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 11-12, 2018
Atlanta, Georgia

Record of the Proceedings

TABLE OF CONTENTS

Page

Minutes of the Meeting 1
Opening Session: December 11, 2018 1
Overview of the DTBE-Funded Demonstration Project on LTBI Testing and Treatment 3
Overview of the CDC/DVH Hepatitis B Virus (HBV) Campaign 8
Update on DTBE's Communications Messaging and Campaigns 13
DTBE Director's Report 18
LTBI Treatment: Insights from Human Immunology Studies and Opportunities for Collaboration 22
Update on the *Guidelines for the Treatment of Latent TB Infection* 25
Update on the Draft Treatment of Drug-Resistant TB Guidelines 29
NCHHSTP Office of the Director's (OD) Report 34
Preparation for the ACET Business Session 36
Opening Session: December 12, 2018 37
Update by the Essential Components Workgroup 37
Update by the Congregate Settings Workgroup 38
Update by the Child and Adolescent Workgroup 38
Update by the LTBI Workgroup 39
Update by the TB Drug Supply Workgroup 39
CDC Office of Infectious Diseases Board of Scientific Counselors 41
ACET Business Session 42
Business Item 1: Approval of Previous ACET Meeting Minutes 42
Business Item 2: ACET Vote on the New LTBI Workgroup Charge 42
Business Item 3: Advice Requested from ACET 43
Business Item 4: ACET Vote on the TB Drug Supply Letter 45
Business Item 5: Proposed Public Charge Rule 47
Business Item 6: HHS Secretary's Response to ACET 48
Business Item 7: Future Agenda Items 48
Public Comment Session 49
Closing Session 50
Attachment 1: Participants' Directory 51
Attachment 2: Glossary of Acronyms 54

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ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
December 11-12, 2018
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 11-12, 2018 at the CDC Corporate Square Campus, Conference Room 1A/B/C, in Atlanta, Georgia.

ACET is formally chartered under the Federal Advisory Committee Act (FACA) to provide advice and recommendations to the HHS Secretary, HHS Assistant Secretary for Health, and CDC Director regarding the elimination of tuberculosis (TB). The charter authorizes ACET to make recommendations regarding policies, strategies, objectives and priorities; address the development and application of new technologies; provide guidance and review on CDC's TB Prevention Research portfolio and program priorities; and review the extent to which progress has been made toward TB elimination.

Information for the public to attend the ACET meeting in person or participate remotely via webinar or teleconference was published in the *Federal Register* in accordance with FACA regulations and rules. All sessions of the meeting were open to the public (*Attachment 1: Participants' Directory*).

Opening Session: December 11, 2018

Hazel Dean, ScD, DrPH (Hon), MPH, FACE
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 confirm the attendance of the ACET voting members, *ex-officio* members, and liaison representatives. She announced that ACET meetings are open to the

public and all comments made during the proceedings are a matter of public record. She informed 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.

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
Robert Belknap, MD (Denver Metro Tuberculosis Control Program)	Recipient of federal funding from CDC for the Tuberculosis Epidemiologic Studies Consortium (TBESC) and the Tuberculosis Trials Consortium (TBTC)
Barbara Cole, RN, MSN, PHN (Riverside County Department of Public Health)	No conflicts disclosed
Jennifer Flood, MD, MPH (California Department of Public Health)	No conflicts disclosed
David Horne, MD, MPH (University of Washington School of Medicine)	No conflicts disclosed
Robert Horsburgh, Jr., MD, MUS (Boston University School of Public Health)	Recipient of federal funding from CDC for TBESC, TBTC, and the NCHHSTP Prevention Epidemiologic and Economic Modeling Agreement
Lixia Liu, PhD, MP, (ASCP), D(ABMM) (New Mexico Department of Health)	Recipient of federal funding from CDC for the TB Cooperative Agreement (CoAg)
Jeffrey Starke, MD (Baylor College of Medicine)	Member of the Otsuka Pharmaceutical Company Data Safety Monitoring Board for pediatric studies of Delamanid

Dr. Dean confirmed that the 18 voting members and *ex-officio* members in attendance (or their alternates) constituted a quorum for ACET to conduct its business on December 11, 2018. She called the proceedings to order at 10:00 a.m. and welcomed the participants to the ACET meeting.

Dr. Dean made several announcements regarding the changes that have occurred in ACET's membership since the previous meeting in August 2018.

- CDR Geri Tagliaferri will serve as the alternate *ex-officio* member for the U.S. Department of Homeland Security (DHS), U.S. Immigration and Customs Enforcement (ICE) in the absence of Dr. Diana Elson.
- CDC sent a letter to the Association of Public Health Laboratories with a request to identify a new liaison representative to replace Dr. Jennifer Rakeman.
- CDC sent a letter to the Agency for Healthcare Research and Quality with a request to identify a new *ex-officio* member to replace Ms. Kali Crosby.
- CDC sent a letter to the HHS Office of Global Affairs with a request to identify a new *ex-officio* member for the U.S. Section of the U.S.-Mexico Border Health Commission.

- CDC sent a letter to the Health Resources and Services Administration (HRSA) with a request to identify a new *ex-officio* member.

Barbara Cole, RN, MSN, PHN, ACET Chair
TB Controller
Riverside County (California) Department of Public Health

Ms. Cole also welcomed the participants to the ACET meeting. She explained that the meeting was called to order 1.5 hours later than the time on the published agenda due to inclement weather. To accommodate all of the agenda items, she announced that the formal presentations would begin at 10:00 a.m. as scheduled. However, the two preceding updates by the NCHHSTP Office of the Director and the DTBE Director would still be presented later during the meeting.

Ms. Cole concluded her opening remarks by reviewing the key agenda items.

- Several presentations would address ACET's ongoing focus on issues related to latent TB infection (LTBI), including an LTBI demonstration project in Lynn, Massachusetts; DTBE's LTBI communication and messaging campaign; human immunology studies on LTBI treatment; and a draft of the new *LTBI Treatment Guidelines*.
- The Division of Viral Hepatitis (DVH) would make a presentation in direct response to ACET's previous request to learn about the experiences, lessons learned, and successes of the other NCHHSTP divisions that potentially could be applied to TB. During the August 2018 ACET meeting, for example, the Division of HIV/AIDS Prevention (DHAP) described its strategy of adopting HIV treatment as prevention.
- Day 2 of the meeting would be devoted to updates by the ACET workgroups and the ACET Business Session.

Overview of the DTBE-Funded Demonstration Project on LTBI Testing and Treatment

Jennifer Cochran, MPH
TB Program Manager
Director, Division of Global Populations and Infectious Disease Prevention
Massachusetts Department of Public Health

Advice requested from ACET by DTBE:
1. What are the lessons learned from the LTBI demonstration project?
2. How can CDC and state programs use the findings from the LTBI demonstration project to expand partnerships with Community Health Centers (CHCs) and testing and treatment programs?

