunction with a planned randomized trial.

The review panel provided guidance on several overarching areas. Collaboration should be increased with laboratory scientists to address biomarkers, AIDS clinical trial groups to address HIV/TB co-morbidity, and other TB trial groups. Funding problems should be resolved through better collaboration with NIH. The external peer review process of TBTC should be continued.

The review panel had a very positive impression of the value of TBTC overall and reached consensus on the need to continue to support and protect this effort. Most notably, TBTC's needs in the areas of laboratory standardization, stable funding indexed to inflation, and adequate support for investigators have not been addressed to date. Fiscal attrition of TBTC remained a major concern during the Scientific Advisory Group of Experts meeting in March 2008. In 2008, another TBTC site was eliminated and eight sites were reduced to closeout mode. In addition to executing trials, TBTC also develops science and determines the most important trials to conduct.

The review panel acknowledged the significant impact of TBTC on TB therapy and diagnostics. If Study 26 is successful, the non-inferiority of a three-month/once-weekly LTBI regimen could be demonstrated by 2010. If Studies 29 and 31 are successful, the efficacy of a three-month TB treatment regimen could be demonstrated by mid-2013. If both studies are successful, tens of

millions of dollars could be saved domestically by a combination of shorter treatment durations for both active TB and LTBI.

The 2009-2019 re-competition of TBTC will start in 2009 and all applications will be formally peer reviewed. The configuration of TBTC will be determined by public health and scientific needs, availability of patients from the proposed sites and funding. The development of 4-6 new agents is expected to primarily occur in the public sector. Two agents that are currently in MDR-TB trials are not likely to advance further without external support. The development of agents for drug-susceptible TB will require many trials. Careful selection of the most promising agents and the identification of agents that are unlikely to advance further without public support will be a major challenge for TBTC during the 2009-2019 re-competition.

In the 2009-2019 re-competed of TBTC, more resources will be needed to support additional costs: increased business at overseas sites, more regulatory and registration costs for clinical trials, management of experimental active drugs and placebos, centralized and standardized laboratory activities, oversight of clinical trials conducted by laboratories, expanded clinical site monitoring and data management activities, increased travel and shipping costs, and increased investigator support in light of local cost pressures.

TBTC will operate under a new vision in the 2009-2019 re-competition. Domestic and high-burden sites will be combined. Capacity will be strengthened for TBTC to enroll ~1,000 patients in treatment trials each year. New international sites will be established with leading external partners and new relationships with CDC field research sites. Complementary animal modeling and microbiology studies will be incorporated. International experts will be formally engaged.

To begin implementing the new vision for TBTC in 2009, 6-10 contract and Veterans Affairs sites will be funded domestically; at least four international sites with capacity to enroll 200 patients per year and receive federal dollars will be added; efforts to engage at least one CDC field station will be continued; and 1-2 external expert positions will be funded.

The development of materials for the 2009-2019 re-competition of TBTC is underway. The funding opportunity announcement is expected to be released in early 2009 and will remain open for a minimum of 60 days. A pre-proposal conference is planned for mid-November 2008, Investigators who are unable to attend the CDC meeting in Atlanta can participate by conference call. All participants will be required to register for the conference.

In terms of global TB trial capacity, TBTC potentially could enroll ~1,000 patients per year. The European Developing Country Clinical Trials Partnership and the TB Alliance are supporting five large global TB trials. The National Institute of Allergy and Infectious Diseases (NIAID) has expressed interest in collaborating in TBTC clinical trials. Médecins Sans Frontières will hold meetings to explore its potential involvement in global TB trials. The U.S. Agency for International Development awarded a ceiling of $80 million to a research consortium over the next five years. TBTC will explore collaborations with this new consortium.

ACET made several comments and suggestions in two key areas for DTBE to consider in the 2009-2019 re-competition of TBTC.

First, DTBE should consider adding vitamin D to TBTC clinical trials due to its potential impact on cancer, falls and other diseases or injuries. This approach might increase NIH's interest in funding TB clinical trials in institutes other than NIAID, such as the National Institute of Dental and Craniofacial Research and the National Institute of Diabetes and Digestive and Kidney Diseases.

TBTC clinical trials could be designed to determine an association between the baseline vitamin D status of patients and their response to TB regimens. TBESC was interested in addressing the impact of vitamin D on TB treatment outcomes, but no action was taken due to the lack of available data that demonstrate a strong positive effect. DTBE should explore this issue in more detail through a TBTC/TBESC collaboration.

