

**U.S. 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



**Meeting of the
Advisory Council for the Elimination of Tuberculosis
December 2-3, 2014
Atlanta, Georgia**

Record of the Proceedings

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**ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
December 2-3, 2014
Atlanta, Georgia**

Minutes of the Meeting

The U.S. 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 December 2-3, 2014 in Building 8 of CDC's Corporate Square Campus, Conference Room A/B/C, in Atlanta, Georgia.

ACET is chartered to provide advice to the Secretary of HHS and the Director of CDC regarding the elimination of tuberculosis (TB); make recommendations regarding policies, strategies, objectives and priorities; address the development and application of new technologies; provide guidance on CDC's TB Prevention Research portfolio and program priorities; and review the extent to which progress has been made toward eliminating TB.

Opening Session: December 2, 2014

Hazel Dean, ScD, MPH

Deputy Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
ACET Designated Federal Officer (DFO)

Dr. Dean conducted a roll call to determine the ACET voting members, *ex-officio* members and liaison representatives who were attending the meeting either in person or remotely. She announced that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record.

Dr. Dean reminded the ACET voting members of their responsibility to disclose any potential individual and/or institutional conflicts of interest for the public record and recuse themselves from voting or participating in these matters.

CONFLICT OF INTEREST DISCLOSURES	
ACET Voting Member (Institution/Organization)	Potential Conflict of Interest
Ana Alvarez, MD, FAAP (University of Florida College of Medicine)	No conflicts disclosed
Lisa Armitige, MD, PhD (Heartland National Tuberculosis Center)	No conflicts disclosed
Jennifer Cochran, MPH (Massachusetts Department of Public Health)	No conflicts disclosed
Barbara Cole, RN, MSN, PHN (Riverside County Department of Public Health)	No conflicts disclosed
Susan Dorman, MD (Johns Hopkins University School of Medicine)	No conflicts disclosed
Robert Horsburgh, Jr., MD, MUS (Boston University School of Public Health)	No conflicts disclosed
Eric Houpt, MD (University of Virginia)	No conflicts disclosed
Michael Lauzardo, MD, MSc (University of Florida College of Medicine)	Recipient of federal funding from CDC for the Southeastern National Tuberculosis Center, a Regional Training and Medical Consultation Center (RTMCC)
James Sunstrum, MD (Wayne County, Michigan TB Clinic)	No conflicts disclosed
David Warshauer, PhD (Wisconsin State Laboratory of Hygiene)	No conflicts disclosed

Dr. Dean announced that the voting members and *ex-officio* members in attendance constituted a quorum for ACET to conduct its business on December 2, 2014. She called the proceedings to order at 8:38 a.m. and welcomed the participants to day 1 of the ACET meeting. Dr. Dean noted the temporary and permanent changes to ACET's membership.

- Biographical sketches of five new ACET members were included in the meeting packets:
 - Lisa Armitige, MD, PhD; Medical Consultant, Heartland National TB Center
 - Eric Houpt, MD; Professor, Division of Infectious Diseases and International Health, University of Virginia
 - Michael Lauzardo, MD, MSc; Chief, Division of Infectious Disease and Global Medicine, University of Florida College of Medicine
 - James Sunstrum, MD; TB Consultant, Wayne County TB Clinic
 - David Warshauer, PhD; Deputy Director, Communicable Disease, Wisconsin State Laboratory of Hygiene
- Dr. Shama Ahuja has replaced Dr. David Trump as the liaison representative for the Council of State and Territorial Epidemiologists.
- Dr. Michael Bartholomew would serve as the *ex-officio* member for the Indian Health Service in the absence of Dr. Susan Karol.
- Ms. Marla Clifton would serve as the *ex-officio* member for the Department of Veterans Affairs in the absence of Dr. Gary Roselle.
- CDR Edward Chin has replaced Ms. Tiffany Moore as the *ex-officio* member for the United States Marshals Service.
- Mr. Kenyon Farrow would serve as the liaison representative for the Treatment Action Group in the absence of Ms. Colleen Daniels.
- Dr. Ameer Patrawalla has replaced Dr. Lee Reichman as the liaison representative for the American College of Chest Physicians.
- Dr. Chana Rabiner has replaced Dr. Warren Hewitt as the *ex-officio* member for the Substance Abuse and Mental Health Services Administration.
- Dr. Susan Robilotto and Ms. Marlene Matosky would serve as alternate *ex-officio* members for the Health Resources and Services Administration (HRSA) HIV/AIDS Bureau in the absence of Dr. Rupali Doshi.

Dr. Dean asked the participants to join her in welcoming the new members, *ex-officio* members and liaison representatives to their first ACET meeting.

Barbara Cole, RN, MSN, PHN, ACET Chair

TB Controller

Riverside County (California) Department of Public Health

Ms. Cole joined Dr. Dean in welcoming the participants to day 1 of the ACET meeting. She explained that ACET would continue to address issues related to TB elimination. She thanked the ACET members for contributing their valuable time and expertise to assist CDC in achieving this important national goal.

NCHHSTP Office of Director's Report

Hazel Dean, ScD, MPH

Deputy Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
ACET Designated Federal Officer (DFO)

Dr. Dean covered the following topics in the NCHHSTP Office of Director's (OD) report to ACET. At the agency level, CDC, other U.S. government agencies, the World Health Organization (WHO) and international partners are continuing their response to the rapidly changing ebola outbreak in West Africa. The ebola outbreak is the largest outbreak of this disease in history and has accounted for 5,689 deaths to date.

As of December 1, 2014, 10,050 of the total 15,935 ebola virus disease cases were laboratory-confirmed. Guinea, Liberia and Sierra Leone have accounted for the vast majority of cases. The deployment of 259 CDC staff as of December 1, 2014 includes 89 staff throughout the United States, 2 staff to other countries with reported ebola cases, and 168 staff to West Africa for surveillance, contact tracing, data management, laboratory testing and health education. CDC also activated its Emergency Operations Center to coordinate ebola-related assistance with partners.

CDC is operating under a continuing resolution that authorizes FY2015 appropriations through December 11, 2014 at the FY2014 enacted levels. The continuing resolution also provides additional funding to support the ebola outbreak response in Africa, including \$30 million to CDC's global health programs.

CDC established a new Laboratory Safety Improvement Workgroup in July 2014 that will be responsible for specific tasks. The moratorium on the movement of biological material outside of Biosafety Level 3 and 4 Laboratories will be addressed. The CDC Director will be advised on the resumption of transfers. To date, 49 packages have been submitted for review of the moratorium on laboratory safety, 33 packages have been released, 12 packages have been released with provisions, 3 packages are under review, and 4 packages are pending submission.

Laboratory safety recommendations will be implemented to address recent laboratory incidents at CDC. Oversight will be provided of corrective actions and an inventory of biologic material in all CDC laboratories (*i.e.*, a "Clean Sweep"). Recommendations will be developed to establish a permanent single point of accountability for laboratory safety. CDC recently released a job posting for a new Associate Director for Laboratory Science.

The workgroup primarily will focus on two major aspects of laboratory safety. First, the use of protocols for key control points (e.g., pathogen inactivation) by trained and supervised staff will be demonstrated. Second, redundant control/secondary verification of critical control points will be established via direct observation by supervisors or staff and critical actions recorded on camera.

At the National Center level, NCHHSTP is pleased to announce changes in its leadership at the OD level. Dr. Philip LoBue was appointed as the new Director of the Division of Tuberculosis Elimination. Dr. Eugene McCray was appointed as the new Director of the Division of HIV/AIDS Prevention (DHAP). Dr. Richard Wolitski was appointed as the new Senior Advisor for Indicator Monitoring and Program Improvement.

NCHHSTP deployed >125 staff to the ebola response over the past few months, including >40 staff to Africa. All NCHHSTP laboratories currently are active due to the release of three of its laboratories from the moratorium on the movement of biological material.

NCHHSTP established three goals for its draft 2020 Strategic Plan. The incidence of infection, morbidity and mortality, and health disparities across affected groups will be decreased for HIV, viral hepatitis, STDs and TB. Efforts are underway to develop indicators, targets and strategies to measure progress on achieving the Strategic Plan goals. NCHHSTP expects to finalize the draft Strategic Plan early in 2015.

NCHHSTP published the latest edition of its State Health Profiles. NCHHSTP launched a new policy web page for TB, HIV and STD prevention programs. The new web page serves as a “one-stop shop” with tools and resources of legal assessments across all of NCHHSTP’s focus areas. NCHHSTP hosted a Program Collaboration and Service Integration training session for public health officials in the U.S.-Affiliated Pacific Islands. This event provided a platform to build capacity in these resource-limited areas.

DTBE Director’s Report

Philip LoBue, MD

Director, Division of Tuberculosis Elimination
Centers for Disease Control and Prevention

Dr. LoBue focused his Director’s report to ACET on strategies for TB elimination in the United States. Since systematic recording of TB began in 1953, 2013 marked the fewest number of cases reported (9,582) and the lowest TB case rate (3.0/100,000). However, a tremendous gap still exists between current TB morbidity and the elimination goal of ~300 cases (or a case rate of <0.1/100,000).

The key risk groups for TB have remained the same for over 10 years. Foreign-born persons (FBPs) account for 63% of TB cases and have a case rate that is 11 times higher than in U.S.-born persons. China, India, Mexico, the Philippines and Vietnam account for the top five countries of the TB burden in FBPs. Racial/ethnic minorities account for 84% of TB and have a case rate that is 7-17 times higher than in whites. Other key risk groups for TB include HIV-infected persons (~7%), homeless persons (~6%), incarcerated persons (~4%), and substance abusers (7%-12%).

CDC identified several challenges to reaching the national TB elimination goal. Political commitment has weakened as the number of cases continues to decrease. Resources are at risk because TB is less of a priority to policymakers and the general public. Clinical, laboratory and public health expertise and experience have been lost.

Drug and biologic shortages are more problematic due to the lack of a market. Regulatory requirements limit access to the Global Drug Facility (GDF) or other mechanisms for the larger global market. Efforts are concentrated to the remaining cases and outbreaks in more difficult-to-reach populations (e.g., FBPs and homeless persons). Latent TB infection (LTBI) accounts for <10,000 TB cases, but the large pool of 11 million persons with LTBI needs to be addressed.

The recent Hill study modeled TB trends in the United States and described actions that would need to be taken to reach the TB elimination goal of <1 case/1 million population. The study showed that combining the two strategies of decreasing the LTBI prevalence among FBPs entering the United States and substantially increasing LTBI treatment would nearly reach the TB elimination goal.

CDC's position is that the 2000 Institute of Medicine (IOM) Report, *Ending Neglect: The Elimination of Tuberculosis in the United States*, still should guide current TB elimination efforts. CDC's response to the report included six fundamental goals that are elements of a national elimination strategy. Dr. LoBue described newer approaches CDC is considering to achieve the six TB elimination goals since the release of the IOM Report nearly 15 years ago.

Goal 1 is to maintain control of TB. Efforts for complete and rapid detection of persons with active TB disease are successful in the United States because all cases ultimately are located. Gene Xpert and other new technologies can assist in minimizing delays in case detection. Clinical decision support tools and other educational efforts also can help primary providers to "think TB" and order diagnostic tests for suspected cases. A new, innovative approach would be to develop a multiplex test for TB and other respiratory infections that would not require providers to order a separate TB test.

Current TB treatment is adequate to maintain high treatment completion rates among persons with active disease. Shorter-course regimens are now being studied and would be particularly beneficial in lowering costs. Several TB programs are using more efficient and effective video and wireless technologies to substantially decrease the cost of directly observed therapy (DOT).

However, CDC acknowledges that a large, rigorous evaluation study is needed before definitive recommendations can be made on the use of these technologies.