Ms. Cochran presented an overview of a DTBE-funded demonstration project that aimed to scale-up LTBI testing and treatment in a CHC environment. CDC issued a Notice of Funding Opportunity (NOFO) in March 2016 that provided a clear framework to conduct the LTBI demonstration project. First, the grant recipient would demonstrate a feasible, scalable program to expand LTBI testing and treatment within a defined high-risk community. Second, the grant recipient would intensify community-based efforts, independent of contact investigations or other routine public health activities, to locate and treat high-risk people with LTBI or exposure

to infectious TB. Third, the grant recipient would implement targeted testing and treatment to prevent future TB cases.

CDC outlined ambitious goals in the NOFO. Most notably, the grant recipient would be required to complete the demonstration project in a short, three-year time frame from September 30, 2016-September 29, 2019. The grant recipient would be required to test 2,500 additional people per year and identify approximately 500 people per year who were positive for LTBI. The language in the NOFO defined "high-risk populations" as those with an LTBI prevalence rate of 20 percent. The grant recipient also would be required to achieve high evaluation and treatment outcomes, such as a treatment acceptance rate of 90 percent and a treatment completion rate of 80 percent. Moreover, the grant recipient was expected to achieve the evaluation and treatment outcomes with short-course regimens, such as a 12-dose regimen of isoniazid/rifapentine (3HP) or a four-month regimen of rifampin (4R).

CDC awarded the CoAg for the LTBI demonstration project to the Massachusetts Department of Public Health (MDPH) at funding of $500,000 per year for three years. MDPH selected the Lynn Community Health Center (LCHC) in Lynn, Massachusetts as the setting to conduct the project. LCHC is a Federally Qualified Health Center (FQHC) that has a "high-risk population" based on CDC's definition. Of approximately 40,000 LCHC patients, 82 percent are minorities; 59 percent speak a language other than English; and 94 percent live at or below 200 percent of the Federal Poverty Level.

MDPH established five workgroups to guide the LTBI demonstration project and maintain clear communications among concurrent activities. The "Clinical Workgroup" is responsible for overseeing the overall workflow of the demonstration project as well as implementing and achieving CDC's LTBI testing and treatment requirements. The "EMR/IT/DATA Workgroup" (i.e., Electronic Medical Record/Information Technology/Data) is responsible for collecting, managing, and analyzing data.

The "Community Engagement Workgroup" is responsible for conducting outreach to engage the family and community members of LTBI patients who are enrolled in the demonstration project. The "Education Workgroup" is responsible for educating key audiences on LTBI, including clinicians and other providers, non-clinical staff, patients, and community members. The "Evaluation Workgroup" is responsible for conducting formal assessments at various time points over the course of the three-year demonstration project.

Ms. Cochran presented a flowchart to illustrate MDPH's three major points of intervention in the LTBI demonstration project.

Use Primary Care Teams to conduct LTBI risk assessment testing

- Determine whether results of the interferon gamma release assay (IGRA) or tuberculin skin test (TST) are positive
- Document negative test results in the patient's electronic medical record (EMR)

Use the patient's EMR to provide regular updates and facilitate communications between the Primary Care and TB Teams (for positive test results)

- Order a chest X-ray
- Refer the patient to the TB Team

Use the TB Team for direct follow-up with the patient

- Ensure that follow-up with the patient includes a chest X-ray, evaluation, education, treatment/directly observed therapy (DOT), and adherence support
- Ensure adequate TB Team staffing: two physicians, one nurse, one patient navigator, two community health workers (CHWs), and one project manager

The data collection design of MDPH's LTBI demonstration project is summarized as follows. LCHC uses an EMR system. The goal was to use data already collected in the EMR system for LTBI surveillance and make modifications as needed. The 55 high-priority fields for LTBI surveillance that MDPH and LCHC jointly identified are now extracted and electronically transmitted to MDPH. The high-priority fields include demographics, LTBI test results, and LTBI treatment outcomes. EMR modifications are available to other users of the Oregon Community Health Information Network (OCHIN) EPIC system.

LCHC created a TB flowsheet to collect data that are not found in core EMRs in structured fields (e.g., reasons for not initiating treatment or health outcomes at the completion of treatment). Data are automatically extracted from LCHC's EMRs on a biweekly basis, transmitted to MDPH via a secure mailbox, and processed and uploaded into the MDPH surveillance system. This data process allows MDPH to develop and distribute aggregate reports to its project partners, ensure the accuracy of the information, and monitor progress in the field.

Ms. Cochran presented preliminary data that MDPH has collected to date from the LTBI demonstration project, but she emphasized three key disclaimers. First, the data are "live" and updated every two weeks. Second, the dataset is still not "clean" at this point due to errors in data collection, addition of the TB flowsheet at the halfway point of the project period, and discrepancies in definitions between the EMRs and surveillance data. Third, the quality assurance and improvement processes are ongoing.

LCHC has been successful in scaling up TB testing to date. LTBI risk assessment and testing are implemented at the primary care team level with a focus on non-U.S.-born people/populations (USBP). The increase in testing from quarter (Q) 1 to Q7 of the project is all in the increased use of IGRA. LCHC has consistently reported a 15 percent positive TB infection rate.

Of the 5,327 patients who were tested for LTBI in Q1 to Q6 of the demonstration project, 64 percent were female (by gender); 61 percent were Hispanic (by ethnicity); and 40 percent were White (by race). Due to data quality issues across the LCHC EMR, however, race was not known for 19 percent of patients who were tested. Of the 775 patients who had a positive test result, 61 percent were females (by gender); 51 percent were non-Hispanics (by ethnicity); and 46 percent were African American (by race).

Of all 499 patients who initiated treatment, 59 percent were females (by gender); 51 percent were Hispanics (by ethnicity); and 46 percent were African American (by race). Of all 336 patients who completed treatment, 56 percent were females (by gender); 52 percent were Hispanics (by ethnicity); and 48 percent were African American (by race).

In addition to these demographics, the country of origin also was reviewed. Of all 5,327 patients who were tested for LTBI, the top five countries of birth were the Dominican Republic (24 percent), Guatemala (20 percent), Haiti (4 percent), Nigeria (3 percent), and El Salvador (3

percent). Although only 4 percent of patients tested were from Haiti, patients from this country accounted for 12 percent of positive test results.

The care cascade was based on six key components for each patient: positive screening result, chest X-ray, evaluation, treatment eligibility, treatment initiated, and treatment completed. To monitor progress over time, the components of the care cascade were compared using six-month cohorts (i.e., two quarters). Volume increases were reported for all six components from Q1-Q2 to Q3-Q4. With the exception of the treatment completion rate, increases were reported for all of the other five components from Q3-Q4 to Q5-Q6. However, data analysis of the treatment completion rate has not yet been completed.

A treatment regimen variable was included in the project design to address challenges with extracting medication data from the EMR. Of 350 patients who initiated treatment and have reportable data, 80 percent are on short-course regimens: 4R (57 percent) and 3HP (23 percent). The remaining 18 percent of patients are on a nine-month regimen of isoniazid (INH), generally due to drug-drug interactions. Of all 499 patients who initiated treatment, 67 percent completed therapy and 20 percent are still on therapy. The following factors accounted for the remaining 13 percent of treatment outcomes: discontinued by the patient (4 percent), adverse reaction (3 percent), discontinued by a clinician (2 percent), unknown reason (2 percent), lost (2 percent), and relocated (less than 1 percent).