Second, the recommendation by the external review panel to conduct pediatric TB trials only after new regimens have been evaluated in adults is problematic to many TBTC investigators. A number of pediatricians and investigators in HIV pediatric trials also strongly disagree with this recommendation. Basic data are lacking at this time on the pharmacokinetics of first-line TB therapeutic drugs in key subgroups of children.

Clinical trials for TB drug development in children should not be delayed until new regimens have been evaluated in adults. Although pediatric trials are time-consuming and resource-intensive, the current data gaps in TB drug development for children are "inexcusable" and "shameful." Pediatric TB trials might provide an opportunity for DTBE to leverage additional resources for TBTC from NIH and other funding entities. Overall, the public sector must provide leadership in assuring adequate data for new TB agents and regimens for children and TBTC should substantially contribute to this effort.

Update by the BCG Workgroup

Dr. Elsa Villarino, of DTBE, reported that CDC asked ACET to determine whether the 1996 BCG vaccine guidelines should be revised. To fulfill its charge, ACET formed a workgroup in 2007 with DTBE staff and ACET members, liaisons and *ex-officios*. The workgroup considered a number of factors to support the revision of the guidelines. TB epidemiology has changed globally due to the increasing incidence of MDR-TB and the emergence of XDR-TB. Increased humanitarian efforts and academic programs often require activities with high-risk populations that place HCWs, volunteers and students at risk for transmission of drug-resistant strains of TB.

International areas with a high prevalence of MDR-TB typically do not adequately or completely implement infection control measures. Transmission of TB in facilities and amplification of TB due to HIV co-infection are common in areas with a high prevalence of MDR-TB. IGRA is now

available as a diagnostic tool for LTBI and eliminates concerns regarding false-positive TST results with BCG vaccination.

The workgroup drafted recommendations that focus on the prevention of TB in HCWs and other groups at high risk for transmission of TB as a result of traveling to overseas areas with a high prevalence of MDR-TB. The draft guidance covers administration of BCG vaccine prior to travel and evaluation of the traveler's vaccination status pre-/post-travel. The workgroup developed the recommendations with a number of caveats.

Experience and knowledge of BCG vaccine among U.S. medical providers is limited, including its administration and efficacy in adults. Minimal studies on BCG vaccine have been published since the 1996 guidelines were released. Information is needed on product availability and administration instructions. Further guidance is needed on specific screening tests that would be needed to determine persons who are eligible for BCG vaccine, such as HIV testing, a complete patient history for other conditions with immune suppression, and testing to exclude LTBI and active TB.

Similar to the 1996 BCG guidelines, the updated recommendations would be released as a joint ACET/Advisory Committee on Immunization Practices (ACIP) statement. ACIP formed a small workgroup to review the BCG vaccine recommendations that were drafted by the ACET workgroup. During a recent conference call, however, the ACIP workgroup outlined several reasons for its strong reluctance to endorse the draft BCG recommendations.

BCG vaccine data are outdated and most likely will not be reanalyzed in a formal clinical trial in the near future. The recommendations were drafted with old data and limited experience of U.S. medical providers on this issue. This practice is not consistent with CDC policy for new guidance to be supported by strong and recent evidence. BCG vaccine is not readily available in the United States.

The ACIP workgroup informed the ACET workgroup that a thorough review of the BCG vaccine efficacy data would be required before a joint ACET/ACIP statement on the use of BCG vaccine for the prevention of TB in HCWs in high-risk situations overseas could be endorsed and released. The ACET workgroup agreed to provide the ACIP workgroup with the clinical trial data.

Additional details on efforts to revise the 1996 BCG vaccine guidelines were provided by other members of the ACET workgroup: Dr. Barbara Seaworth, chair of the workgroup and an ACET member; Dr. Naomi Aronson, ACET's *ex-officio* member for the Department of Defense; and Ms. Rachel Stricof, ACET's liaison member for the Association for Professionals in Infection Control and Epidemiology (APIC).

During the recent conference call, an ACIP workgroup member was in favor of conducting a clinical trial to collect additional data and inform future decisions on BCG vaccination. This suggestion could be supported by developing a form that would be completed by any individual who is vaccinated with BCG in the United States prior to travel overseas. The form would facilitate systematic follow-up of HCWs and other persons who are deployed to high-risk areas.