Investigation, appropriate evaluation and treatment of contacts of infectious TB cases will continue to be important to goal 1 because up to 1%-2% of contacts have active disease. The ability to detect and treat LTBI is limited because the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) poorly predict persons who will develop TB in the future. The specificity of IGRAs is weaker in some low-risk populations, but IGRAs are more beneficial in FBP with Bacillus Calmette-Guérin (BCG) vaccination because only one visit is required. Short-course regimens will provide greater opportunities to improve treatment, such as the 3-month, once-weekly Isoniazid/Rifapentine (3HP) regimen and the 4-month Rifampin regimen.

Infection control measures have been effective in preventing transmission of TB in the United States, particularly in healthcare settings. Healthcare-associated outbreaks of TB have not been reported since the 1990s, but more focus is needed on infection control and prevention measures in homeless shelters and correctional facilities. These settings account for most of the recent TB outbreaks. Initiatives to improve infection control standards in these settings include the DTBE Homeless Workgroup, the ACET and DTBE Corrections Workgroups, and DTBE's ongoing collaboration with the Interagency Council on Homelessness.

Goal 2 is to accelerate the decline of TB. The primary focus should be placed on FBPs from medium- and high-incidence countries to improve targeted testing and treatment of persons with LTBI. Because this pool of persons is extremely large and resources are limited, efforts initially should be targeted to the high priority subpopulation of FBPs who have the greatest risk of progression to active disease (e.g., FBPs with HIV or diabetes, FBPs who smoke, and FBPs on immune-suppressing drugs). IGRAs should be used in BCG-vaccinated FBPs, while short-course regimens should be used in all persons with LTBI to increase completion rates.

Due to limited resources that are not expected to increase in the near future, testing and treatment should be expanded beyond health departments. CDC has identified three potential strategies in this effort: (1) leverage resources from the Affordable Care Act (ACA); (2) conduct LTBI testing in primary care settings for at-risk groups and obtain reimbursement for this service based on a U.S. Preventive Services Task Force (USPSTF) Grade A or B recommendation; and (3) scale-up successful program models that have identified and extensively engaged service providers of target populations in the community.

CDC-funded RTMCCs can continue to be used to assure appropriate regionalization of TB control activities. CDC is developing a Laboratory Center of Excellence to increase the availability of high-quality drug susceptibility testing, particularly in low-incidence jurisdictions that cannot maintain proficiency. Genotyping is nationalized and completed by one laboratory for the entire country. Legal and practical challenges will need to be addressed to expand regional approaches when the number of TB cases decline even further.

Rapid outbreak response is essential to interrupt transmission of TB. Homeless persons, substance abusers and incarcerated persons account for the vast majority of recent outbreaks. Universal genotyping has facilitated earlier recognition of TB transmission and earlier response to outbreaks because alerts have been incorporated into the genotyping database. More knowledge and understanding of predictors of the growth of TB clusters have increased the ability to prioritize clusters and more rapidly respond to outbreaks. However, implementation of infection control and prevention measures in homeless and correctional settings needs tremendous improvement.

Goal 3 is to develop new tools for the diagnosis, treatment and prevention of TB. Efforts are underway to identify the most effective approaches to implement new tools: IGRAs, Gene Xpert, the feasibility of overcoming barriers to DOT in order for patients to self-administer 3HP, the role and utility of whole-genome sequencing in genotyping, molecular detection of drug resistance for other drugs beyond Gene Xpert, and Bedaquiline (BDQ) and Delamanid for multidrug-resistant-TB (MDR-TB).

New drugs and regimens are in various stages of development, including 4-month shorter-course regimens for drug-susceptible TB, a 9-month regimen for MDR-TB, and new tests for diagnosis and detection of drug resistance. Despite these advances, basic research funded by the National Institutes of Health (NIH) and Gates Foundation is needed to achieve broader, more transformative changes.

- An LTBI test that is highly predictive of persons who would progress to active TB disease
- Inexpensive and simple point-of-care tests to diagnose TB disease and detect drug resistance, particularly for global TB control
- Ultra-short regimens with a duration of no more than 4 weeks for TB disease and LTBI treatment to increase completion rates to nearly 100% and reduce cost
- A highly effective TB vaccine

Goal 4 is to reduce the global burden of TB by increasing U.S. involvement in international TB control activities. Support should continue to be provided to WHO and other global or multilateral organizations in developing evidence-based policy. Strategic partnerships should be established with individual countries. Emphasis should be placed on countries that overlap in terms of their high TB burden and significant contributions to domestic TB cases among their immigrants who enter the United States. A transition should be made from short-term projects that originate from CDC in Atlanta to longer-term, in-country technical assistance to increase impact. The strong focus on TB drug resistance and HIV should continue due to their greater role globally.

CDC's current overseas screening program of persons entering the United States has been extremely effective in detecting and treating TB disease in permanent immigrants and refugees. Most foreign-born TB cases occur from reactivation of LTBI after their residence in the United

States for several years. CDC is considering the feasibility of incorporating LTBI testing and treatment with short-course regimens into the current overseas screening program and expanding screening to include other long-term visitors (e.g., students and work visa recipients).

Goal 5 is to mobilize and sustain support for TB elimination by engaging policy and opinion leaders, healthcare providers, affected communities and the general public. CDC will enhance its existing partnerships with both domestic and international organizations to ideally increase support for TB elimination. CDC currently is conducting a “cases-averted” analysis to make a stronger argument. For example, >200,000 TB cases have been averted since the response to the TB resurgence in the 1980s-1990s. Other initiatives CDC is considering to increase support for TB elimination include quantifying cost-savings and benefits, documenting the return on investment, and conveying powerful stories from individual TB patients.

Goal 6 is to monitor progress toward reaching the TB elimination goal and regularly report on progress to all target audiences. CDC currently uses outcome and process measures in the National Tuberculosis Indicators Project to track overall progress, but improvements will be made in the future to better evaluate individual TB elimination projects and programs. The performance of funded TB programs and laboratories will be assessed on a regular basis. The DTBE Research Workgroup recommended periodic internal and external reviews of research projects. Approaches are needed to compile key outcomes from these evaluation processes to demonstrate improvement. The National TB Program objectives and performance targets for 2015 were displayed for ACET’s review.

Dr. LoBue concluded his update by summarizing the five key strategies for TB elimination in the United States.

1. *Sustain commitment*
 - Utilize critical partnerships
 - Make a strong argument by documenting the return on investment and conveying stories of persons affected by TB
2. *Maintain basic TB control functions*
 - Improve the effectiveness and efficiency of TB case finding and treatment, contact investigations and infection control
3. *Expand effective LTBI testing and treatment*
 - Broaden efforts beyond health departments
 - Target FBPs as a high priority population
 - Implement new TB regimens and tools
4. *Strategically engage in global TB efforts*
 - Maximize the impact of limited resources because the national TB elimination goal cannot be achieved without more progress globally

5. *Minimize the difficulties and complexities associated with TB control*

- Promote and take advantage of scientific and technological advancements

ACET agreed with Dr. LoBue that three key areas must be prioritized in order to achieve the TB elimination goal in the United States: TB in FBP, TB in correctional settings, and global TB efforts. ACET discussed the following topics with Dr. LoBue in this regard.

- The need to revise strategy 4 to describe funding and other efforts by CDC and its partners in the Global TB Strategic Plan.
- The extent to which TB elimination continues to be a “motivational” or “inspirational” factor for the nation.
- The need to shift messaging to focus more on the larger pool of 11 million persons with LTBI rather than the smaller number of <10,000 TB cases attributed to LTBI.
- The role of ACA in TB elimination.
- CDC’s rationale for not finalizing, clearing and releasing ACET’s Foreign-Born TB Guidelines.
- CDC’s difficulties in updating the Report of Verified Case of Tuberculosis.
- The need to build strong relationships with diabetes national organizations and engage these groups as key partners in TB elimination, particularly since current diabetes guidelines do not mention TB and diabetes/TB co-infection is as high as 15% in some jurisdictions.

Overview of NCHHSTP’s Health Equity Activities

Wayne Duffus, MD, PhD

Associate Director for Health Equity

National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention

Centers for Disease Control and Prevention

Advice Requested from ACET by the NCHHSTP Office of Health Equity (OHE):

- What are the essential issues for TB elimination that should be considered when developing training and educational materials aimed at increasing knowledge of health equity concepts?
- What key issues other than funding should be addressed to achieve health equity for TB elimination at state and local levels?
- What specific strategies should be operationalized to achieve health equity for TB elimination?

Dr. Duffus presented an overview of NCHHSTP's health equity activities. NCHHSTP's vision is "a future free of HIV, viral hepatitis, STDs and TB" and its mission is to save lives, protect individuals and reduce disparities associated with these diseases. NCHHSTP's three goals in the draft 2020 Strategic Plan are aligned with its vision and mission. The incidence of infection, morbidity and mortality, and health disparities across affected groups will be decreased for HIV, viral hepatitis, STDs and TB.

NCHHSTP adopted the definition of "health equity" as optimal health for all with no persons being disadvantaged from achieving this potential because of their socially determined circumstances. Regardless of age, gender, race/ethnicity, income, education, geographic location, disability or sexual orientation, all persons in every community across the nation deserve equal access to their best health. "Health inequity" is defined as the difference or disparity in health outcomes that is systematic, unfair and avoidable.

A holistic approach to reducing the rates of HIV, viral hepatitis, STDs, TB and other diseases is needed in order to ensure all persons have an opportunity to achieve optimal health. In addition to individual and behavioral factors, environmental and social factors also must be addressed (e.g., education, housing, access to employment and transportation). NCHHSTP adopted and modified the WHO Conceptual Framework on Social Determinants of Health (SDH) to better understand common conditions and health inequities in its target populations that negatively impact health outcomes.

The SDH model demonstrates that adults with a higher level of education are likely to live longer. College graduates are likely to live at least 5 years longer than non-high school graduates. Adult life expectancy also increases with a higher level of income. Adults in the highest income groups are likely to live at least 6.5 years longer than adults in poverty. Lower positions are associated with worse health, while higher positions are associated with better health. Compared to white adults, for example, poor or fair health is much more common in black and Hispanic adults due to lower incomes in these populations.

The SDH model further illustrates the impact of residential segregation on access to care or high-quality care. Moreover, food deserts in specific communities limit the ability of residents to access fresh fruits and vegetables that are necessary for a balanced diet. Homelessness and correctional systems might be associated with higher rates of mental health and substance abuse. The prevalence of HIV/STD infections in some communities might place persons at risk without an actual increase in their individual risk behaviors.

The health impact pyramid describes different types of public health interventions and provides a framework to improve health. The five tiers of the pyramid from the lowest to highest level are socioeconomic factors, contextual changes to make individuals default to healthy decisions, long-lasting protective interventions, clinical interventions, and health counseling and education. Interventions at the lower levels of the pyramid are more effective in increasing population-based impact, while interventions at the higher levels are less effective because more individual

participation and behavioral changes are required on an ongoing basis. However, the implementation of interventions at each level can achieve and sustain public health benefits to the maximum extent possible.

In addition to the NCHHSTP's center-wide OHE and Health Equity Workgroup, DHAP and the Division of STD Prevention also have an OHE as part of their organizational structures. Moreover, DTBE appointed a new Health Equity Coordinator earlier in 2014 to promote health equity concepts in research, policy and programs. NCHHSTP also supports a number of cross-center workgroups to address health equity in priority populations and settings, including corrections, drug users, youth and men who have sex with men.

The NCHHSTP Office of Health Disparities was established in 2003 and eventually was re-branded as the current "Office of Health Equity." Several notable accomplishments have been made since that time. A "Lunch and Learn Health Equity Scientific Lecture" is held on the third Thursday of each month. These events are well received and accounted for >400 participants in FY2014. The lecture series has featured several TB-related presentations over the past two years, particularly TB disparities in African Americans and TB in homeless populations.