Overall, the outcomes of the LTBI demonstration project to date in a CHC environment are higher than in TB clinics. Most notably, the 12-dose regimen in the LCHC patient population played a major role in the successful uptake of the short-course regimens. Other key accomplishments were due to specific components of the patient-centered care model, such as time devoted to teaching, flexibility in DOT visits, and the engagement of CHWs and a patient navigator on the TB Team to support patients. In Q1-Q4 of the project, 77 percent of patients with IGRA- or TST-positive results who initiated therapy have a documented record of treatment completion. In Q5-Q6, 88 percent of patients completed treatment or are still on therapy.

Ms. Cochran presented two posters in English and Spanish that are displayed in LCHC to increase patient/community awareness of TB. The posters include simple, positive messages: (1) “Getting tested and treated for TB infection can help keep you and your family healthy.” (2) “Getting tested and treated is easier than in the past.” (3) “New tests and treatments are available.” Efforts are underway to test other messages and obtain more feedback to design posters in additional languages.

Several community education and awareness projects were successfully launched as part of the LTBI demonstration project. A Community Advisory Board was established with representation by key agencies that serve the target population in the city of Lynn and individual community members. The board meets on a quarterly basis. Community conversations are held to provide opportunities to listen to community members discuss LTBI and consider education on this topic. English as a Second Language classes, Levels 3 and 4, are used to hold one-hour workshops on LTBI. The workshop includes a video with key messages and facilitated discussions. Education also is offered to community providers outside of LCHC, including academic detailing for primary care practices and a Continuing Medical Education update that was held in September 2018.

Ms. Cochran concluded her presentation by describing MDPH’s next steps to complete the year 3 activities of the LTBI demonstration project by September 29, 2019. The ongoing efforts

include reviewing the data on a quarterly basis to identify improvements and efficiencies; engaging the LCHC Primary Care Teams; and conducting community engagement and education activities. Because the final year of the project is underway, MDPH also will conduct new activities, such as launching planning efforts for long-term sustainability at LCHC; identifying key lessons learned from the project for replication in other CHCs; and cleaning and analyzing the final dataset. MDPH already has initiated efforts to apply lessons learned from the LTBI demonstration project to expand LTBI services in eight other CHCs in Massachusetts. MDPH also will collaborate with DTBE to conduct an economic assessment of the time and costs associated with the LTBI activities in a CHC setting.

ACET DISCUSSION: LTBI DEMONSTRATION PROJECT

Ms. Cochran provided additional details on the following topics in response to ACET's questions.

- Funding allocations of MDPH's $1.5 million award to support the LTBI demonstration project (approximately 70 percent to LCHC for staff and a significant portion to the evaluation contractor that will include the economic assessment).
- Key outcomes from the regimen data: the process LCHC used to offer 3HP versus 4R to patients; uptake of the self-administered 3HP-DOT regimen; side effects that caused 3 percent of patients to discontinue treatment; and differences in treatment completion rates between the 3HP and 4R regimens.

ACET GUIDANCE

ACET commended MDPH on its ongoing efforts to expand the LTBI demonstration project from one CHC at the local level to eight CHCs at the state level. Several members made suggestions for DTBE to consider to further scale-up the LTBI demonstration project at the national level.

- The "TB Team" model has been successfully implemented in healthcare settings outside of TB clinics to provide TB prevention, treatment, and care. DTBE should explore strategies and leverage funding with its federal partners to replicate the TB Team approach in FQHCs, primary care, and other healthcare settings throughout the country.
- DTBE and MDPH should use their upcoming economic assessment as an opportunity to highlight cost-saving measures for TB programs and CHCs. For example, the specific components of an LTBI testing and treatment program (e.g., chest X-rays, DOT, and TB drugs) that are billable and reimbursable should be identified and widely publicized.
- DTBE should reach out to its partners at the HRSA Bureau of Primary Health Care to explore the possibility of including LTBI testing and treatment as a new quality metric and incentive for FQHCs.

Dr. LoBue followed up on ACET's guidance for DTBE to scale up the LTBI demonstration project nationally. A sound proof of principle will be needed to inform the next steps in this effort, but his position was that wide-scale replication is feasible based on the preliminary data MDPH has collected and reported to date. However, important issues will need to be resolved at the outset, such as the specific needs, capacity, and resources of the local jurisdiction.

Dr. LoBue emphasized that MDPH allocated the majority of its $1.5 million award to LCHC, but dedicated CDC funding for LTBI testing and treatment will not be available to other programs. As a result, other programs will be required to rely on their existing TB CoAg funds and leverage additional state or local resources to scale-up LTBI testing and treatment. He confirmed that

DTBE would prioritize and invest in the national scale-up of LTBI testing and treatment if funds were available.

Overview of the CDC/DVH Hepatitis B Virus (HBV) Campaign

Cynthia Jorgensen, DrPH
DVH Education, Training, and Communication Team Lead
Centers for Disease Control and Prevention

Dr. Jorgensen highlighted the lessons learned from the CDC/DVH HBV campaign to reach Asian Americans and described the implications of viral hepatitis for TB control. HBV is a chronic infection that results in the premature death of one in four people from liver disease and liver cancer. HBV is treatable if the individual is diagnosed early and monitored, but the treatments are life-long and can be expensive. Moreover, HBV is a vaccine-preventable infection. Universal HBV vaccination for infants was adopted in the United States in 1991.

Current data show that one in 12 Asian Americans has chronic HBV, but 66 percent are unaware of their infection. Asian Americans represent approximately 5 percent of the U.S. population, but account for more than 50 percent of chronic HBV cases. HBV affects multiple subgroups in the Asian American population in the United States, including Chinese, Korean, Vietnamese, Cambodian, Hmong, and Laotian people. The sizes of these subgroups range from 210,000 people (Laotian) to 3.3 million people (Chinese). The percentages of non-USBP in these subgroups range from 44 percent (Hmong) to 74 percent (Korean). The percentages of people who prefer their native language in these subgroups range from 78 percent (Korean) to 92 percent (Hmong).

DVH allocates funding of approximately $5 million in total to nearly all state health departments (SHDs) in the country. Due to their small federal CoAg awards, SHDs have limited capacity, no program resources, and minimal staff to focus on HBV. Asian Americans typically have not been included as a key audience in these activities in the past because SHDs historically have targeted their efforts and resources to address hepatitis C virus (HCV).

DVH partnered with national Asian American organizations, particularly the Association of Asian Pacific Community Health Organizations and the Hepatitis B Foundation Fund, to implement a strategic plan to more effectively reach Asian Americans/Pacific Islanders (AAPIs). In collaboration with its partners, DVH released a competitive NOFO to achieve three key goals: (1) build local coalitions to reach Asian Americans in their communities; (2) provide linkage to care services; and (3) integrate these activities with other major issues facing the Asian American community.