The ACET workgroup described possible reasons for the ACIP workgroup's reluctance in endorsing the draft BCG vaccine recommendations. The ACIP workgroup had limited knowledge and understanding of the actual risks, illnesses and deaths from MDR-/XDR-TB, LTBI and active TB when HCWs, volunteers and students are deployed to high-prevalence areas overseas. Despite the controversy with the draft BCG vaccine guidelines, CDC should encourage medical centers and humanitarian organizations to follow the guidance on pre-travel screening, education regarding fit-testing of masks and infection control while in-country, and post-travel evaluation.

ACET and ACIP have different missions. ACET provides evidence-based guidance on the elimination of TB, while ACIP provides evidence-based guidance on the use of vaccines. Although joint ACET/ACIP statements have been developed and released in the past, the difference in the missions of the two advisory groups served as a barrier to reaching agreement on revising the BCG vaccine guidelines. This problem might be resolved if the BCG vaccine guidelines are viewed as a guidance document for overseas travelers rather than as a formal ACIP recommendation on a vaccine that requires federal funding or guarantees third-party reimbursement.

The draft BCG vaccine guidelines were presented to and reviewed by an ACIP workgroup with four members rather than the full membership. Moreover, a decision has not been made on whether the HCW, travelers, pediatric or another ACIP workgroup should have responsibility for evaluating the draft BCG vaccine guidelines.

Dr. Castro advised ACET to reframe its entire approach in which BCG vaccination would serve as only one of several measures in the entire hierarchy of infection control precautions. The guidelines would place equal emphasis on pre-travel screening, education and post-travel evaluation. Dr. Castro also pointed out that ACET and ACIP might benefit from discussing infection control policies of other groups when individuals are deployed overseas. DTBE could ask Family Health International, Partners in Health, CARE, the President's Emergency Plan for AIDS Relief and similar organizations to provide feedback on this issue.

The ACET members made two key suggestions to assist the workgroup in revising the BCG vaccine guidelines. First, ACET should ensure that the recommendations are usable and actually will help HCWs and other overseas travelers. The guidelines should be structured to overcome the prevailing consensus in the United States that BCG vaccine has no value, merit or benefit to populations other than children.

Second, ACET could resolve the problem with ACIP by developing evidence-based guidance on the use of BCG for vaccinating HCWs and other overseas travelers. ACIP typically does not endorse recommendations with language to "consider or encourage the use of" a vaccine because this guidance does not result in payment.

ACET should present the evidence-based BCG recommendations to ACIP with a request to forward the guidance to appropriate workgroups, such as the HCW, adult immunization or

traveler's workgroup. This approach would allow ACIP workgroups to incorporate "consider or encourage the use of" language into their respective statements.

Dr. Fleenor confirmed that ACET would revisit this issue during its next meeting to determine whether the BCG vaccine guidelines should be released as a sole ACET guidance document or as a joint ACET/ACIP statement. In the interim, he asked the workgroup to discuss Dr. Castro's proposal to reframe the guidelines with BCG vaccination as only one measure in a set of infection control precautions. Dr. Fleenor agreed that less emphasis on BCG vaccine might facilitate ACIP's endorsement of the guidelines.

Update by the Isolation Guideline Workgroup

Dr. Sundari Mase, of DTBE, explained that ACET formed a workgroup in April 2008 to review the existing literature and make summary recommendations on the discontinuation of isolation for patients with MDR-TB. The ultimate outcome of this effort will be to develop national evidence-based guidelines. The workgroup members include DTBE staff, ACET members and external TB experts.

The workgroup acknowledged the clear public health importance for developing the guidelines. Transmission of MDR-/XDR-TB, particularly in institutional settings and to high-risk persons, continues to be a threat to communities across the world. Morbidity and mortality among individual TB patients who need treatment for 2-3 years with extremely toxic regimens have been documented. More resistant and deadly TB strains have emerged. Treatment of MDR-TB is extremely resource-intensive.

The workgroup's comprehensive literature review included an assessment of all national guidelines. For pan-sensitive disease, existing guidelines recommend adequate treatment for two weeks, three negative AFB smears and clinical improvement of the patient. For MDR-TB, existing guidelines recommend more caution and collection of AFB cultures as the gold standard. The guidelines also state that culture conversion could be considered as a goal for non-infectiousness of MDR-TB patients.