NCHHSTP celebrated the 10th anniversary of OHE in November 2013 with the theme, "From Theory to Action: Applying Social Determinants of Health to Public Health Practice." Distinguished keynote speakers and other stakeholders highlighted the role of public health in reducing health inequities, shared key accomplishments, and facilitated discussions on strategies to advance health equity efforts.

NCHHSTP published three supplements in *Public Health Reports* in 2010-2013. The papers focused on SDH in the prevention and control of HIV/AIDS, viral hepatitis, STDs and TB; data systems and SDH; and the application of SDH to public health practice. NCHHSTP's 2014 publications in peer-reviewed journals focused on health equity among incarcerated female adolescents and adult women, HIV/STD risks for young blacks in high prevalence areas, and training to racial/ethnic minority students for careers in public health sciences. Dr. Jonathan Mermin, Director of NCHHSTP, was a keynote speaker at the 2014 Conference on Correctional Health Care and described HIV/AIDS, viral hepatitis, STDs and TB in correctional settings.

NCHHSTP revised its existing policies to ensure that health equity is an overarching goal in the center-wide Strategic Plan. NCHHSTP's 2010 SDH white paper highlighted public health approaches to eliminate health disparities in HIV/AIDS, viral hepatitis, STDs and TB in the United States. NCHHSTP increased the number of funding opportunity announcements with health equity and SDH language from 20 in FY2012 to 55 in FY2014.

NCHHSTP has, currently is and will continue to identify and address key SDH issues for programs. Completed initiatives include launching the SDH web page on the CDC.gov website in 2009; releasing the 2013 SDH Activities Report; and publishing the *HIV/AIDS, Other Sexually*

Transmitted Diseases, Viral Hepatitis and TB in State and Federal Prisons Report in the spring of 2014.

Ongoing initiatives include the dissemination of various communication products: health equity and SDH glossary of terms, SDH frequently asked questions, press releases and surveillance reports. Future initiatives include the provision of training and educational resources (e.g., slide sets and webinars) to internal and external partners to increase their knowledge of health equity concepts. Moreover, Centers for Medicare and Medicaid data for all 50 states will be used to conduct analyses and develop research questions related to SDH.

NCHHSTP maintains a strong and diverse group of partnerships to conduct its health equity activities. These partnerships include federal agencies and academic institutions; public health ethics, health equity and sexual health experts; fellowship programs; and national organizations with a disease-specific focus on HIV, viral hepatitis, STDs and TB. NCHHSTP also targets recruitment efforts to racial/ethnic minorities to ensure that this student population considers public health as a top career choice. Moreover, NCHHSTP attempts to include health equity issues when new curricula are developed.

NCHHSTP will conduct its first health equity site visit with stakeholders for HIV, viral hepatitis, STD and TB prevention on December 4-5, 2014 in Tennessee. NCHHSTP will aim to achieve several learning objectives for staff.

- Understand barriers to achieving health equity in Tennessee from the perspectives of persons who live and work in the state.
- Identify new and existing activities to increase health equity between advantaged and disadvantaged populations.
- Understand Tennessee's process to establish priorities; allocate state, local and private resources among social groups with disproportionate levels of need; and determine adverse health outcomes in the context of current national programs and priorities.
- Identify Tennessee's innovative approaches to improve healthcare access and address the impact of preventive services in a non-Medicaid expansion state.

Dr. Duffus encouraged ACET to obtain additional information on health equity from websites of the WHO Commission on Social Determinants of Health, the HHS Healthy People 2020 Initiative, and the Robert Wood Johnson Foundation.

ACET discussed the following topics with Dr. Duffus on NCHHSTP's health equity activities related to TB.

- The need for NCHHSTP to include "country of origin" as an additional characteristic in its health equity definition.
- The feasibility of NCHHSTP examining inadequate vitamin D levels as a health disparity for TB and LTBI, particularly in African Americans.

- NCHHSTP's efforts to engage, partner with and provide education to national provider and healthcare organizations that serve African Americans and Hispanics, particularly since TB/diabetes co-infection disproportionately impacts these minority populations.

Panel Presentation: Perspectives from the Field on the Status of TB Elimination

A panel of ACET liaison representatives described perspectives from the field on the status of TB elimination in the United States.

Robert Benjamin, MD, MPH

Deputy Health Officer, Marin County Department of Health and Human Services

Chair, Stop TB USA and

ACET Liaison Representative, National Association of County and City Health Officials

Advice Requested from ACET by Stop TB USA:

- Will ACET resolve to reaffirm and endorse the 2010 TB Elimination Plan recommendations?
- Will ACET strongly encourage HHS and CDC to implement the 2010 TB Elimination Plan recommendations and ask the Federal TB Task Force to present an updated overview?
- Will ACET perform periodic assessments and submit progress reports to HHS as recommended in the original TB Elimination Plan?
- Will ACET members convey TB messages to their individual organizations?
- Do ACET members expect their individual organizations to partner with Stop TB USA and the National Tuberculosis Controllers Association (NCTA)?

Dr. Benjamin presented an update on the "Call for Action on the Tuberculosis Elimination Plan for the United States." Stop TB USA initiated the Call for Action by convening a retreat with CDC, NTCA and other TB partners in August 2007. The participants extensively reviewed recommendations in the 2000 IOM Report to determine the need for a new document. The participants discussed the five goals in the IOM report to begin fulfilling its charge:

- Maintain TB control despite the decline in the number cases
- Accelerate the decline in TB by increasing targeted testing and treatment of LTBI
- Develop new diagnostic, treatment and prevention tools for TB
- Increase U.S. involvement in global TB control
- Mobilize and sustain public support for TB

The participants agreed that despite the passage of seven years between the release of the IOM report in 2000 and the Stop USA retreat in 2007, the recommendations were still valid. However, the participants noted that the IOM recommendations had not been fully implemented.

The participants reached consensus on updating the IOM report with a newer TB elimination plan that would focus more on the involvement of stakeholders in TB elimination efforts in the United States and describe specific action steps to implement the IOM recommendations. The participants agreed that the following stakeholders should be engaged: policymakers at all levels of government, the public health sector, medical practitioners, professional societies, community-based organizations (CBOs) and voluntary organizations.

Stop TB USA's 2010 TB Elimination Plan serves as a realistic appraisal of the current status of TB elimination efforts in the United States and includes a description of unique challenges to specific populations. ACET provided advice during the development of the report and formally endorsed the final document that was released in 2010.

The executive summary of the 2010 Elimination Plan notes that recent trends have prompted the reevaluation of national plans and efforts for TB elimination in the United States. Several points are emphasized in this regard. TB remains a serious and persistent threat to health in communities throughout the country. Interim targets for TB elimination have not been met. The rate of decrease in TB incidence is slowing, but not accelerating. TB elimination will require nearly 100 years if the current trends continue.

The 2010 TB Elimination Plan summarizes whether Stop TB USA's previous recommendations have been met and if its action plans have been accomplished.

Recommendation	Met?
Maintain public awareness of the threat of TB and the importance of TB elimination through collaborative efforts among Stop TB USA, partners and other stakeholders	Yes
Renew and/or expand the commitment to TB elimination in the United States, including adequate resources and funding	No
Fully engage partners and stakeholders to assure that all U.S. citizens are provided with timely access to lifesaving TB services for the diagnosis, treatment and prevention of TB	Yes/No
Action Plan	Accomplished?
Make a commitment to implement the 2000 IOM recommendations and conduct a periodic review on the progress toward TB elimination	Uncertain
Develop new timelines and interim goals for TB elimination	Uncertain
Obtain assistance from various organizations to leverage infrastructure funding that would enable Stop TB USA to collaborate with CDC and other partners in generating political will to implement the 2000 IOM recommendations and action plans	Uncertain

Address the federal funding gap by obtaining an independent assessment of the extent to which increased funding levels authorized in the Comprehensive Tuberculosis Elimination Act of 2007 effectively could accelerate the development and implementation of new tools for the diagnosis, treatment and prevention of TB	No
Engage policymakers at federal, state and local levels, the public health sector, medical practitioners, professional societies, CBOs and voluntary organizations in a commitment to TB elimination	Yes/No

The 2010 TB Elimination Plan conveys several key messages. The plan to eliminate TB in the United States failed and is projected to require over 90 years. The failure to implement the U.S. plan leaves TB and drug-resistant TB as a growing, yet largely ignored global microbial threat. Major advances in diagnostics have been made, but implementation of these tools has been slow. Current TB treatment regimens are weak, poorly tolerated and toxic. Major governmental funding will be required.

The 2010 TB Elimination Plan describes specific action steps. Action step 1 is to develop new long-term objectives. Stop TB USA's new long-term strategic plan includes two objectives and timelines that are aligned with those in the WHO Global TB Program Framework Toward TB Elimination in Low-Incidence Countries.

Objective 1 is to eliminate TB in the United States by 2050 as defined by <1 case/1 million population and no TB deaths. Interim milestones have been established for 2025 and 2035 to reduce TB deaths, decrease TB incidence, and assure that no families are affected by catastrophic costs related to TB. Objective 1 will require a marked increase in funding for TB research and development; ongoing funding by federal, state and local governments and other industrialized countries; and a commitment to meet public health infrastructure needs.

Objective 2 is to collaborate with the Global Stop TB Partnership to leverage adequate funding to produce three safe and effective short-course regimens for all TB patients regardless of prior drug-resistance patterns by 2035. Interim milestones have been established for 2020, 2025 and 2035 to increase research and development funding to within 75% of the World Health Assembly goal of \$2 billion per year, ensure the safety and efficacy of a new MDR-TB regimen, and assure the availability of three safe and effective regimens for all TB patients.

Action step 2 is to support policy and education efforts. Funds authorized in the TB Elimination Act should be appropriated. State and local public health funding for TB control should be maintained. Membership on the U.S. House of Representatives TB Caucus should be increased from 38 representatives.

Action step 3 is to consider TB in the context of public health preparedness. The HHS Biomedical Advanced Research and Development Authority (BARDA) provides an integrated, systematic approach to the development and purchase of necessary vaccines, drugs, therapies

and diagnostic tools for public health medical emergencies. Stop TB USA is now represented on the new national stakeholder group on antimicrobial resistance.

The failure to rapidly develop and implement new tools for the diagnosis and treatment of TB and LTBI has left state and local health departments inadequately prepared for MDR-TB and entirely unprepared for extensively drug-resistant TB (XDR-TB). Continued occurrence of MDR-TB outbreaks in communities should be widely publicized.

Action step 4 is to identify visionary leadership for drug-resistant TB. WHO should partner with the International Labour Organization (ILO) to ensure a healthy, productive and TB-free workforce that migrates throughout the world.

Action step 5 is to elevate TB as a national priority for funding. For example, NIH allocated ~\$2.9 million to HIV/AIDS research and \$207,000 to TB research in 2013. The Global Plan annual targets for TB research funding have not been met in the areas of basic science, new diagnostics, new drugs, new vaccines and operational research. The purchasing power of CDC's annual TB budget has decreased by 52% from FY1990 to FY2014.

The Gates Foundation recently committed \$258.3 million to malaria research and development, but similar philanthropic funding has not been allocated to TB. HHS recently announced that \$2.2 billion in grants would be supported by the HRSA-funded Ryan White HIV/AIDS Program for care and medications. The new grants will support efforts to achieve the goal of an AIDS-free generation, but similar federal funding has not been allocated for a "TB-free generation."