In addition to releasing the competitive NOFO, DVH also launched other efforts to support the strategic plan. Priorities were established by identifying a subgroup of the Asian American population and limiting the number of languages to Mandarin/Cantonese, Vietnamese, and Korean. An Asian American communications firm was hired to guide the activities. Agreement was reached for CDC to serve as a centralized source to widely disseminate the high-quality materials that were developed and ensure a national presence for this initiative.

The communities of the Asian American subgroups were provided with high-quality materials in their native languages to support their local efforts. This approach struck an appropriate

balance between consolidating limited resources at CDC versus allocating small funding awards to multiple Asian American subgroups to develop materials. The multi-lingual "Know Hepatitis B™" campaign was jointly created and launched by DVH and Hep B United (HBU) in 2013 to increase testing for chronic HBV. The campaign is targeted to Asian Americans and is implemented in Chinese, Korean, and Vietnamese. A different phase of the campaign has been launched in each year since 2013.

The campaign materials were distributed to the target Asian American communities in their languages in various formats, including video and radio broadcasts of public service announcements; print advertisements; social media and digital media (e.g., buttons/badges and banner advertisements); patient education materials (e.g., posters, infographics, advertisement templates/flyers to address local needs, fact sheets, and a risk assessment card); and provider clinical tools.

DVH's approach throughout the campaign planning phase was to implement a research-, theory-, and systematically-based process, including audience analysis, formative research, theory-based message development, cultural communication expertise, pre-testing messages and strategies, and strategic channel selection. The campaign was designed to be disseminated at both national and community levels. The "audience analysis" component of the campaign allowed DVH to prioritize the three largest subgroups in the Asian American population (e.g., Chinese, Vietnamese, and Korean), maximize limited resources, balance the audience size, and identify effective outreach strategies.

DVH has identified new trends in the Asian American population based on a review of recent data. More Asian immigrants are relocating to the United States to take advantage of education and employment opportunities. The new group of Asian immigrants are younger and have a higher level of educational attainment. This trend has caused the Asian American population to have the greatest gap in income inequality of all racial/ethnic groups in the United States. For example, Asians with a socioeconomic status (SES) at the top 10 percent have incomes that are 10.7 times higher on average than those with an SES at the bottom 10 percent. Based on the current immigration pattern, more non-U.S.-born Asians are older, while U.S.-born Asians are younger.

DVH reviewed key findings from the 2015 American Community Survey to learn more about its three target audiences (Chinese, Korean, and Vietnamese) of the Know Hepatitis B™ campaign. The percentages of non-USBP in these three subgroups are 52 percent (Korean), 61 percent (Chinese), and Vietnamese (77 percent). The percentages of people who prefer their native language in these subgroups are 43 percent (Korean), 58 percent (Chinese), and 66 percent (Vietnamese).

DVH took steps to better understand its Asian American audience by integrating various research techniques into a formative study design, such as a literature review, key informant interviews, needs assessments, exploratory focus groups, media use profiles, and quantitative surveys. The goal of the formative research was to identify barriers and determinants of behavior among Asian Americans who do and do not present for HBV screening; propose potential concepts for messages; and inform the development of other necessary strategies. The formative research showed that across the individual subgroups, the Asian American population shared common misconceptions about HBV and will require additional educational efforts.

- "I'd have symptoms if I was infected."
- "Only Asians in Asia have hepatitis B. We are hygienic here."
- "It's not very serious. It's not like cancer."
- "You can get hepatitis B from sharing food."

DVH applied several theories to develop the Know Hepatitis B™ campaign messages and translated the formative research findings into theory-based messages. The individual theories included the "Social Cognitive Theory," "Precaution-Adoption Process Model," "Health Belief Model," and "Theory of Reasoned Action." The campaign messages also were matched to specific channels. Moreover, behavioral science and communication theories were implemented to enhance the acceptability and relevance of the campaign messages. The following campaign messages demonstrated that a theory-driven approach was more effective than others.

- *Credibility and Significance:* "CDC recommends Asian Americans get tested for Hepatitis B." Testing of this theory-based message showed that the Asian American community highly regards, trusts, and is fully aware of CDC.
- *Severity and Susceptibility:* "Hepatitis B is the leading cause of liver cancer for Asian Americans."
- *Call to Action:* "Ask your doctor about getting tested for Hepatitis B."
- *Outcomes:* "A lesson on Hepatitis B could save your life."
- *Knowledge and Awareness:* "Sharing food or utensils will not spread the Hepatitis B virus." Testing of this theory-based message showed that progress has been made, but baseline knowledge of HBV in the Asian American population has remained low over time.

DVH made every effort to avoid translating the materials and messages from English to another language for the Know Hepatitis B™ campaign. The Asian American communication contractor engaged native speakers and cultural experts to develop the campaign materials and messages in the native language at the outset. This approach resulted in the campaign messages and materials being effective and well received by the Asian American target audiences.

DVH implemented a six-point strategy to prioritize the materials and messages for the Know Hepatitis B™ campaign. More concepts than needed were "created." The concepts were "tested." Reactions to the concepts were "analyzed" to determine unintended consequences and identify potential areas of improvement. Concepts that performed poorly were "dropped." The concepts were "revised" as indicated. The best concepts were "selected" as campaign materials and messages. The selected materials and messages were retested whenever possible. For example, two rejected concepts were "Take a moment to get tested for Hepatitis B so you can continue making memories" and "You are looking at a big threat to you and your family."

The materials and messages of the Hepatitis B™ campaign were designed to (1) clearly communicate and provide education on modes of transmission and describe the link between HBV and liver cancer; (2) dispel myths; and (3) select channels that were matched to the communication objectives. For example, Asian American community newspapers were used to publish articles or other content requiring a longer format. A poster or flyer was used to supplement patient education materials.

DVH launched a strategic, comprehensive approach to select as many communication channels as possible that would match the media habits of the Asian American audience. All nine of the selected channels were feasible, practical, and aligned with the National Educational Campaign.

- News Media Advocacy
- Digital Media
- Public Service Advertising
- Social Media
- Collateral Materials
- Public/Private Partnerships
- Community Mobilization and Outreach
- Professional Education
- Opinion Leader Outreach

Dr. Jorgensen presented examples of the different types of products that were developed for the National Educational Campaign and distributed with a two-prong implementation strategy. DVH led the national implementation efforts by disseminating materials to in-language media outlets throughout the country and using earned media to promote stories and speakers. The National Educational Campaign was disseminated via traditional media (e.g., television, radio and print advertisements) and targeted to Asian media markets in select cities: New York/New Jersey, Los Angeles, Houston, District of Columbia, Boston, Dallas, Seattle, and San Francisco.

Digital advertisements were posted on in-language sites throughout the country. News media outreach featured interviews with speakers from HBU coalitions. In-language social media also was a key component of the national implementation strategy. To date, the National Educational Campaign has resulted in 461 million impressions with a media value of approximately $3.7 million.