CDC and United Kingdom guidelines advise treating physicians to make judgments regarding MDR-TB patients, while the Canadian guidelines recommend airborne isolation of MDR-TB patients until three negative AFB cultures are collected. Both WHO and CDC air travel guidelines require two negative AFB cultures prior to commercial airline travel for MDR-TB patients.

The workgroup developed a list of questions to guide the development of the isolation guidelines. What evidence exists to support MDR-TB isolation guidelines? What evidence exists to support transmission of MDR-TB in different settings? What variables are associated with transmission? Does evidence exist on a duration of time to safely discontinue isolation

after initiation of appropriate treatment? Does evidence exist to support microbiologic criteria for isolation discontinuation?

The workgroup performed a narrative review that was adapted from a systematic review. Terms used in the review were both inclusive and specific. Multiple electronic databases were searched and primary reports with confirmed MDR-TB transmission were included in the review. Two reviewers independently selected reports for inclusion and discrepancies were resolved by consensus. Full-text English language articles were retrieved. Descriptive population-based and molecular epidemiology studies were noted, but were excluded from the final analysis due to the lack of specific data. Cost-analyses and review articles were excluded from the review as well.

A number of characteristics were reviewed in the studies, such as geographic locations and settings; recommendations regarding airborne infection isolation; AFB smear and culture results of source cases; HIV status of source cases and contacts; and genotyping and epidemiologic linkages. The workgroup acknowledges a number of limitations of the review. No studies directly addressed the relationship between different variables and transmission in the context of airborne isolation precautions. Only English language articles were included in the review. The narrative review was limited by existing articles and other data.

Of 720 potentially relevant citations that were initially identified, 250 duplicates were excluded. Of the 470 remaining citations, 282 were excluded based on a review of titles. Of 188 citations that were identified as relevant to MDR-TB transmission, 135 were excluded based on the inclusion criteria, such as non-English language articles and population-based, molecular or epidemiologic studies. Of 53 full-text articles that were screened, 28 were included in the review and 25 were excluded based on the inclusion criteria.

Of 28 articles included in the review, 64% reported transmission in a hospital or congregate setting, 29% reported community transmission, and 7% reported transmission in both settings. Isolation precautions were not initiated or reported in 82% of the articles. Transmission primarily occurred in facilities that did not initiate recommended isolation precautions. Of eight articles that reported MDR-TB treatment, none reported an association between treatment and transmission. Smear status of source cases was reported in 36% of the articles. Of the cases reported in these ten articles, 80% were smear-positive and 20% were smear-negative. Two articles reported transmission from smear-negative MDR-TB patients.

Cavitation was reported in 18% of the articles. Extent of disease was not reported in 86% of the articles. HIV status was reported in 46% of the articles. Transmission from both HIV-negative and HIV-positive patients was reported in these articles. Transmission of fluoroquinolone-resistant strains was reported in 18% of the articles. Confirmation of transmission was reported in 93% of the articles through genotyping and in 96% of the articles through epidemiologic links.

The workgroup reviewed two additional studies to gather further evidence on MDR-TB transmission. One study showed that transmission of TB from humans to guinea pigs occurred even after initiation of MDR-TB treatment, but not in pan-sensitive disease. Another study

showed that MDR-TB patients in South Africa on standardized treatment regimens remained highly infectious to guinea pigs for at least four months.

The workgroup's literature review confirmed that transmission of MDR-TB is occurring in both hospital and community-based settings. The failure to initiate airborne isolation precautions, particularly in institutional settings, was associated with transmission. Transmission occurred from both smear-positive and smear-negative patients. Data were limited on transmission sources, treatment regimens, culture status or the influence of other variables on transmission.

Culture negativity appeared to be the standard to characterize cases as non-infectious. The Canadian guidelines were found to be the most conservative and require three negative AFB cultures to discontinue isolation. The workgroup's literature review resulted in minimal evidence to inform the development of the isolation guidelines. Further research might be needed to determine factors that are associated with infectiousness. Existing policies and guidelines might serve as a basis for future studies.

After completing the literature review, the workgroup explored different options to develop the isolation guidelines. Option 1 would be to maintain the existing policy, but recommend the application of more stringent criteria to discontinue isolation of MDR-TB patients. The workgroup was not in favor of option 1.

Option 2 would be to develop setting-dependent recommendations with more stringent criteria in certain settings, such as returning to work, school, congregate or high-risk settings. Less stringent criteria would be recommended for other settings, such as discharge from the hospital to home isolation. Option 3 would be to require three negative AFB cultures for discontinuation of airborne isolation precautions in all settings. The workgroup agreed was not in favor of option 3.