Action step 6 is to change TB-related messaging. Most notably, the word "latent" should be removed from the term "latent TB infection." Recent scientific research into the nature and dynamics of granulomas reveals that there is nothing "latent" about granulomatous lesions. In addition, because the term "latent" implies that it is not serious, the term has become politically ineffective and adversely impacts the ability to leverage and increase funding for TB.

Action step 7 is to identify new partners and strengthen existing partnerships. A larger and stronger pool of partners might influence CDC to include TB in its list of "winnable battles."

John Bernardo, MD

Professor of Medicine and Biochemistry, Boston University School of Medicine
ACET Liaison Representative & President, National Tuberculosis Controllers Association

Dr. Bernardo described perspectives from NTCA and the nation's TB control programs on the status of TB elimination in the United States. NTCA is a professional organization of TB program staff that represents all TB workers regardless of their NTCA membership. NTCA derived its name because of the role of state and large-city TB controllers as the decision-makers for their respective jurisdictions.

NTCA's strategic planning process in 2013 resulted in defining its vision as "a world free of TB" and clarifying its mission "to protect the public's health by advancing the elimination of TB in the United States through concerted actions of state, local and territorial government programs." NTCA is aware that the focus should be placed on four key areas to better understand TB elimination in the United States.

First, "domestic TB elimination" should be clearly defined. A clear distinction should be made between goals that can and cannot be achieved. Second, various strategies should be identified due to differences between public health and community priorities. Implementation plans described in the "Essential Elements of TB Control" should continue to serve as valid resources. Third, infrastructure needs at multiple levels should be addressed, including geographic, cultural, clinical and scientific factors. Fourth, the fiscal base should be specified in terms of direct patient costs, infrastructure costs and ACA.

The Essential Elements of TB Control include overall planning and policy, management of TB cases and suspects, identification of persons with TB disease, identification and management of persons infected with *Mycobacterium tuberculosis*, laboratory and diagnostic services, data collection and analysis, and training and education.

A major challenge in TB elimination efforts is the perception among Congressional staff that TB is no longer a problem in the United States. TB has markedly declined over the past 30 years, but 9,588 cases were reported in 2013. Los Angeles, Fulton County, Georgia and Springfield, Massachusetts reported 113 TB cases that were linked to homeless populations in 2008-2014. Of the 94 TB cases reported by Los Angeles and Georgia, 14 resulted in deaths.

Massachusetts identified significant health disparities in 201 TB cases reported in 2013. Case rates were 0.8/100,000 in whites, 19.1/100,000 in Asians, 13.6/100,000 in African Americans, and 4.9/100,000 in Hispanics. Foreign-born residents of the state represent >50 countries each year and have accounted for >80% of TB cases in Massachusetts since 2011.

Access requires engagement at multiple sectors. Engagement of the public includes at-risk communities and the population at large. The language, fears, priorities, needs, health beliefs and health-seeking behaviors of the community should be understood, particularly since these factors typically are discordant with clinical and public health views on the diagnosis, prevention and treatment of TB.

Public health messaging should address personal concerns, stigma, and financial fears related to healthcare costs and the potential loss of employment. Trusted and credible sources for the community to obtain health information should be identified (e.g., pharmacists, non-traditional practitioners, CBOs and faith-based organizations). The best method to communicate with the community should be determined (e.g., printed materials and radio advertisements).

Public health messaging should be designed to engage at-risk communities. Dialogue should be initiated to build trust with the community. Access to public health services should be provided on the community's terms. Effective community engagement will result in access to reliable information and services, better understanding of TB and public health, and improved public and personal health.

Engagement of health providers includes direct care providers and public health. Direct care providers typically have poor understanding of and limited information on the epidemiology of TB in their patient populations and jurisdictions. TB education and training are lacking in medical/nursing schools and residency/fellowship programs. TB frequently competes with many other priorities in clinical settings. Resources are limited for TB radiography, laboratory and community outreach services.

Direct care providers should be identified for groups that are at risk for TB. Healthcare systems should be engaged to determine TB needs, resources and expertise in the provider community. Evidence-based and credible educational programs should be offered to build competency in TB. Educational strategies should be adapted to meet local needs, such as academic detailing in emergency departments, rotations of infectious disease grand rounds to medical students and residents, and workshops. TB experts should be available to assist direct care providers.

TB programs are unique in clinical and public health domains, but are being integrated into other public health department programs. Public health services are considered to be no longer needed due to the inaccurate assumption that all persons are covered by private insurance or Medicaid. Resources are needed to support the unique needs of the TB infrastructure, but public health decision-makers have competing priorities and legislators are unaware of problems and needs related to TB.

Engagement of policymakers includes those at both national and jurisdictional levels. The public should be educated to raise awareness of TB as both an individual and public health problem and generate public support. Legislators should be engaged to encourage and support federal and local funding for categorical TB functions and programs. Alliances should be established and strengthened with CBOs to support joint public health efforts.

Access to TB services should be assured to develop trust and remove social, behavioral and financial barriers. The TB infrastructure should be maintained by interacting and collaborating with programs to foster understanding of the unique needs of TB control in public health. Cross-jurisdictional strategies should be developed to assure compliance with the Essential Elements of TB Control, particularly clinical, laboratory and public health competencies.

The TB infrastructure is in jeopardy at this time due to the reduced incidence of disease. TB is now restricted to disadvantaged populations that account for the majority of morbidity. TB programs have less staff in the field. Cuts to TB funding appear to be based on perceptions rather than the realities of ACA. The aging TB workforce continues to lose medical, nursing and

laboratory expertise. A strong alliance with CDC, NIH and other federal partners is needed to emphasize the need for TB prevention in high-risk populations.

Poor TB tools have been developed and scientific understanding of the organism-host relationship continues to be limited. Clinical and translational TB research is difficult to conduct. The ability to generalize TB research findings outside of laboratory settings is difficult. Relevant TB clinical trials are lacking and often are redundant. Minimal attention has been given to TB drug alternatives and drug development. The focus on antibiotics has increased resistance to TB drugs.

FDA Panel Presentation: TB Drug Shortages

A panel of speakers from the U.S. Food and Drug Administration (FDA) presented overviews on TB drug shortages.

David Roeder

Associate Director for Regulatory Affairs, Office of Antimicrobial Products
U.S. Food and Drug Administration

Mr. Roeder described the FDA approval process for non-U.S.-based manufacturers. FDA ensures that safe and effective drugs are available in adequate supplies for the long-term to treat TB patients in the United States. However, FDA faces two key challenges in this effort: (1) the ability to maintain older TB drugs on the market and (2) and the provision of effective incentives to encourage the development of new TB therapies.

Most of the current FDA-approved TB therapies are older, off-patent drugs with a limited market in the United States. Many TB drugs are approved and available in other countries. Foreign manufacturers might not have sufficient experience with the U.S. drug regulatory system. The three key factors that should be considered for FDA drug approval are highlighted below.

Factor 1 is regulatory considerations. A 505(j) application is for generic drug approval. The application is submitted as an abbreviated new drug application (ANDA) to copy an already-approved drug. The generic drug and already-approved drug must have the same ingredients, route of administration, dosage form, strength, and conditions of use recommended in labeling. An ANDA must be submitted to FDA with manufacturing information, bioequivalence study results, labeling and administrative documents (e.g., patent certification).

A 505(b)(2) application is submitted as a new drug application (NDA) to change an already-approved drug that might require additional studies to fully establish safety and efficacy. An NDA does not qualify for submission as a generic drug. The applicant neither owns nor has a right of reference to all information necessary to support approval, but the literature or FDA's

previous approval of another drug can be used. A new dosage form or new combination product (e.g., fixed dose or co-package) likely would be a 505(b)(2) NDA for TB drugs.

A 505(b)(1) full application is submitted as an NDA. TB drugs, such as BDQ, typically require a new molecular entity. The applicant either owns or has a right of reference to all information necessary to support approval. New molecular entities likely would be regulated as 505(b)(1) NDAs for TB drugs.

Factor 2 is scientific considerations. An ANDA requires bioequivalence studies unless a waiver is granted. A 505(b)(2) NDA requires all studies necessary to support the change from the already-approved drug. A 505(b)(1) NDA requires all studies necessary to support the safety and efficacy of the drug.

Factor 3 is economic considerations. ANDAs are charged user fees under the Generic Drug User Fee Act. The fees are highly variable and primarily are influenced by the number of both domestic and foreign manufacturing facilities. The law has no provisions for waivers or fee reductions. ANDA user fees could range from \$100,000 to \$500,000, plus an annual fee for one facility at a cost ~\$270,000, plus fees for post-market changes at a cost ~\$32,000.

NDAs are charged user fees under the Prescription Drug User Fee Act, but waivers can be obtained for orphan drugs, small businesses with <500 employees, drugs with a public health necessity, and barriers to innovation. User fees for NDAs or Biologics License Applications (BLAs) can cost ~\$2.3 million if clinical data are required, ~\$1.2 million if clinical data are not required, or ~\$1.2 million for supplements if clinical data are required; plus an annual fee for establishments at a cost of ~\$569,000; plus an annual fee for products at a cost of ~\$110,000. However, these fees likely would be waived for TB drugs that qualify as orphan drugs.

Mr. Roeder highlighted the President's Emergency Plan for AIDS Relief (PEPFAR) as a case study in using FDA's existing regulatory framework to address urgent public health needs. Most U.S. antiretroviral drugs were still under patent and were too expensive to use in PEPFAR when the program was launched in 2004. Generic copies of these drugs could not be approved in the United States until the existing patents had expired. Foreign generic products were available at a low cost, but their quality was unknown. A pathway was sought to allow FDA oversight of product quality for the purchase of foreign generic products to be used in PEPFAR.

Foreign firms submitted generic and 505(b)(2) applications with a goal of obtaining "tentative approval" from FDA. Tentative approval allows FDA to review applications in their entirety to ensure standards for approval are met prior to the expiration of innovator patents. Because tentatively approved drugs cannot be marketed in the United States, these products do not compete with innovators in the U.S. market. However, tentatively approved drugs could be purchased for use in overseas PEPFAR programs with an assurance that the products meet FDA standards. To date, 179 antiretroviral products, including new combination products and pediatric dosing forms, have been approved or tentatively approved for use in PEPFAR.

Monetary incentives are available to develop new TB therapies. Incentive 1 is orphan drug designation and exclusivity. This incentive is for diseases affecting <200,000 persons in the United States. Orphan designation provides grants and tax incentives for drug development. An orphan drug is eligible for marketing exclusivity for seven years at the time of approval, but this incentive is not relevant to generic drugs.

Incentive 2 is tropical disease priority review vouchers (PRVs). This incentive is authorized by the FDA Amendments Act of 2007 and provides a list of eligible tropical diseases, including TB. Sponsors of applications for a new molecular entity for treatment of TB can be eligible for a PRV at the time of approval. The owner of a PRV can use this incentive to obtain a priority review for any NDA or BLA. Priority reviews can shorten the time of an NDA or BLA review by four months. A PRV can be sold on the open market for use by another sponsor. A recent sale of a PRV was \$125 million.

Incentive 3 is the Generating Antibiotic Incentives Now legislation. Antibacterial and antifungal drugs, including TB drugs, that are intended to treat a serious or life-threatening infection can be granted a Qualified Infectious Disease Product (QIDP) designation. Drugs with QIDP designation are eligible for fast-track designation, while NDAs for drugs with QIDP designation are eligible for priority review. At the time of approval, drugs with QIDP designation are eligible for a five-year extension of any exclusivity granted with that approval. As of November 21, 2014, 62 QIDP designations have been granted.

CAPT Jouhayna Saliba, PharmD

Team Leader, Drug Shortage Staff, Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Dr. Saliba described FDA's role and response in addressing drug shortages. FDA established its Drug Shortage Staff (DSS) in 1999 due to a shortage of Isoniazid (INH). The overarching responsibility of DSS is to facilitate the prevention and resolution of shortages by collaborating with key stakeholders from FDA, other government agencies, industry and the public.