HBU and other Asian American partners led the local implementation efforts to extend the reach of the campaign, support local educational and outreach activities, leverage the trust and credibility of community leaders, and provide critical testing and linkage to care. The CDC/HBU partnership resulted in a co-branded campaign that built strong endorsement at the community level.

HBU is a national coalition that receives CDC CoAg funds of approximately $270,000 per year to specifically focus on HBV. Based on testing data that the 30 HBU coalitions across 19 states have collected to date, more than 5,500 people have been screened with a median infection rate of 5.6 percent (or a range from 1-19 percent). HBU is structured as a “coalition of coalitions” to engage groups that have an interest in Asian community health issues, including TB. The HBU coalitions include academic research groups, community-based organizations (CBOs), clinics, student organizations, businesses, and health departments.

The mission of HBU is to reduce health disparities associated with HBV by increasing awareness, screening, vaccination, and linkage to care for high-risk communities across the United States. HBU has established three major goals to achieve its mission. For the “awareness” goal, HBU raises the profile of HBV and liver cancer as an urgent public health priority. For the “prevention” goal, HBU increases HBV testing and vaccination, particularly among AAPIs and other communities at higher risk. For the “intervention” goal, HBU improves access to care and treatment for individuals living with HBV to prevent end-stage liver disease and liver cancer.

HBU conducts several activities under the prevention goal to increase HBV testing. Education and training are provided to improve the ability to manage, grow, and sustain local coalitions. Capacity development is offered by using best practices to conduct and evaluate community-

based HBV screening as well as by collecting, managing, and sharing HBV-related data. Resources are disseminated to enhance the usage of linguistically and culturally competent materials, particularly those within the Hepatitis B™ campaign. Technical assistance (TA) is available to improve usage of social media and other technology. HBU conducts these activities through a range of innovative formats, including peer-to-peer mentoring, conference calls, mini-grants, webinars, journal clubs, in-person summits, toolkits, and contests.

DVH learned several valuable lessons in effectively engaging local groups. Non-traditional partners should be considered, such as organizations with a focus on other disease areas, social services groups, and local business owners. The priorities, areas of interest, and ongoing activities of these community partners should be identified to determine opportunities to share resources and provide assistance.

The assets and capabilities of local groups should be identified. For the Hepatitis B™ campaign, for example, the key assets of the local coalitions included population-based and community-specific data, community connections through existing partners and stakeholders, trust among diverse communities, and culturally and linguistically appropriate resources. Moreover, the local coalitions were able to disseminate testing, care, and treatment resources to the community; host educational events, training sessions, and webinars; secure expert speakers for events; provide advice on effectively reaching specific Asian audiences (e.g., Koreans); and building connections with other groups.

Dr. Jorgensen concluded her overview by presenting the following series of photographs.

- Community resources that were developed by the local coalitions: posters, infographics, flyers that can be easily modified with HBV testing locations in specific communities, HBV quizzes, vaccination cards, and fact sheets in 14 different languages.
- Various events in which the community resources were prominently displayed and blood was drawn for HBV testing.
- The HBU Annual Summit to promote team building, develop capacity, share resources and lessons learned, and unveil new phases of the Hepatitis B™ campaign.
- The HBU Advocacy Day with Congressional staff to raise awareness of the disease burden of HBV, positively shape policies that impact the HBV community, offer training to participants, and provide education on the importance of continued HBV funding.
    - HBU's key achievements on Advocacy Day 2017 included visiting approximately 60 Congressional members, convening a debriefing session, recognizing key community champions and policymakers, and creating a model for advocacy at the state level.

ACET DISCUSSION: CDC/DVH HBV CAMPAIGN

Dr. Jorgensen provided additional details on the following topics in response to ACET's questions.

- Measures to determine success of the Hepatitis B™ campaign, such as a higher level of knowledge and awareness of HBV; increased HBV testing and treatment rates; and the number of people tested for HBV and linked to care.
- HBU's funding from non-governmental sources, such as a large biomedical research group.
- HBU's efforts to use its holistic "coalition of coalitions" structure to incorporate LTBI testing into HBV screening in the Asian American community.

Update on DTBE's Communications Messaging and Campaigns

Nick DeLuca, PhD
Chief, DTBE Communications, Education, and Behavioral Studies Branch
Centers for Disease Control and Prevention

Advice requested from ACET by DTBE:

1. What are ACET's general comments on the presentation? Does ACET have any ideas on further promotion of the U.S. Preventive Services Task Force (USPSTF) guidelines and recommendations?
2. What is ACET's feedback on the proposed LTBI campaign and network?
3. Does ACET agree with the focus on high-priority populations (e.g. Asians and Hispanics) in light of current resources?
4. What are ACET's suggestions on the provider component of the campaign?
5. What are ACET's suggestions on the evaluation component of the campaign?

Dr. DeLuca covered two major topics in his update to ACET on DTBE's communications messaging and campaigns: (1) a proposal of an LTBI campaign and network and (2) CDC's activities to promote the USPSTF Grade B recommendation for LTBI screening that was issued in September 2016.

PROPOSAL OF AN LTBI CAMPAIGN AND NETWORK

CDC and the broader TB community have recognized for some time that expanded LBTI testing and treatment will be required to achieve the TB elimination goal in the United States. As a result, CDC and USPSTF currently recommend testing of populations that are at increased risk for LTBI, including people who were born in or frequently travel to countries where TB disease is common. Moreover, the development of targeted LTBI campaigns and collaborations with community partners can be effectively used to increase awareness of LTBI and encourage LTBI testing and treatment of at-risk populations.

DTBE is proposing to create and launch a new "Take on Latent TB Infection" campaign to expand LTBI testing and treatment. The two key goals of this effort will be to (1) target a communications campaign to encourage LTBI testing and treatment among at-risk populations and (2) build a strong partner network with at-risk communities to assist with outreach and other activities as well as to encourage LTBI testing and treatment.

DTBE will target the new LTBI campaign to two key audiences: Hispanics and Asians, including Chinese, Vietnamese, Filipino, and Indians. However, DTBE also will design a separate component of the campaign specifically for healthcare providers/personnel (HCP) who serve these at-risk populations. CDC's recent surveillance data provided a strong rationale for DTBE to select the two target audiences.

- Compared to Whites, the current TB case rates are 33 times higher for Asians and eight times higher for Hispanics.
- Of all TB cases in the United States that were reported to CDC in 2017 by race/ethnicity, Asians accounted for 36 percent and Hispanics accounted for 28 percent.
- Of all TB cases in the United States among non-USBP that were reported to CDC in 2017 by country of birth, the Philippines, India, Vietnam, and China collectively accounted for 36 percent and Mexico accounted for 19 percent.

DTBE's methodology will include developing the LTBI campaign and building the network as parallel efforts. The campaign messages will be influenced by DTBE's extensive formative research and its ongoing pilot project to test LTBI terminology and messaging with the at-risk populations. The campaign materials will be developed and translated in-language to be culturally and linguistically appropriate.