The workgroup explored option 2 in further detail. On the one hand, more stringent criteria would be beneficial in addressing a number of public health problems. Transmission has been documented in hospital, congregate and community settings. Both public health and individual impacts of transmission of highly drug-resistant strains of TB are significant. Treatment and containment of MDR-TB are resource-intensive. Escalation of drug resistance is a threat to global and national TB control efforts.

On the other hand, more stringent criteria would lead to hardships to patients and their families. The potential for and impact of transmission in a hospital setting would be greater. Isolation in a hospital setting is resource-intensive. MDR-TB strains are "less fit." Many individuals oppose hospitalizing MDR-TB patients for 4-5 months to await culture conversion.

The workgroup's draft recommendations are outlined as follows. Smear-positive or smear-negative MDR-TB patients should be hospitalized at diagnosis for the purpose of isolation in two situations. The patient lives with high-risk persons at home, such as small children <5 years of age and immunocompromised persons on tumor necrosis factor-alpha blockers and those with HIV, end-stage renal disease or cancer. The patient lives in a congregate setting, such as a

skilled nursing facility, long-term care facility, correctional institution without adequate isolation capability or a homeless shelter.

Hospitalized patients should be discharged to home isolation when the home environment is stable and no high-risk persons or previously unexposed persons, regardless of risk status, are present. Airborne isolation precautions should be discontinued while the patient remains in the hospital in the following situations: (1) adherence to an adequate MDR-TB regimen tailored to susceptibility results; (2) clinical improvement with resolution of cough; (3) smear-negative and three negative cultures read at three weeks; and (4) confinement of the patient to a private room until culture-negative if possible.

Patients should be discharged from either hospital or home isolation to the community in the following situations: (1) adherence to an adequate MDR-TB regimen tailored to susceptibility results; (2) clinical improvement with resolution of cough; and (3) smear-negative and three negative cultures read at three weeks.

More caution should be taken and more stringent criteria should be used in special situations, such as persons with no previous exposure to the MDR-TB patient, immunocompromised patients, patients who are still symptomatic despite three negative cultures over three weeks, patients with extensive or cavitary disease at diagnosis, unclear ability to achieve isolation, a virulent strain with transmission, HCWs returning to a neonatal intensive care unit or other high-risk setting, and XDR-TB patients, particularly those who are incurable.

The workgroup acknowledges the need to obtain input on the draft recommendations from NTCA, MDR-TB experts, state and local TB programs, pediatric TB experts and other key stakeholders after ACET's discussion. The draft recommendations will be revised based on input from stakeholders and presented to DTBE leadership. The workgroup expects to formulate the isolation guidelines by June 2009.

ACET made a number of suggestions for the workgroup to consider during its ongoing effort to refine the isolation guidelines.

- The recommendations to discharge hospitalized patients to home isolation and from either the hospital or home isolation to the community are the same. However, a clear distinction should be made between these two recommendations with language to "carefully evaluate the work, school or other community environment of the patient."
- The recommendations are not based on sound data. Most notably, strong evidence has not been collected to date to support the current practice of isolating MDR-TB patients for two weeks. The allocation of program resources to isolate MDR-TB patients for 4-5 months would be extremely difficult to justify without a solid scientific basis.
- The recommendations should acknowledge patients who are smear-positive/culture negative.
- Specific intervals of time should be suggested for the recommendation to read smear-negative and three negative cultures within three weeks, such as "three consecutive days."

- ACET and NAACHO should jointly administer a national survey to determine standard practices in applying legal authorities to discontinue isolation of MDR-TB patients at the local level. The survey results should be summarized and widely distributed to assist local jurisdictions in making decisions regarding isolation.
- CDC should administer a survey to all states to identify specific locations to place MDR-/XDR-TB patients on treatment until cured. This information is a critical need because MDR-/XDR-TB patients who committed no crimes have been isolated in U.S. detention/correctional facilities as "inmates."
- The recommendation to discharge patients to home isolation should include language for public health departments to perform psychosocial and medical assessments. The evaluations would provide helpful information on the willingness, ability, behaviors, social factors, medical needs and other characteristics of the patient to comply with home isolation.
- The recommendations should clearly distinguish between the "isolation" and "discharge" components of the guidelines because these two issues are entirely different. Isolation focuses more on treatment of the patient, while discharge focuses more on potential transmission to the community.
- The isolation guidelines should not address XDR-TB due to its significant difference with MDR-TB. XDR-TB patients should remain isolated out of the home until culture-negative results are collected.
- The workgroup should engage APIC as another key stakeholder to provide input on the isolation guidelines.
- The recommendations on isolation of MDR-TB patients in detention/correctional facilities should be placed in a separate section of the guidelines to highlight the unique nature of this setting. For example:
  - The recommendation to hospitalize MDR-TB patients at diagnosis in detention/correctional facilities should not be limited to settings without isolation capability. This language might cause facilities with adequate isolation capability to ignore the guidance.
  - The guidelines should address patients in detention/correctional facilities or other congregate settings who are released from isolation and are later found to have MDR-TB based on culture results. The guidelines should recommend placing these individuals back in isolation.