FDA collects drug shortage data from multiple sources across the supply chain. The FDA Safety and Innovation Act (FDASIA) was enacted in July 2012 and requires manufacturers to notify FDA about the potential for disruption in the supply of any drug for any reason six months in advance. However, FDASIA does not require reporting of drug shortage data from all points in the supply chain. Other data sources include voluntary information submitted by industry, FDA staff in the field, and reports from individual members of the public.

FDA requires notification by manufacturers of interruptions in the supply that could lead to a meaningful supply disruption or discontinuation as well as any changes in manufacturing. FDA sends a letter to manufacturers that do not comply with notification requirements. Although a monetary penalty is not imposed, non-compliance letters are posted on the FDA website for

public viewing. FDA cannot require a company to manufacture a drug, increase its drug supply, or target distribution of a drug to specific populations or jurisdictions.

The number of drug shortages reported to FDA decreased from 251 in 2011 to 44 in 2013. In 2013, sterile injectables (e.g., chemotherapy, anesthesia and other acute medications) accounted for 80% of shortages. This is due to the complex, highly-specialized manufacturing process of these products. A manufacturing process that is not meticulous could pose a high risk to patients. A shortage of sterile injectables is likely if quality or production problems arise with these products. In 2013, oral solid drugs account for 18% of shortages. The top three factors for drug shortages in 2013, are quality issues related to manufacturing (37%), quality issues related to delays and capacity (27%), and raw materials (27%).

The HHS Assistant Secretary for Planning and Evaluation released a report in 2011 that described the major causes of shortages for sterile injectables.

Cause of the Shortage	Specific Problem
State of the industry	<ul style="list-style-type: none">• The vast majority of the market is represented by only 7 manufacturers.• Contract manufacturers act as both primary contract and secondary subcontract manufacturers.
Lack of redundancy	<ul style="list-style-type: none">• Multiple products are made on existing manufacturing lines.• The 24-hour/7-day week production schedule provides no cushion of time.
Complex manufacturing processes	<ul style="list-style-type: none">• Complex molecules do not allow for simple resolutions.• Problems typically affect multiple products at once.
Investment economics uncertainties	<ul style="list-style-type: none">• For example, the ability to make a profit from producing propofol is questionable because a 20-mL vial sells for only \$0.48. At this time, there are 3 manufacturers of propofol.
Quality and manufacturing issues	<ul style="list-style-type: none">• Sterility due to bacterial and fungal contamination• Particulates in glass, metal or fiber in vials• The potential for drugs to form crystals• Reaction between the drug and container or diluent• Potentially toxic impurities (e.g., heavy metals)• Degradants that result in less effective drug products• Breakdown of equipment• Natural disasters

FDA's role in drug shortages is to prioritize patient care as the top concern and ensure products are safe, effective and available. Early notification of drug shortages is critical to FDA's

involvement in developing prevention and mitigation strategies with manufacturers. However, some shortages cannot be prevented due to an unforeseen breakdown in the manufacturing line or longstanding quality issues. Some drug shortages can be addressed more rapidly than others, but FDA always considers the risks to patients at the outset.

FDA's prevention and mitigation strategies for drug shortages include prioritizing medically necessary products; weighing the risks and benefits of the drug; maintaining availability of the drug while minimizing the risk to patients; providing manufacturers with advice, assistance and expedited approaches to address problems; and offering flexible, creative and quick resolutions. FDA defines a "medically necessary drug" as a product used to treat or prevent a serious disease or medical condition for which no other alternative drug exists that is available in adequate supply and judged to be an adequate substitute by medical staff. FDA solicits external expertise in the process of defining a medically necessary drug.

FDA takes actions to promptly and efficiently respond to notifications of drug shortages by performing risk-based analyses and utilizing other tools. FDA's regulatory discretion allows the manufacture of medically necessary drugs to continue. This tool is best suited for products that present a minor or low risk to patients, but additional safety controls might be required: filters with the product, extra testing at the plant, third-party oversight of drug production, or special instructions for safe use.

FDA requests other firms to increase production of the drug to address a public health need. FDA expedites inspections and reviews of proposals submitted by manufacturers, including longer expiration dates for drugs in the existing inventory, new manufacturing sites, new sources for raw materials, or changes in specifications. FDA makes critical drugs temporarily available from unapproved sources in rare cases.

FDA formed a Drug Shortage Task Force with staff from DSS and other offices. FDA released its Strategic Plan on October 31, 2013 to strengthen its ability to respond to notices of a disruption in supply and improve its mitigation tools and communications. FDA enhanced its "Drug Shortage Website" to more effectively communicate with stakeholders. FDA is creating long-term prevention strategies to address the underlying causes of supply disruptions and prevent future drug shortages.

FDA has identified three long-term prevention strategies to date: (1) develop methods to incentivize and prioritize manufacturing quality; (2) establish a new Office of Pharmaceutical Quality that would use regulatory science to identify early warning signals of drug shortages; and (3) overcome existing limitations of data to increase knowledge and identify new approaches to address drug shortages.

Overall, FDA will continue to strongly focus on drug shortages through a multidisciplinary approach involving clinicians, pharmacists, chemists, biotechnology firms, regulatory tools, manufacturers and public communication. FDA also will strongly emphasize the need for

industry to commit to and institutionalize a new culture of quality manufacturing processes, methods and testing.

The new culture of quality ideally will include redundancy of production through additional facilities and manufacturing lines, appropriate inspection and maintenance of facilities, prompt reporting and correction of even small production and quality problems, and ongoing dialogue with FDA on the best strategies to support quality manufacturing. FDA will continue its close collaborations with manufacturers to prevent and mitigate shortages of critical drugs, but strong and multidisciplinary partnerships will be needed to resolve drug shortage problems.

Dr. Saliba confirmed that the TB drug supply currently has no shortages.

TB Drug	Current Status
INH Tablets	No supply issues; available from 2 manufacturers
INH Injection	No supply issues
Rifampin Injection	Available from a sole-source manufacturer; ability to meet demand
Ethambutol	Available from 2 manufacturers
Amikacin Injection	Available from 2 manufacturers
Cycloserine	Available
Capreomycin	Available from a sole-source manufacturer

ACET discussed the following topics with the FDA panel on TB drug shortages.

- The ability of U.S. TB programs to obtain INH tablets from Canada.
- The role of high user fees in hindering the ability to update older TB drug labels with newer clinical data and preventing overseas manufacturers from introducing their TB drugs to the U.S. market.
- Ethical concerns and barriers to using quality, less expensive TB drugs sold through GDF in other countries, but not in the United States.
- FDA's regulatory restrictions on importing second-line drugs (SLDs) for TB patients, particularly if no other products are available in the United States to treat this patient population.
- The definition of a "medically necessary drug" for an individual patient or public health.
- Benefits to individual TB patients and the broader TB community due to FDA's strong relationships with drug manufacturers.

Update by the DTBE Drug Shortages Workgroup

Ann Cronin

Associate Director for Policy and Issues Management, DTBE
Centers for Disease Control and Prevention

Ms. Cronin reported that the workgroup's most recent discussions have focused on TB drug shortages and proactive approaches to prevent or mitigate future shortages. She reviewed a table of TB drugs in the United States that are available or vulnerable to shortages. The table illustrates the current status of 15 TB drugs:

- Essential, first-line use (4 of 15 drugs)
- Sole-source manufacturer in the United States (9 of 15 drugs)
- Unavailable in the United States (1 drug only)
- FDA approved and sold in the United States by specific manufacturers (14 of 15 drugs)
- Non-FDA approved and sold through GDF by specific manufacturers (13 of 15 drugs)
- Non-FDA approved and not sold by GDF (2 of 15 drugs)

Ms. Cronin informed ACET of several key points in her review of the drug shortage table. Oral and injectable Levofloxacin and oral Moxifloxacin were removed from the table because many manufacturers have FDA approval and sell these products in the United States. Of all 15 drugs, Kanamycin is the only product that is unavailable in the United States.

The FDA website maintains up-to-date company information on the manufacturer and the current status of TB drugs, including temporary disruption in supply and longer-term shortages. In this case, FDA can work with manufacturers to ship product (as it becomes available) to TB programs. However, CDC has no role or oversight of local drug purchasing agreements with manufacturers.

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ANTI-TB DRUGS THAT ARE VULNERABLE TO SHORTAGES IN THE UNITED STATES

Drug*	Essential, First Line Use	Sole Source in U.S.	Unavailable in U.S.	FDA Approved, Sold in U.S. by these manufacturers	Not FDA Approved, Sold through GDF by these manufacturers	Not FDA Approved Not Sold by GDF
Amikacin				Teva; Emcure Pharmaceuticals for Heritage Pharmaceuticals	Medochemie; Cipla; Pharmatex/Fisiopharma; Vianex	
Capreomycin		X		Akorn	Vianex	
Cycloserine		X		The Chao Center	Dong -- A ST Co; Macleods; Lupin	
Ethambutol	X			Lupin Limited for Lupin Pharmaceuticals; STI Pharma; X-GEN Pharmaceuticals	Labatec; Fatol/Riems; Macleods; Cadila; Svizera	
Ethionamide		X		Norwich Pharmaceuticals for Wyeth Pharmaceuticals (Pfizer)	Macleods; Lupin; Microlabs; Cipla	
Isoniazid (oral)	X			Barr Laboratories for Teva; Epic Pharma for Sandoz; Mylan	Labatec; Lupin; Macleods; Fatol/Riems	
Isoniazid (injectable)		X		Sandoz		
Kanamycin			X		Meiji; Panpharma	
Moxifloxacin (Injectable)		X		Schering	Bayer Germany; Cipla; Macleods	

ANTI-TB DRUGS THAT ARE VULNERABLE TO SHORTAGES IN THE UNITED STATES

Drug*	Essential, First Line Use	Sole Source in U.S.	Unavailable in U.S.	FDA Approved, Sold in U.S. by these manufacturers	Not FDA Approved, Sold through GDF by these manufacturers	Not FDA Approved Not Sold by GDF
p-Aminosalicylic acid		X		Jacobus Pharm	Olainfarm; Macleods	
Pyrazinamide	X			ULTRAtab Laboratories for DAVA Pharmaceuticals; MIKART for VersaPharm	Macleods; Cadilla; Labatec	
Rifabutin				Pfizer Italia for Pharmacia & Upjohn Co; Lupin Limited for Lupin Pharmaceuticals		
Rifampin	X	X		sanofi-aventis for sanofi- aventis U.S.	GDF only sells fixed-dose combinations: Lupin; Macleods; Strides; Svizera	Patheon Italia for AKORN; Agila Specialties for Mylan; Agila Specialties for Pfizer;
Rifapentine		X		sanofi-aventis for sanofi- aventis U.S.	Not sold by GDF	
Streptomycin		X		X-GEN Pharmaceuticals	Reig Jofre	Roerig (Pfizer)

Ms. Cronin asked ACET to consider long-term strategies that could be recommended to assure the availability of more TB drugs in the United States. She pointed out that the workgroup has explored the pros and cons of several innovative approaches in this effort. For example, an HHS facility could house a new mini-formulary for TB drugs, but DTBE does not have \$20 million to support this initiative. BARDA could include TB in its list of necessary products for public health medical emergencies, but the start-up purchase of TB drugs from the BARDA stockpile and ongoing sustainability costs would require a tremendous amount of resources.

Manufacturers that sell non-FDA-approved drugs through GDF could be encouraged to seek FDA approval to expand their market to the United States, particularly since these companies sell 13 of 15 first-line drugs (FLDs). However, the level of interest in the manufacturing community for this small market is unknown. Companies that do have FDA approval to sell product in the US may view encouragement of other companies to enter the US market as a disincentive to providing TB drugs. Incentives could be offered to manufacturers that produce old TB drugs to renew and maintain their interest in the market; however DTBE does not have resources or authority to provide these kinds of incentives.