DTBE aims to achieve three major objectives with the LTBI communications campaign. First, awareness will be raised about LTBI, its risk, and the link between infection and disease to address common misperceptions, decrease stigma, and encourage LTBI testing and treatment. Second, awareness will be increased about treatment for LTBI, particularly shorter regimens. Third, providers will be encouraged to offer LTBI testing and treatment to at-risk populations.

DTBE intends to take a systematic approach to develop, launch, and disseminate the LTBI campaign with six key strategies and activities. Formative research will be conducted to increase understanding of cultural attitudes, knowledge, and practices of LTBI. The activities that will be included in the formative research are listed below:

- Literature review
- Environmental scan
- Ethnic media market and channel analyses
- Primary or secondary audience research
- Focus groups
- Key informant interviews
- Discussions with Asian and Hispanic TB leaders and HCP
- Input from community stakeholders and partners
- Needs assessment of community health and social service providers in areas with at-risk populations

A strategy and plan for the LTBI campaign will be developed based on outcomes of the formative research activities. These elements will include target audiences for the first phase of the campaign; prioritized media markets; effective messages and channels; and key stakeholders, partners, and influencers.

The creative development process will be initiated to launch the in-language development and pilot testing of materials. Creative materials, including resources for providers, will be developed for a variety of channels to best reach the target audiences. Traditional platforms will include print, television, and radio advertising, while digital platforms will include social media, video, and digital advertising.

The initial LTBI campaign will be launched and disseminated through innovative methods, such as traditional and new media channels and news media opportunities. Partnerships will be leveraged to expand the reach of the LTBI campaign and increase engagement. The campaign materials will be available for download and dissemination by partners outside of the initial target markets.

A process evaluation will be conducted through media monitoring, analyses of uptake of the campaign, and media impressions. The process evaluation will help to inform future phases of the LTBI campaign, the development of additional materials, and expansion opportunities. An outcome evaluation will be conducted to determine the impact of the LTBI campaign at specific

sites. The TBESC sites and OCHIN will be engaged to pilot the outcome evaluation at one or two select sites. The potential models will include pre-/post-evaluation of LTBI testing and/or treatment rates in select markets; evaluation of awareness of LTBI and exposure to the campaign; and knowledge assessments among the target audiences.

An LTBI network will be established as a major component of the LTBI campaign to engage communities and other partners. The network will be designed to achieve four key goals: (1) provide TA and training to the network members to conduct culturally competent outreach to the target populations; (2) build capacity to test and treat at-risk populations for LTBI; (3) share strategies, materials, and lessons learned; and (4) leverage the network membership to implement national LTBI campaigns.

The LTBI network will aim to achieve several important outcomes. Regional, state, and local organizations will increase their efforts to collaborate and share resources, strategies, and lessons learned to serve the target populations. Capacity will be increased to deliver education and outreach. LTBI testing and treatment will be increased among the target populations. The reach of and exposure to CDC's LTBI campaign will be increased.

Several strategies and activities will be implemented to support the LTBI network. The "networking" strategy will be targeted to traditional and non-traditional partners, such as CBOs, health centers, and professional associations. The network members will actively serve their respective target populations. The "capacity building" strategy will provide educational outreach to the target populations and offer TA on LTBI testing and treatment. The "campaign implementation" strategy will provide feedback on the materials and strategies of the LTBI campaign and assist with the dissemination of the campaign materials.

CDC'S ACTIVITIES TO PROMOTE THE USPSTF LTBI SCREENING RECOMMENDATION

The USPSTF Grade B recommendation for LTBI screening that was issued in September 2016 acknowledged the critical role of clinicians, health care agencies, and community organizations in TB elimination, particularly those serving at-risk populations. CDC took several actions to widely publicize the USPSTF LTBI recommendation. An online hub was created that served as a "one-stop shop" for resources, materials, and links to LTBI and USPSTF materials. Since 2016, the online hub has generated 31,629 views, 22,388 unique visitors, and 7,681 downloads.

CDC partnered with three leading medical application providers (Epocrates, Up-to-Date® Anywhere, and Medscape Mobile) to ensure that their content on LTBI screening and treatment was current. CDC also is conducting preliminary research with providers to determine the need for developing a standalone LTBI application. CDC and Medscape jointly produced and broadcast an expert commentary article and video on the USPSTF LTBI recommendation. A follow-up expert commentary article and video on the updated 3HP recommendations will be released in January 2019.

CDC targeted a video to the public, "5 Things to Know About Tuberculosis," in both English and Spanish that has generated over 44,000 views to date. The USPSTF LTBI recommendation is being promoted through various platforms, including the social media channels of CDC, DTBE, and partner organizations; articles published in peer-reviewed journals by DTBE staff; and LTBI infographics, graphics and web buttons.

CDC incorporated the USPSTF LTBI recommendation into messaging and communication efforts for related activities, such as the updated guidance on the 12-dose treatment regimen for

LTBI in June 2018 and the United Nations General Assembly High-Level Meeting on the Fight Against Tuberculosis (UN HLM) in September 2018.

CDC published the updated 3HP recommendations in the June 28, 2018 edition of the *Morbidity and Mortality Weekly Report* (*MMWR*). The *MMWR* article aimed to (1) raise awareness of the updated recommendations among clinicians and public health professionals; (2) develop new patient and clinician web content and educational materials; and (3) update existing web content and educational materials.

CDC strategically engaged clinical partners by developing a new TB partners listserv to connect with over 260 organizations and agencies that have an interest in TB topics. CDC directly reached out to the following primary care associations to widely promote the 3HP guidance and messaging through their individual networks and social media channels:

- American Academy of Family Physicians
- American Medical Association
- National Commission on Correctional Health Care (NCCHC)
- American College of Physicians
- American Academy of Pediatrics
- American Academy of Physicians Assistants
- National Hispanic Medical Association
- National Council of Asian Pacific Islander Physicians
- National Association of Community Health Centers
- American Association of Nurse Practitioners

Several trade media outlets published articles in 2018 on the USPSTF LTBI recommendation and CDC's most recent LTBI treatment guidelines, including *Monthly Prescribing Reference*, *Infectious Diseases in Children*, and *Contagion Live*. The CDC-funded TB Centers of Excellence (COEs) for Training, Education, and Medical Consultation will co-host a webinar on December 13, 2018 to provide an overview of the updated 3HP guidelines and their practical implications.

The UN HLM was convened on September 26, 2018. The meeting was only the fifth time that the United Nations has called for a high-level meeting devoted to a health issue. The meeting also served as an opportunity to showcase the commitment and achievements of the United States to domestic and global TB. CDC highlighted LTBI to showcase the domestic focus on TB, particularly its message to "expand testing and treatment for LTBI as the final frontier of TB elimination in the United States." CDC also used the UN HLM as an opportunity to publish an opinion editorial in *The Hill*, "The Time is Now for Global Commitment to Address the Leading Infectious Disease Killer: Tuberculosis."

CDC's next steps will be to continue its communication research to test LTBI messages, concepts, and terminology, including the USPSTF recommendation. The "Our Personal Stories" project will be further developed by gathering stories from people who have been tested and treated for LTBI and widely sharing this information. Efforts will be continued to integrate and promote the USPSTF LTBI recommendations in additional communication activities.