Dr. Fleenor confirmed that updates by the workgroup in developing guidelines to discontinue isolation of MDR-TB patients would be an ongoing agenda item.

Update on After-Action Reports (AARs)

Ms. Ann Cronin, of DTBE, reported on the outcomes of AARs involving travelers with TB. The GAO, HSC and CDC AARs all focused on a TB patient who traveled by air from Atlanta to Europe and Canada. The GAO AAR also addressed a TB patient who traveled by land between the United States and Mexico. GAO conducted its AAR by interviewing DHS and HHS

staff and reviewing documents submitted by both agencies. GAO concluded that the lack of coordination and procedures between DHS and HHS resulted in delays of the overall response.

HSC evaluated the incident from a disease transmission perspective and questioned the outcomes if a bioterrorism or naturally occurring disease threat crossed the border. HSC conducted its AAR by attempting to identify the root cause of challenges to the response. HSC documented the unusual and unprecedented nature of the incident. CDC evaluated the incident from the perspectives of emergency operations, privacy and public health issues, assistance to state and local health departments, and transmission of disease across borders. CDC conducted its AAR by focusing on actual actions that were taken in the field during the incident.

GAO made the following recommendations in its AAR. DHS should enhance capacity to search for TB patients in its computer system with names and dates of birth. DHS and HHS should inform state and local health officials about new tools and procedures to locate TB patients. DHS and HHS should develop and issue a joint strategy for completion of coordination plans.

HSC listed 22 corrective actions in its AAR. Most notably, education and outreach should be enhanced to state and local partners. Guidance for state and local legal authorities should be refined. Standard operating procedures should be developed for the containment of persons who pose a health threat. The International Health Regulation notification procedures should be modified.

CDC outlined 38 tasks in its AAR to improve readiness. Most notably, investments in rapid TB diagnostic testing should be accelerated. Public health laboratory capacity should be assured in all jurisdictions. A mechanism should be developed with greater flexibility to use diagnostic tests. Standard operating procedures for laboratories should be created.

CDC has completed a number of activities in response to the AARs of travelers with TB. An algorithm was developed to ensure infectious TB patients do not board aircraft. DNB restrictions were published in the September 19, 2008 edition of the *MMWR*. An expert panel formally evaluated implementation of the 2007 TBTIs for TB screening in the Philippines.

ACET Business Session

Dr. Fleenor announced that he wrote two letters to Dr. Gerberding in August 2008 regarding formal resolutions ACET passed during its June 2008 meeting: unintended consequences of the Paperwork Reduction Act as well as funding and expedited implementation of currently available drug resistance assays. Both letters were distributed to ACET for review.

Dr. Fleenor led ACET in a review of the business items that required formal or informal action.

ISSUE 1: Dr. Fleenor entertained a motion for ACET to approve the previous meeting minutes. Drs. Castro and William Baine, ACET's *ex-officio* member for the Agency for Healthcare Research and Quality, submitted two changes into the record:

- Page 4: Change the second sentence under the "DTBE Director's Report" as follows: "The ACET BCG Workgroup initiated discussions with the CDC Advisory Committee on Immunization Practices (ACIP) to develop joint *Guidelines on the Role of BCG Vaccine in the Prevention and Control of TB in Healthcare Workers Traveling to High-Risk Areas*."
- Page 9: Add a new paragraph after Dr. Baine's existing comments: "Dr. Baine also urged ACET to advocate, encourage and promote wider performance of acid-fast smears, in full compliance with CLIA, as a targeted screening test on unconcentrated sputum by clinical laboratories that perform gram-staining of sputum specimens, but refer processing for mycobacteriology, including microscopy on concentrated sputum, to reference laboratories."