NTCA's Perspective on the TB Drug Supply

Donna Wegener

Executive Director

National Tuberculosis Controllers Association

Ms. Wegener described NTCA's perspective on the TB drug supply. NTCA is aware that the TB drug supply in the United States prevents the spread of disease. As a result, the new web-based NTCA Reporting System was launched in November 2013 to collect and maintain various data elements on the TB drug supply. The NTCA Reporting System provides real-time information and is a rich source of data to assess national TB drug shortages.

NTCA acknowledges that the TB drug supply currently does not have significant or severe shortages as in the past, but weaknesses and vulnerabilities could lead to adverse changes. Most notably, only a few options exist for multi-drug TB regimens. Drug shortages are continuing to worsen due to a procurement system that is decentralized across individual states. The number of manufacturers is limited. The cost of TB drugs continues to increase. A safety net has not been established for the TB drug supply. Of 4 FLDs, 3 have a shortage or have experienced a large price increase. Of 8 SLDs, 5 have a single manufacturer.

The NTCA Reporting System captured several recent changes to the TB drug supply in 2014 at the state level. A change in packaging for Cycloserine created confusion for suppliers. The 125% price increase for para-aminosalicylate sodium significantly impacted TB programs across

the country, particularly those with limited budgets. Capreomycin had a limited, short-dated supply in California.

Priftin was unavailable from a local supplier in Texas. The “piecemeal” allocation of Tubersol in some states has affected TB contact investigations. For example, TB controllers in North Dakota are only given 100 vials of Tubersol per month. A large, low-incidence state encountered difficulties in acquiring Pyridoxine and was required to divert TB drugs from rural areas.

NTCA currently is addressing key challenges in the TB drug supply. The ability to maintain a sense of urgency is difficult because no TB drugs or diagnostics are in short supply or stock-out status at this time. Problems with allocating TB drugs have not been resolved, particularly in the context of clearly defining roles of manufacturers, suppliers, distributors and state contractors. The cost of TB drugs is continuing to increase due to sole-source manufacturers, generic drugs and TB-specific drugs. The cost of TB drugs is driving prescribing patterns. For example, BDQ has a better safety and efficacy profile, but providers are continuing to prescribe Pyrazinamide more often due to its lower cost.

Market forces are allowing large pharmaceutical companies to purchase smaller companies that produce TB drugs. For example, Akorn received U.S. approval in August 2014 to purchase VersaPharm that manufactured a generic TB drug. ACA has led to unintended consequences for some TB patients. In California, for example, a previously healthy middle-aged immigrant with health insurance was diagnosed with MDR-TB.

The patient purchased a health plan through the ACA Health Insurance Marketplace, but could not afford MDR-TB drugs that cost ~\$5,000 each month. The local health department in California attempted to apply wraparound services, but its resources are limited and cannot be sustained throughout the duration of the patient’s treatment. To address TB-specific flaws in ACA, MDR-TB should be included in the Medicaid reimbursement exception for end-stage renal disease.

Despite these challenges, NTCA is focusing its efforts on new partners and tools to improve the TB drug supply in the United States. Ongoing communications, relationships and collaborations with industry have been strengthened. The release of the President’s Executive Order, “Combating Antibiotic-Resistant Bacteria,” has given BARDA new authority to include TB and MDR-TB drugs in its list of necessary products for public health medical emergencies. The U.S. Agency for International Development (USAID) has funded a new system to enhance access to pharmaceuticals and services. USAID’s new electronic forecasting tool will be reviewed to determine potential opportunities to address issues in the domestic TB drug supply.

Overall, risks to the U.S. TB drug supply are persistent despite progress that has been made over the past two years. Sole-source manufacturers account for a large proportion of FLDs and SLDs. Short- and long-term strategies need to be expedited to address vulnerabilities and

weaknesses in the current procurement system, such as interruptions in the TB drug/diagnostic supply, cost increases and limited access.

ACET discussed the following topics with the DTBE Drug Shortages Workgroup and NTCA on the current status of the TB drug supply in the United States.

- The feasibility of FDA pre-qualifying companies that could rapidly and temporarily import TB drugs when production problems arise with sole-source manufacturers.
- The ability of NTCA to facilitate effective communications on the TB drug supply within and between TB programs.

Status Report on the ACET Workgroups

Barbara Cole, RN, MSN, PHN, ACET Chair

TB Controller

Riverside County (California) Department of Public Health

Ms. Cole announced that the terms of two former ACET members who chaired workgroups have expired. In accordance with Federal Advisory Committee Act rules and regulations, current voting members of the parent company must chair workgroups. Ms. Cole presented brief status reports and proposed next steps to ensure that the charges of the workgroups are fulfilled.

ACET Essential Components Workgroup. Ms. Cole reported that the workgroup was charged with reviewing and recommending updates to CDC's 1995 document, "Essential Components of a TB Program." The workgroup presented several updates to ACET on its ongoing activities and progress in drafting a new document. Ms. Cole expected the new Essential Components document to be presented during the next meeting for ACET's review and discussion. ACET's formal vote on the draft document would fulfill the workgroup's charge.

ACET Corrections Workgroup. Ms. Cole reported that ACET agreed by consensus to reestablish the workgroup during the June 2014 meeting with the following charge: (1) evaluate activities DTBE has conducted to address ACET's previous recommendations on TB in correctional settings; (2) review recent publications on the dramatic contribution of correctional settings to TB cases; and (3) serve as a liaison between ACET and the DTBE Corrections Workgroup.

Ms. Cole noted that the workgroup has an existing charge, ongoing DTBE support to convene teleconference meetings, and DTBE staff to provide technical expertise. She confirmed that the future direction of the workgroup would be revisited during the Business Session on the following day because no ACET voting members volunteered to serve as the new chair.

Update by the ACET Latent TB Infection Workgroup

Robert Horsburgh, Jr., MD, MUS

Professor of Epidemiology, Biostatistics and Medicine & Department of Epidemiology Chair
Boston University School of Public Health
ACET Member & Workgroup Chair

Dr. Horsburgh covered the following topics in his update to ACET on the workgroup's recent activities. The workgroup was established during the June 2014 ACET meeting and soon learned that the NTCA TB Infection Survey Committee was addressing the same issues. As a result, the workgroup began fulfilling its charge by engaging the NTCA Survey Committee as a key partner and reviewing the current LTBI literature.

- Of all TB cases in the United States, 80% are attributed to reactivation of LTBI.
- The current LTBI burden in the United States includes 11.2 million persons.
- Only 50% of 200,000-300,000 persons who are treated for LTBI each year in the United States complete treatment.
- TB regimens of shorter durations are expected to improve treatment completion rates.
- The recently completed National Health and Nutrition Examination Survey (NHANES) is expected to provide an estimate of the proportion of LTBI patients who still need treatment.

The workgroup described the rationale for developing an LTBI registry or reporting system. An accurate estimate of the burden of LTBI would be provided. Changes in LTBI would be monitored over time. Populations at high risk for LTBI and in need of screening would be identified. Source case investigations of LTBI would be facilitated, particularly for pediatric infections. Awareness of and advocacy for the importance of LTBI would be increased.

If the LTBI registry or reporting system also captured data on TB treatment initiation and completion, process indicators would be provided to assess progress toward TB elimination. Populations in need of assistance with TB treatment adherence would be identified. Providers in need of TB education and outreach would be determined.

The workgroup discussed the experiences of individual states in collecting and reporting LTBI data. Kansas, Massachusetts, Mississippi, Missouri, New Hampshire and Rhode Island have mandatory LTBI reporting systems. Massachusetts receives ~5,000 LTBI reports annually in its passive system and does not distinguish between the proportion of IGRAs and TSTs. Missouri receives ~3,000 LTBI reports annually. The system is extremely useful in conducting source case investigations and assuring that preventive therapy was offered. Massachusetts and Missouri do not capture and monitor data on LTBI treatment completion rates.

New Hampshire receives ~1,200 LTBI reports annually and uses its system for targeted case management. Maine and Tennessee have voluntary LTBI reporting systems. Arizona, Georgia, New York City (NYC), Virginia and West Virginia have LTBI reporting systems for specific populations only, such as children.

The workgroup analyzed the NYC LTBI reporting system as an initial case study. The NYC system only captures pediatric LTBI cases at an incidence of 133-396 cases per year. The NYC system could be used for locating source cases, but decreased funding has resulted in low reporting. The NYC system has the capacity to retrospectively indicate potentially preventable cases that previously were identified as contacts. The NYC system can serve as a source for baseline results that could be used to assess conversions in future contact investigations. The NYC system also could serve as a source to evaluate underreporting of TB infection.

The workgroup extensively discussed the NTCA TBI Survey that will be administered to TB controllers in the field in early 2015. The workgroup noted that CDC is continuing to use “LTBI,” while NTCA has shifted to the terminology of “TB infection” (TBI). In general, the survey will ask TB controllers to summarize any TB test result and describe both mandatory and voluntary TBI reporting practices. In particular, the survey will ask TB controllers to respond to the following questions.

- What data elements currently are reported and targeted to specific populations?
- What level of patient and TBI information is reported to TB programs?
- What is the extent to which TB programs are interested in receiving TBI test results and diagnoses?
- What are the perceived benefits and challenges of a national reporting system for TBI test results and diagnoses?
- What is the extent to which TB programs are interested in participating in activities to support reporting of TBI test results or diagnoses?

The workgroup’s next steps will be to review NHANES data to identify the proportion of LTBI patients who previously were treated; analyze results of the NTCA TBI Survey of TB Controllers; estimate the workload for various LTBI reporting strategies; specify the costs and benefits of LTBI reporting; collaborate with the Tuberculosis Epidemiologic Studies Consortium to determine whether LTBI surveillance should be active or passive; and assess whether a new LTBI reporting system could be built on the existing contact investigation registry.

Based on the discussion with ACET, Dr. Horsburgh confirmed that the workgroup would identify additional sources to collect and review LTBI data in an effort to estimate the true burden of LTBI in the United States.

Preparation for the ACET Business Session

Barbara Cole, RN, MSN, PHN, ACET Chair

TB Controller

Riverside County (California) Department of Public Health

Ms. Cole summarized key points and outcomes from the day 1 presentations. She asked ACET to consider topics that potentially could be developed as formal resolutions during the Business Session on the following day.

Presentation	Topic to Consider
DTBE Director's Report	<ul style="list-style-type: none">• Strategies to leverage and apply components of CDC's ebola response to TB• The 5 strategies for TB elimination in the United States
NCHHSTP's Health Equity Activities	<ul style="list-style-type: none">• Approaches to include health equity concepts in TB elimination efforts
Status of TB Elimination in the Field	<ul style="list-style-type: none">• ACET's formal support of the Stop TB USA 2010 TB Elimination Plan
TB Drug Shortages	<ul style="list-style-type: none">• Long-term strategies to assure the availability of more TB drugs in the United States
LTBI Workgroup	<ul style="list-style-type: none">• New and more effective messaging to shift to TB elimination (e.g., replace "LTBI" with "TBI")

With no further discussion or business brought before ACET, Ms. Cole recessed the meeting at 4:34 p.m. on December 2, 2014.

Opening Session: December 3, 2014

Hazel Dean, ScD, MPH

Deputy Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention

Centers for Disease Control and Prevention

ACET Designated Federal Officer

Dr. Dean conducted a roll call to determine the ACET voting members, *ex-officio* members and liaison representatives who were attending the meeting either in person or remotely. She announced that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record.