ACET GUIDANCE: DTBE'S COMMUNICATION MESSAGING AND CAMPAIGNS

- DTBE should make every effort to ensure that adequate funding and resources are leveraged to launch and widely disseminate the LTBI campaign and other communication activities as soon as possible. Several ACET members reiterated that over two years have passed since the USPSTF LTBI recommendation was issued in September 2016.
- The primary care associations that DTBE engaged in 2018 to promote the updated 3HP guidelines also should be educated on the 2016 USPSTF LTBI recommendation.
- DTBE should conduct a demonstration project of its proposed LTBI campaign, messaging, and other communication activities with civil surgeons. Civil surgeons are required to test status adjusters with an IGRA, but these providers do not routinely promote, offer education, or emphasize the importance of LTBI treatment to their patients. Moreover, a demonstration project with civil surgeons and status adjusters can be designed to measure critical outcomes.
- DTBE should fully engage state and local public health departments to ensure that the messages of the LTBI campaign are well coordinated and consistent nationally.
- DTBE should develop both general and culturally-specific tools, such as talking points or scripts, to assist providers in discussing LTBI with their routine and at-risk patient populations.
- DTBE should design the LTBI campaign to be as simple as possible to ensure that this initiative can be scaled up nationally. For example, EMRs should be utilized to accurately capture "at-risk" patients. This approach will eliminate the need for providers to make these types of decisions during a short 15-minute visit with their patients. Moreover, the HBV and emergency preparedness communities have successfully used EMRs to capture at-risk patients and destigmatize this characterization.
- DTBE should clarify the terminology in its campaign messages and communication activities by replacing "latent TB infection" with "TB infection" or "Class 2 TB." For example, "latent" is an important word in the English language to U.S. providers, but its meaning likely will not be relevant or appropriately translated to the target populations of non-USBP. DTBE's campaign messages should be created to resonate with the target audiences, such as (1) "TB infection has no symptoms, but treatment is critical to prevent the development of TB in the future" or (2) "Your Class 2 TB will progress to Class 3 without treatment." Overall, clear and understandable messaging should be the cornerstone of all aspects of the LTBI campaign, including the education, information dissemination, training, social marketing, branding, and advertising components. Culturally appropriate messaging also should be specifically developed for non-U.S.-born clinicians and other providers who will treat the target audiences.
- DTBE is commended for its direct outreach to NCCHC to promote and widely disseminate the updated 3HP guidelines. Most notably, the NCCHC membership includes hundreds of accredited facilities that test for TB among approximately 500,000 people who are in correctional settings in the United States.
- DTBE should ensure that its LTBI campaign messages are inclusive of non-USBP who legally reside in the United States at this time, but are not U.S. citizens. Trustworthy and motivational messaging will be needed to ensure that this at-risk population presents for LTBI screening without fear of deportation and has access to appropriate medical care.
- DTBE is commended for proposing an LTBI campaign with outstanding education, outreach, and health promotion components. However, DTBE should establish rigorous standards or criteria for systematic data collection and surveillance of LTBI testing and treatment outcomes in the field. Because the United States is a low incidence country,

many domestic public health programs have limited capacity in this area. DTBE has tested its Surveillance for TB Elimination Management System (STEMS) at all of the current TBESC sites, initiated discussions with non-TBESC sites, and launched preliminary efforts to include STEMS as a platform of the National Tuberculosis Controllers Association (NTCA). As a result, DTBE could use the results of the STEMS pilot to inform the development of standards for LTBI data collection and surveillance.

- DTBE should reconsider its approach of targeting some of the LTBI campaign messaging and communication activities to consumers because the general public is not at risk. Instead, attention should be solely directed to the at-risk community at both provider and patient levels. DTBE should closely collaborate with state and local health departments because these agencies have the most knowledge and best understanding of their local data, providers, and specific at-risk neighborhoods.

DTBE Director's Report

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

Dr. LoBue presented an outline of the seven key topics that he would address in the DTBE Director's report to ACET.

- CDC's fiscal year (FY) 2019 budget
- Revised Report of Verified Case of Tuberculosis (RVCT)
- 2018 "Recommendations for TB Screening and Testing of U.S. Healthcare Personnel"
- Revision of the CDC Youth Risk Behavior Survey (YRBS) to include TB questions
- Modified and new codes in the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10)
- TBTC Study 31
- U.S. Food and Drug Administration (FDA) Drug Shortages Task Force

CDC'S FY2019 BUDGET
CDC's FY2019 budget has been funded for the entire fiscal year through September 30, 2019. DTBE received level funding of $142.6 million.

REVISED RVCT
The pilot for the 2020 RVCT has been completed and the revised form has been essentially finalized. Approval by the Office of Management and Budget (OMB) is needed to comply with the Paperwork Reduction Act, but the 2020 RVCT was submitted to OMB for approval as part of the Nationally Notifiable Diseases Surveillance System package for CDC. The pilot of the message mapping guide also needs to be completed to ensure that data can be successfully transmitted from reporting areas to CDC, but this effort is underway.

DTBE expects to finalize the training plan for the 2020 RVCT by the end of December 2018. The training plan will be implemented over the course of 2019 and various training products will be offered, including a detailed instruction manual, online webinars, training courses, and other job aids for the TB reporting areas. DTBE will begin implementing the revised RVCT for reported TB cases in 2020.

2018 RECOMMENDATIONS FOR TB SCREENING AND TESTING OF HCP

The draft 2018 HCP recommendations were presented to ACET during the April 2018 meeting. Since that time, the document has been cleared by NCHHSTP and other centers; reviewed by the CDC Office of the Associate Director for Science (OADS); and revised by the authors based on the comments that were submitted. After OADS gives approval during the final clearance step, the document will be submitted for publication.

TB QUESTIONS IN THE YRBS

CDC developed the YRBS in 1991 to monitor health behaviors that contribute to the leading causes of death, disability, and social problems among youth in the United States. The NCHHSTP Division of Adolescent and School Health (DASH) administers the YRBS as a national survey to provide data that are representative of students in grades 9-12 in public and private schools in the United States. In addition to DASH's administration of the YRBS at the national level, health and education departments at state, territorial, tribal, and local levels also can conduct their individual surveys with additional questions. These surveys provide data that are representative of primarily public high school students in each jurisdiction.

ACET made a recommendation during the August 2018 meeting for DTBE and DASH to explore the possibility of adding TB-related questions to the YRBS. In response to ACET's request, DTBE is coordinating efforts with DASH leadership to develop new TB-specific questions for the YRBS and review any existing questions in the survey that address social determinants related to TB. Moreover, an opportunity exists to propose TB-related questions for both the national and local surveys in 2021. This goal can be achieved by state and local TB programs encouraging their health and education departments to include TB questions in the local surveys.

DASH administers the YRBS every two years. The 2017 survey results currently are available and the 2019 survey is being conducted in the field at this time. New TB-specific questions will need to be submitted to DASH by December 2019 to be included in the 2021 YRBS. To meet this timeline, DTBE will need to present the draft TB-related questions to ACET during the April 2019 meeting rather than the August 2019 meeting.