A motion was properly placed on the floor and seconded by Mr. Kinney and Ms. Taylor, respectively, for ACET to accept the previous minutes with the changes Drs. Castro and Baine submitted into the record. ACET **unanimously approved** the June 17-18, 2008 Draft Meeting Minutes as amended with no further discussion.

ISSUE 2**.** Dr. Fleenor returned to Dr. LoBue's proposal for ACET to serve as a peer reviewer of DTBE's intramural program and research activities. A motion was properly placed on the floor and seconded by Drs. Burman and Seaworth, respectively, for ACET to undertake this effort. ACET **unanimously agreed** to serve as the peer reviewer of DTBE's intramural program and research activities.

ISSUE 3**.** Dr. Baine asked ACET to formally approve a recommendation for technicians in CLIA-approved laboratories who perform gram-staining to also perform AFB smears. He made a number of comments to support his request. The capacity of small community hospitals that only perform gram-staining of sputum specimens should be expanded to include AFB smears on unconcentrated specimens as a targeted screening test whenever the possibility of TB is present. Negative and positive specimens should be referred to reference mycobacteriology laboratories for concentrated smear and culture testing.

Hospitals should perform direct specimen examination by microscopy with gram, methylene blue, Wright, acid-fact or other stains on specimens from patients under their care in the context of clinical evaluation without requiring compliance with CLIA when the examination is not billed as a separate service.

ACET agreed that Dr. Baine's proposal could avoid isolation or expedite the release of TB patients from isolation, but several members did not support placing a formal motion of the floor.

- Small community hospitals do not have adequate capacity, sufficient personnel or 24-hour access to certified laboratory technicians to perform and read AFB smears.
- The number of fields that would need to be read for unconcentrated smears has not been determined.
- Studies have demonstrated that unconcentrated smears are less sensitive than concentrated smears. Many clinicians have limited knowledge of the difference between

concentrated and unconcentrated smear results and might inappropriately use this information.
- The value of small community hospitals in performing AFB smears has not been documented.

None of the voting members placed a motion on the floor to formally approve Dr. Baine's proposal. Dr. Baine confirmed that he would clarify his proposal during the next meeting and again ask for ACET's formal approval.

***ISSUE 4*:** Dr. Fleenor returned to Dr. Vernon's request for ACET's formal action on CDC's revision of the 2005 IGRA guidelines. He summarized the key points of this issue based on ACET's discussion. Research should be increased to determine the positive predictability of IGRAs for future TB disease and the effect of PPD boosting on IGRA positivity.

CDC is considering postponing the December 2008 *MMWR* publication of the updated IGRA guidelines to allow more time for ACET, NTCA and other stakeholders to review the document. However, the publication should not be postponed because TB controllers are in critical need of the guidelines at this time. Moreover, a delay of the December 2008 publication would affect the timeline for the release of the ATS/CDC/IDSA Diagnostic Guidelines.

A motion was properly placed on the floor and seconded by Drs. Burman and Narita, respectively, for ACET to form a workgroup to conduct an in-depth review of CDC's updated IGRA guidelines in advance of the next ACET meeting. ACET **unanimously approved** the motion.

Dr. Fleenor summarized the process for ACET to undertake this effort. Dr. Narita will chair the new IGRA Workgroup; Mr. Griffin and Drs. Bakhtawar and Burman will serve as members. The updated IGRA guidelines and the workgroup's comments on the document will be shared with the entire ACET membership for feedback. ACET will take a formal vote on the updated IGRA guidelines during the next meeting.

Dr. Narita will closely collaborate with Dr. Fleenor and Ms. Margie Scott-Cseh, the Committee Management Specialist for ACET, to schedule conference calls and disseminate materials. DTBE will submit the updated IGRA guidelines to the CDC clearance process in December 2008 in conjunction with the workgroup's deliberations.

***ISSUE 5*:** Dr. Charles Wallace, ACET's alternate liaison member for the International Union Against Tuberculosis and Lung Disease-North American Region, asked ACET to formally approve the following recommendation. DTBE should formally establish a cap on indirect rates for cooperative agreements that involve TB prevention/control, laboratories and RTMCCs.

Dr. Fleenor pointed out that ACET's discussion on Dr. Wallace's proposal primarily focused on indicators to measure the performance of TB cooperative agreement grantees. He clarified that indirect rates are completely separate from performance indicators and only apply to the overall cost and expenses for grantees to operate a project under a cooperative agreement.