Dr. Dean reminded the ACET voting members of their responsibility to disclose any potential individual and/or institutional conflicts of interest for the public record and recuse themselves from voting or participating in these matters. None of the voting members publicly disclosed any individual or institutional conflicts of interest for the record that were new or different than those declared on day 1 of the meeting.

Dr. Dean announced that the voting members and *ex-officio* members in attendance constituted a quorum for ACET to conduct its business on December 3, 2014. She reconvened the proceedings at 8:40 a.m. and welcomed the participants to day 2 of the ACET meeting.

ACET Business Session

Barbara Cole, RN, MSN, PHN, ACET Chair

TB Controller

Riverside County (California) Department of Public Health

Ms. Cole opened the business session and called for ACET's review, discussion and/or formal action on the following topics.

Topic 1: ACET's Process to Respond to Requests for Advice

Ms. Cole was pleased that ACET initiated a process during the June 2014 meeting to monitor the status of its recommendations to CDC in a more formal, systematic and ongoing manner. However, she emphasized that a similar process is needed to ensure ACET responds to specific advice requested by CDC. She moderated a discussion on the current status of ACET's responses to CDC's previous requests for advice.

Request for Advice from ACET	Requester	ACET Response
MARCH 4, 2014 MEETING		
ACET's guidance to HHS to prevent TB drug shortages in the future.	NTCA	ACET took a formal vote to establish a new TB Drug Shortages Workgroup. The motion unanimously passed by 10 ACET voting members. Ms. Jennifer Cochran and Dr. Susan Dorman will serve as co-chairs. The workgroup will initiate its activities based on the following draft

Request for Advice from ACET	Requester	ACET Response
		<p>charge.</p> <ul style="list-style-type: none"> Concrete recommendations to the HHS Secretary will be drafted by the next meeting for ACET's review, discussion and formal action. The workgroup will extensively discuss the innovative strategies Ms. Ann Cronin has explored to address TB drug shortages in the United States. The HHS Secretary will be informed that collaborations over the past two years among CDC, FDA, USAID and other federal partners to address TB drug shortages have not generated any resolutions to the problem due to existing regulatory and legal barriers. The public health impact of TB drug shortages will be emphasized as well. The HHS Secretary will be provided with broader recommendations on drug shortages for non-infectious diseases, such as cancer drug shortages, to increase public attention.
<p>ACET's recommendations on CDC's global health activities:</p> <ul style="list-style-type: none"> CDC's global TB measures and targets Global TB Steering Committee Global TB Strategic Framework and the Global TB Strategic Plan TB Building and Strengthening Infection Control Strategies (BASICS) Initiative 	CDC Center for Global Health	<p>ACET agreed to schedule Dr. Susan Maloney, the CDC Global TB Coordinator, on the next agenda to provide an update on CDC's Global TB Strategic Plan. ACET will formulate recommendations at that time.</p>
JUNE 9-10, 2014 MEETING		
<p>ACET's collaboration with the DTBE Corrections Workgroup and other correctional partners to create a national strategic action plan for TB prevention and control in correctional facilities.</p>	DTBE	<ul style="list-style-type: none"> The ACET Corrections Workgroup will suspend all activities until its charge is redefined and a current voting member volunteers to serve as the new chair. ACET agreed to schedule a status report on the workgroup's most recent activities on the next agenda. ACET agreed to schedule the DTBE

Request for Advice from ACET	Requester	ACET Response
		Corrections Workgroup on the next agenda to present an update on its “partially implemented” and “ongoing” activities in response to ACET’s previous resolutions.
ACET’s input on the USPSTF Draft Research Plan on LTBI.	DTBE	ACET submitted its guidance to USPSTF. With the exception of recommending LTBI treatment as primary prevention, all of ACET’s other suggestions were accepted by USPSTF and are included in the final research plan. ACET will continue to monitor this issue over the next year.
DECEMBER 2-3, 2014 MEETING		
<p>ACET’s support of the 2010 TB Elimination Plan:</p> <p>(1) Will ACET resolve to reaffirm and endorse the 2010 TB Elimination Plan recommendations?</p> <p>(2) Will ACET strongly encourage HHS and CDC to implement the 2010 TB Elimination Plan recommendations?</p> <p>(3) Will ACET ask the Federal TB Task Force to present an updated overview?</p>	Stop TB USA	<p>(1) ACET took a formal vote and resolved to reaffirm and endorse the 2010 TB Elimination Plan. The motion passed by a majority vote of 9 in favor and 1 abstention (Dorman).</p> <p>(2) ACET took a formal vote to recommend to the HHS Secretary and CDC Director to implement the 2010 TB Elimination Plan. The motion passed by a majority vote of 7 in favor, 1 opposed (Sunstrum), and 2 abstentions (Cochran and Dorman).</p> <p>(3) ACET agreed that DTBE, as the lead of the Federal TB Task Force, will provide periodic updates on the status of implementing the 2010 TB Elimination Plan. CDC’s federal partners and non-governmental organizations will be invited to the next meeting to present updates to ACET: NIH, USAID, Gates Foundation and the Treatment Action Group (TAG).</p>
<p>(1) ACET’s input on essential issues to consider for TB elimination in developing training and educational materials to increase knowledge of health equity concepts.</p> <p>(2) ACET’s input on key issues to achieve</p>	NCHHSTP Office of Health Equity	ACET agreed to invite the new DTBE Health Equity Coordinator to the next meeting to provide a more focused overview of health equity issues in the context of TB elimination. ACET will formulate recommendations at that time.

Request for Advice from ACET	Requester	ACET Response
health equity for TB elimination at state and local levels and specific strategies to operationalize to achieve health equity for TB elimination.		

Topic 2: Draft ACET Meeting Minutes

Ms. Cole entertained a motion for ACET to approve the previous meeting minutes. A motion was properly placed on the floor by Ms. Jennifer Cochran and seconded by Dr. Ana Alvarez for ACET to approve the previous meeting minutes.

The motion for ACET to adopt the Draft June 9-10, 2014 Meeting Minutes was tied with 5 members in favor and 5 abstentions by the new members: Armitige, Houpt, Lauzardo, Sunstrum and Warshauer.

Topic 3: ACET Report to the HHS Secretary (2011-2013)

Ms. Cole informed the new members that ACET discussed its Report to the HHS Secretary (2011-2013) during the previous meeting. The HHS Secretary sent a letter to CDC acknowledging receipt of the report. Ms. Cole asked ACET to propose next steps in this regard.

Dr. Dean emphasized that progress on implementing the recommendations in ACET's report has been delayed due to changes in leadership within the Office of the HHS Secretary and the ebola outbreak. She advised the Chair to send a follow-up letter to the new HHS Secretary to request a meeting to discuss ACET's report. The report should be attached to the letter.

ACET proposed several topics that should be prioritized in Ms. Cole's meeting with the HHS Secretary.

- TB drug shortages
- TB in correctional settings
- Scale-up of LTBI treatment
- TB funding in the context of the role of ACA in TB elimination
- TB disparities and health equity issues
- TB in foreign-born populations

- The lack of progress on implementing recommendations in the 2000 IOM TB elimination report
- The importance of maintaining a strong public health infrastructure in light of the ebola outbreak
- Alignment of TB issues with the overarching vision, strategic direction and priorities of the HHS Secretary

Dr. Dean reminded ACET of its previous suggestion for the Chair to attend a briefing with Dr. Frieden or his designee after each meeting to summarize key outcomes and elevate the importance of TB at the level of the CDC Director. To advance this suggestion, Dr. Dean confirmed that she would schedule a briefing with Ms. Cole and Dr. Frieden after the March 2015 ACET meeting. If Dr. Frieden is unavailable, Ms. Cole will meet with Dr. Ileana Arias, Principal Deputy Director of CDC.

Topic 4: TB Research Agenda

Dr. LoBue reported that the DTBE Research Workgroup has completed three key tasks since the previous ACET meeting: developed an inventory of ongoing and emerging research projects, formed an internal research oversight board, and identified existing gaps in TB research. The oversight board currently is fulfilling its charge of reviewing DTBE's entire TB research portfolio and ranking individual projects by their level of priority for inclusion in the research agenda.

Dr. LoBue noted that additional tasks need to be completed before the TB research agenda can be finalized, such as hiring a new DTBE Associate Director for Science and conducting an external peer review of the draft research agenda with at least one ACET member and other external experts. Dr. LoBue confirmed that he would notify Dr. Dean when the draft TB research agenda could be presented to ACET for review and comment.

Topic 5: New TB Nurse Consultant

Ms. Cole informed the new members that ACET presented the concept of a resolution during the previous meeting for CDC to hire a new TB Nurse Consultant (TBNC). The important role of a TBNC in DTBE was emphasized, but ACET acknowledged that advising CDC on personnel decisions was outside the scope of its advisory role.

Topic 6: ACET's New Organizational Structure

Ms. Cole moderated ACET's discussion on its new organizational structure in terms of more systematically tracking its formal guidance and action items to CDC, responding to CDC's requests for advice in a timelier manner, and convening in-person meetings versus webinars.

- The Agenda Setting Workgroup is to be commended. The current agenda was extremely responsive to ACET's requests for future agenda items, particularly the series of presentations on the TB drug supply in the United States.
- The new part of the Business Session for ACET to strategically respond to CDC's requests for advice was tremendously helpful. This new process will strengthen ACET's advisory role in providing CDC with the most helpful and useful guidance to advance toward TB elimination.
- Efforts to schedule regular briefings with the CDC Director or his designee and meet with the HHS Secretary will be valuable in promoting the "Think TB" concept at high levels of government.
- Ms. Cole's succinct summary of key points and outcomes from the day 1 presentations are enormously helpful for the ACET members to prepare for the Business Session.
- The change in the schedule that allowed the five new members to attend their first meeting in person rather than by webinar will increase ACET's overall effectiveness in the future.
- CDC should ensure that new members are provided with important materials in advance of attending their first meeting. For the current meeting, for example, the new members should have been given the June 9-10, 2014 minutes, ACET Report to the HHS Secretary (2011-2013), the 2010 TB Elimination Plan, and the USPSTF Final Research Plan on LTBI.
- ACET should continue its efforts to convene two in-person meetings and one webinar per fiscal year. Webinars should be held in conjunction with other events that will be well attended by ACET members, such as the annual NTCA meeting. An additional webinar should be incorporated into the meeting schedule in order for ACET to maintain momentum on TB elimination, particularly the six months between the June and December meetings.
- CDC should hold ACET meetings by video conferencing because this technology is vastly superior to webinars. Moreover, *ex-officio* members count toward a quorum and could meet at an HHS facility in the DC metropolitan area to attend ACET meetings by video conferencing.

Drs. Dean and LoBue responded to some of ACET's suggestions. DTBE has no authority to change federal policy of convening only one in-person meeting per fiscal year. All of CDC's Federal Advisory Committees likely would make the same request if an exception was made for

ACET. CDC will switch to a new technology platform in 2015, but the capability of utilizing video conferencing rather than webinars is unknown at this time.

Topic 7: Potential ACET/BARDA Collaboration

Ms. Donna Wegener, Executive Director of NTCA, reported that efforts have been underway for the past year to build collaboration between ACET and BARDA. NTCA, TAG, the American Thoracic Society, and the Association of State and Territorial Health Officials met with Dr. Robin Robinson, Director of BARDA, in 2013 to raise the visibility of TB preparedness and drug shortage issues. Dr. Robinson expressed an interest in increasing the focus on TB, but was uncertain whether TB was in BARDA's current purview.

Dr. Robinson noted the restrictions in initiating new activities because President's Executive Orders and the HHS Secretary define and establish BARDA's focus and agenda. DTBE and the Infectious Diseases Society of America joined the other professional societies in attending a follow-up meeting with BARDA after a new Executive Order, "Combating Antibiotic-Resistant Bacteria," was released in September 2014. The purpose of the follow-up meeting was to emphasize the critical need to incorporate MDR-/XDR-TB into the BARDA agenda.