Dr. Fleenor also noted that several ACET members were in favor of modifying the "MDR-TB" definition to increase the 5% allocation in the TB funding formula and reflect the actual workloads of programs. The new definition would include patients with MDR-TB or those who are "MDR-equivalent." Because performance indicators for TB cooperative agreement grantees and a modification of the "MDR-TB" definition were new business items, Dr. Fleenor confirmed that these topics would be placed on the next ACET agenda for further discussion.

A motion was properly placed on the floor and seconded by Dr. Burman and Mr. Jones, respectively, for ACET to urge DTBE to formally establish a cap on indirect rates for cooperative agreements that involve TB prevention/control, laboratories and RTMCCs. ACET **unanimously approved** the motion.

ACET proposed an indirect rate cap of 8%-10%, but emphasized that the DTBE should make the final decision. ACET also clarified that jurisdictions with lower indirect rates than the new cap should be required to maintain their current rates. Dr. Theresa Watkins-Bryant, ACET's *ex-officio* member for HRSA, would provide Dr. Castro with language on HRSA's indirect rate cap of 10% to use as a model.

***ISSUE 6*.** Dr. Fleenor returned to Dr. Shinnick's request for ACET to formally adopt three revisions to the CDC NAAT guidelines that were suggested by an expert panel.

1. All U.S. clinicians and public health TB programs should have timely access to molecular tests to aid in the diagnosis of TB.
2. NAATs for the diagnosis of TB should become standard practice for TB suspects.
3. NAATs should be performed on at least one respiratory specimen from each patient with signs and symptoms of active pulmonary TB for whom a diagnosis of TB is being considered (*i.e.*, a TB suspect), but has not been established.

Dr. Fleenor noted that during the discussion, ACET was in favor of suggestions 1 and 2, but several members expressed reservations regarding suggestion 3. To advance ACET's formal action on this issue, he entertained a motion for ACET to formally adopt suggestions 1 and 2 only.

A motion was properly placed on the floor and seconded by Drs. Narita and Bakhtawar, respectively, for ACET to adopt suggestions 1 and 2 regarding CDC's NAAT guidelines. **The motion passed by a majority vote with 1 member opposed.**

A motion was properly placed on the floor and seconded by Drs. Seaworth and Narita, respectively, to include a modified version of suggestion 3 with suggestions 1 and 2. NAATs should be performed on at least one respiratory specimen from each patient with signs and symptoms of active pulmonary TB for whom a diagnosis of TB is being considered (*i.e.*, a TB suspect), but has not been established and for whom the result would influence the management of the patient. **The motion did not pass.**

A motion was properly placed on the floor and seconded by Dr. Seaworth and Ms. Taylor, respectively, to include the original suggestion 3 with suggestions 1 and 2. Several ACET

members pointed out that suggestion 3 is an unfunded mandate and would be extremely difficult for programs to implement. Moreover, NAATs are not practical to perform on all smear-negative patients. **The motion narrowly passed by a majority vote of 4 in favor and 3 opposed.**

***ISSUE 7*:** Dr. Fleenor returned to Dr. Goodman's request for ACET to suggest strategies to disseminate the TB legal preparedness materials. NTCA and NACCHO made commitments to distribute the materials. Suggestions by other ACET members on additional dissemination venues would be submitted to Mr. Kinney due to his role as the ACET liaison to the TB Legal Preparedness Workgroup. CDC noted ACET's request to extend the deadline for the submission of comments on the TB model act from November 30 to mid-December 2008.

***ISSUE 8*:** Dr. Fleenor led ACET in a review of future agenda items that were raised over the course of the meeting.

- Presentation by NIH and CDC regarding coordinated interagency TB research.
- Overview of pediatric TB treatment studies, including a description of unmet needs regarding TB drug development in children.
- Updates by ACET's African American, Foreign-Born, BCG, and Isolation Guideline Workgroups.
- Proposals by DTBE on two new business items: performance indicators for TB cooperative agreement grantees and modification of the "MDR-TB" definition in the TB funding formula.

Public Comment Session

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

Closing Session

The next ACET meeting would be held on either February 17-18 or March 17-18, 2009, but the majority of members expressed a preference for the February date.

With no further discussion or business brought before ACET, Dr. Fleenor adjourned the meeting at 2:23 p.m. on October 8, 2008.

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

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Date

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