Dr. Robinson clarified that a directive from the HHS Assistant Secretary for Health (ASH) would allow BARDA to refocus or reframe a portion of its agenda to include "reemerging" public health issues. TB would be included on this list. ACET was mentioned as a potential mechanism to make the formal request to ASH to allow BARDA to expand its focus.

Chair's call for a vote	Motion properly made by Dr. James Sunstrum for ACET to request that the HHS Assistant Secretary for Health direct BARDA to address MDR-/XDR-TB treatment issues. Motion seconded by Dr. Robert Horsburgh, Jr.
Outcome of vote	Motion unanimously passed by 10 ACET voting members
Next steps	Ms. Cole will convey the request in the same letter that will be sent to the HHS Secretary to schedule a meeting to discuss ACET's report.

Topic 8: Agenda Items

Ms. Cole led ACET in a review of the status of 7 new agenda items that were proposed during the previous meeting. Topics 2, 3 and 4 were presented during the current meeting.

- Topic 1, development of a new Global TB Drug Resistance Database, would be placed on a future agenda.
- Topic 5, HRSA's role in TB elimination, would be placed on a future agenda, but would be expanded beyond HRSA.
- Topic 6, the TB cascade of care, was not revisited.
- Topic 7, national LTBI reporting, would be tabled until the LTBI Workgroup presented its draft recommendations to ACET.

For the current meeting, Ms. Cole noted that ACET proposed several new agenda items during its responses to CDC's previous requests for advice. She opened the floor for ACET to request additional items to place on future agendas.

NEW AGENDA ITEMS	
Presenter(s)	Topic
(DTBE) Dr. Philip LoBue	1. Status report on DTBE's meeting with TB controllers on potential strategies to scale-up TB treatment, particularly for high-risk populations
(DTBE) Dr. Philip LoBue	2. Update on TB drugs in the pipeline
NTCA	3. The impact of funding cuts on TB programs in the field
Select TB Programs & National Organizations	4. Overview of best practices to engage communities in addressing TB in foreign-born populations
ACET Membership	5. Discussion on strategies to publicize the importance of the nursing role in TB control and emphasize the need for a national nursing presence

Topic 9: Action Items

Ms. Cole noted that ACET addressed and obtained status reports on action items 1, 3, 6 and 7 from the previous meeting. Action items 2, 4 and 5 were the responsibility of former or absent ACET members. She planned to follow-up with these individuals to determine whether the action items had been completed.

For the current meeting, Ms. Cole noted that ACET proposed several new action items during its responses to CDC's previous requests for advice. She opened the floor for ACET to request additional tasks.

ACTION ITEMS	
Responsibility	Action Step
DTBE (Ms. Suzanne Marks)	1. Provide the LTBI Workgroup with LTBI test results that DTBE collected from private-sector databases
ACET Committee Management Specialist	2. Provide the five new members with the ACET Report to the HHS Secretary (2011-2013) [completed during the meeting] and the USPSTF Final Research Plan on LTBI
ACET Chair	3. Reestablish the Agenda Setting Workgroup with new members <ul style="list-style-type: none"> • Ms. Barbara Cole, chair • Dr. Lisa Armitige • Dr. Robert Horsburgh, Jr. • Dr. Michael Lauzardo [Completed during the meeting]
Agenda Setting Workgroup	4. Propose strategies to maximize the effectiveness and productivity of ACET meetings that are held via webinar during the next teleconference in early January 2015
ACET Committee Management Specialist	5. Circulate an e-mail message to inform ACET when the public comment period is opened on the USPSTF Final Research Plan on LTBI

Public Comment Session

Donna Wegener

Executive Director

National Tuberculosis Controllers Association

Ms. Wegener made the following comments for ACET's consideration. Nurses are the driving force of TB control programs. A new TB Nurse Consultant (TBNC) position in DTBE would be extremely important to TB programs in the field in terms of having a nursing perspective and a voice at federal, state and local levels. Ideally, the TBNC would be housed in the DTBE Field Services and Evaluation Branch. NTCA is willing to support a national nurse presence if a professional society is a more appropriate or feasible option for the TBNC position than a federal agency.

Closing Session

The next three ACET meetings are tentatively scheduled for March 3, 2015 (a webinar), June 2, 2015 (a webinar), and December 1-2, 2015 (an in-person meeting in Atlanta or a webinar). Based on ACET's comments, CDC confirmed that the December 2015 meeting would be rescheduled due to a conflict with the International Union Against Tuberculosis and Lung Disease conference.

With no further discussion or business brought before ACET, Ms. Cole adjourned the meeting at 12:13 p.m. on December 3, 2014.

Dr. Dean will publish a *Federal Register* notice to inform the public that ACET concluded its business before 2:30 p.m. as noted on the published agenda. The notice also will confirm that the ACET Chair opened the public comment session at 12:10 p.m. rather than at 2:20 p.m. as noted on the published agenda.

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

Date

Barbara Cole, RN, MSN, PHN
Chair, Advisory Council for the
Elimination of Tuberculosis



Participants' Directory

ACET Members Present

Ms. Barbara Cole, Chair
 Dr. Ana Alvarez
 Dr. Lisa Armitige
 Ms. Jennifer Cochran
 Dr. Susan Dorman
 Dr. Robert Horsburgh, Jr.
 Dr. Eric Houpt
 Dr. Michael Lauzardo
 Dr. James Sunstrum
 Dr. David Warshauer

ACET Ex-Officio Members Present

Dr. Naomi Aronson
 Department of Defense

Dr. William Baine
 Agency for Healthcare Research and Quality

Dr. Michael Bartholomew
 (Alternate for Dr. Susan Karol)
 Indian Health Services

Dr. Amy Bloom
 U.S. Agency for International Development

CDR Edward Chin
 United States Marshals Service

Ms. Marla Clifton
 (Alternate for Dr. Gary Roselle)
 U.S. Department of Veteran Affairs

Dr. Diana Elson
 U.S. Immigration and Customs Enforcement

Ms. Caroline Freeman
 U.S. Department of Labor,
 Occupational Safety and Health
 Administration

Dr. Nadine Gracia
 Office of Minority Health
 U.S. Department of Health and Human
 Services

Dr. Mamodikoe Makhene
 National Institute of Allergy and Infectious
 Diseases, National Institutes of Health

Ms. Marlene Matosky
 (Alternate for Dr. Rupali Doshi)
 HIV/AIDS Bureau, Health Resources and
 Services Administration

Dr. Chana Rabiner
 Substance Abuse and Mental Health
 Administration

Dr. Susan Robilotto
(Alternate for Dr. Rupali Doshi)
HIV/AIDS Bureau, Health Resources and
Services Administration

ACET Ex-Officio Members Absent

Ms. Sarah Bur
Federal Bureau of Prisons

Dr. Rupali Doshi
HIV/AIDS Bureau, Health Resources and
Services Administration

Dr. Susan Karol
Indian Health Service

Mr. Stephen Martin
National Institute for Occupational Safety
and Health

Dr. Sheldon Morris
U.S. Food and Drug Administration

Dr. Gudelia Rangel
Mexico Section, U.S.-Mexico Border Health
Commission

Dr. Gary Roselle
U.S. Department of Veteran Affairs

Dr. Bruce San Filippo
U.S. Section, U.S. Mexico Border Health
Commission

ACET Liaison Representatives Present

Dr. Shama Ahuja
Council of State and Territorial
Epidemiologists

Dr. Robert Benjamin
National Association of County and City
Health Officials

Dr. John Bernardo
National Tuberculosis Controllers
Association

RESULTS

Mr. Kenyon Farrow
(Alternate for Ms. Colleen Daniels)
Treatment Action Group

Dr. Amee Patrawalla
American College of Chest Physicians

Dr. Susan Ray
Infectious Disease Society of America

Dr. Randall Reves
International Union Against TB and Lung
Disease

Ms. Tara Wildes
National Commission on Correctional
Health

ACET Liaison Representatives Absent

Ms. Colleen Daniels
Treatment Action Group

Dr. Fran du Melle
American Thoracic Society

Dr. Mayleen Ekiek
Pacific Island Health Officers Association

Mr. Eddie Hedrick
Association for Professionals in Infection
Control and Epidemiology

Dr. Ilse Levin
American Medical Association

Dr. Saul Levin
Association of State and Territorial Health
Officials

Mr. John Lozier
National Coalition for the Homeless

Ms. Eileen Napolitano
Stop TB USA

Dr. Howard Njoo
Public Health Agency of Canada

Dr. Jennifer Rakeman
Association of Public Health Laboratories

Dr. Michael Tapper
Society for Healthcare Epidemiology of
America

Dr. Lornel Tompkins
National Medical Association

ACET Designated Federal Officer

Dr. Hazel Dean
NCHHSTP Deputy Director

CDC Representatives

Ms. Leeanna Allen
Mr. Gustavo Aquino
Mr. Glen Christie
Ms. Ann Cronin
Mr. Justin Davis

Dr. Wayne Duffus
Ms. Teresa Durden
Ms. Maria Fraire-Sessions
Dr. Christine Ho
Dr. John Jereb
Dr. Awal Khan
Ms. Kathryn Koski
Ms. Ann Lanner
Dr. Philip LoBue
Ms. Suzanne Marks
Ms. Margie Scott-Cseh
Dr. Neha Shah
Dr. Andrew Vernon
Dr. Richard Wolitski

Members of the Public

Mr. Sahil Angelo
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Dr. Phillip Nieburg
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Studies

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Glossary of Acronyms

3HP	Three-month, once-weekly Isoniazid/Rifapentine
ACA	Affordable Care Act
ACET	Advisory Council for the Elimination of Tuberculosis
ANDA	Abbreviated New Drug Application
ASH	Assistant Secretary for Health
BARDA	Biomedical Advanced Research and Development Authority
BCG	Bacillus Calmette-Guérin
BDQ	Bedaquiline
BLAs	Biologics License Applications
CBOs	Community-Based Organizations
CDC	Centers for Disease Control and Prevention
DFO	Designated Federal Officer
DHAP	Division of HIV/AIDS Prevention
DOT	Directly Observed Therapy
DSS	Drug Shortage Staff
DTBE	Division of Tuberculosis Elimination
FBPs	Foreign-Born Persons
FDA	U.S. Food and Drug Administration
FDASIA	FDA Safety and Innovation Act
FLDs	First-Line Drugs
GDF	Global Drug Facility
HHS	U.S. Department of Health and Human Services
HRSA	Health Resources and Services Administration
IGRAs	Interferon Gamma Release Assays
INH	Isoniazid
IOM	Institute of Medicine
LTBI	Latent TB Infection
MDR-TB	Multidrug-Resistant TB
NCHHSTP	National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
NDA	New Drug Application

NHANES	National Health and Nutrition Examination Survey
NIH	National Institutes of Health
NTCA	National Tuberculosis Controllers Association
NYC	New York City
OD	Office of Director
OHE	Office of Health Equity
PEPFAR	President's Emergency Plan for AIDS Relief
PRVs	Priority Review Vouchers
QIDP	Qualified Infectious Disease Product
RTMCCs	Regional Training and Medical Consultation Centers
SDH	Social Determinants of Health
SLDs	Second-Line Drugs
TAG	Treatment Action Group
TB	Tuberculosis
TBI	TB Infection
TBNC	TB Nurse Consultant
TST	Tuberculin Skin Test
USAID	U.S. Agency for International Development
USPSTF	U.S. Preventive Services Task Force
WHO	World Health Organization
XDR-TB	Extensively Drug-Resistant TB