MODIFIED AND NEW ICD-10 CODES

A proposal for new and modified ICD-10 codes to address TB and LTBI was presented during the September 2018 meeting of the ICD-10 Coordination and Maintenance Committee. The proposal was generally "well received," but some of the requested modifications were not approved. During the public comment period that ended on November 13, 2018, all of the comments relating to TB were positive. The changes that the committee approved will be added to the master addenda and officially implemented on October 1, 2019. DTBE currently is developing a training plan in preparation of the rollout of the new and modified TB-related ICD-10 codes.

Dr. LoBue presented three tables to illustrate the new and modified TB-related ICD-10 codes that were and were not accepted.

Modifications Accepted

Change Type	ICD-10 Number	Current Code	Final Modification
Modification	Z11.1	Encounter for screening for respiratory tuberculosis	Add one inclusion term: 1. Encounter for screening for active tuberculosis disease

New Codes Accepted

Change Type	ICD-10 Number	Current Code	Final Modification
New Code	Z11.7	N/A	Encounter for testing for latent
New Code	Z86.15	N/A	Personal history of latent
Modification (Originally submitted as modification)	Z22.7	N/A	Add two inclusion terms: 1. Latent tuberculosis infection 2. LTBI Use additional codes R76.11 or R76.12 to identify positive test for tuberculosis infection*

R76.11: Non-specific reaction to the tuberculin skin test without active tuberculosis
R76.12: Non-specific reaction to cell-mediated immunity measurement of gamma interferon antigen response without active tuberculosis

Proposed Codes Not Accepted

Change Type	ICD-10 Number	Current Code	Proposed Modification
New Code	Z09.0	N/A	Encounter for follow-up examination after completed treatment for latent tuberculosis infection
Modification	Z86.11	Personal history of tuberculosis	Add: Personal history of active tuberculosis disease

TBTC STUDY 31
TBTC Study 31 is an open-label randomized controlled trial (RCT) that includes the following study design.[1]

- Standard six-month treatment regimen for drug-susceptible TB: 2HRZE/4HR
- Experimental four-month regimen 1: 2HPEZ/2HP
- Experimental four-month regimen 2: 2HPMZ/2HPM

[1]H=isoniazid, R=rifampin, E=ethambutol, Z=pyrazinamide, P=rifapentine, M=moxifloxacin

The primary outcomes of TBTC Study 31 will be TB disease-free survival at 12 months after assignment of the study treatment and a proportion of participants with grade 3 or higher adverse events during drug treatment.

Enrollment in TBTC Study 31 was completed in October 2018. The 2,516 enrolled participants exceeded the target of 2,500 patients. TBTC's partnership with the National Institutes of Health (NIH)-funded AIDS Clinical Trials Group was instrumental in achieving this goal due to its enrollment of 1,617 patients. The TBTC investigators will analyze results at key time points of Study 31: completion of the study treatment (early May 2019); analysis of the primary efficacy and safety endpoints at 12 months (first quarter in 2020); completion of the study follow-up (early May 2020); and secondary analysis of the endpoints at 18 months (fourth quarter in 2020).

FDA DRUG SHORTAGES TASK FORCE

The FDA Commissioner submitted a report to Congress to establish a task force to identify the root causes of drug shortages and advance potential long-term solutions. In addition to FDA, the task force also includes representatives from the Centers for Medicare & Medicaid Services, HHS Office of the Assistant Secretary for Preparedness and Response, Department of Veterans Affairs, and the Department of Defense.

The task force obtained input from the public by holding stakeholder listening sessions in September and October 2018 and convening a public meeting in November 2018. The task force also released a public docket that will remain open for comments until January 11, 2019. CDC representatives briefed the task force on December 4, 2018 to address drug shortages related to TB, STDs, and influenza. CDC discussed the history of shortages, previous efforts to mitigate these shortages, and gaps in current mitigation strategies. CDC also emphasized the need for solutions that are beyond stop-gap measures.

ACET DISCUSSION: DTBE DIRECTOR'S REPORT

Dr. LoBue provided additional details on the following topics in response to ACET's questions.

- DTBE's plans to address local TB programs that will encounter difficulties in updating their current electronic systems to use the revised RVCT to report TB cases to CDC beginning in 2020.

ACET GUIDANCE

- ACET should submit a letter to the HHS Secretary to express its support of long-term solutions that were proposed by the FDA Drug Shortages Task Force. The proposed solutions include the ability to import drugs during a shortage and utilization of global solutions to increase the number of TB drugs.

LTBI Treatment: Insights from

Jyothi Rengarajan, PhD
Associate Professor of Infectious Diseases
Emory University School of Medicine

Advice requested from ACET by DTBE:

1. What is the potential for collaborating or leveraging ongoing CDC studies, such as TBESC and TBTC, through research sub-studies?
2. What are ACET's suggestions on expanding the potential for TB research in the metropolitan Atlanta area?

Dr. Rengarajan presented insights on LTBI treatment from human immunology studies and described opportunities for collaboration. She began her overview by showing a graphic to illustrate the relationship between antigen-specific T-cell responses and the bacterial load in different infection states of *Mycobacterium tuberculosis* (MTB), including the clinical state, T-cell state, host-pathogen dynamic state, and bacterial state. She explained that the bacterial load is analyzed from an immunological perspective to more effectively understand MTB clearance (elimination of bacteria), MTB persistence (LTBI), and the progression to TB disease.

Emory and its partners have made strong efforts to answer two key research questions to better understand and characterize LTBI. First, what proportion of IGRA-positive asymptomatic individuals have "true" MTB infection? Second, what strategies can be used to identify people who are at highest risk for progression to or reactivation of TB disease and target treatment to those with persistent MTB infection? To address these research questions, Emory applied its existing knowledge of T-cell biology and signatures (e.g., recognized antigens, phenotypes, and functions of antigen-specific T-cells) that are associated with LTBI versus MTB clearance.

The 2015 Adekambi, *et al.* study reported antigen-specific T-cell phenotypes as readouts of bacterial load. The study identified T-cell markers on the surface of TB-specific cells that were able to distinguish between asymptomatic people with LTBI who were IGRA-positive and symptomatic people with active TB who were culture-positive. The addition of phenotypic markers increased specificity and sensitivity and also correlated with treatment response. The findings of the 2015 Adekambi, *et al.* study led Emory and its partners to conduct two research projects.

EMORY RESEARCH PROJECT 1: HUMAN STUDY

Emory and its partners launched this research project to identify MTB-specific T-cell signatures that are associated with resolved and persistent MTB infection in humans. The study was designed to achieve three major objectives: (1) examine the spectrum of antigens recognized by MTB-specific memory T-cells in untreated, asymptomatic IGRA-positive individuals; (2) determine whether a shift occurred in the breadth of antigen-specific T-cell responses following the 3HP treatment regimen; and (3) assess the stability of MTB-specific T-cell responses in the absence of treatment.

The Refugee Health Program at the DeKalb County, Georgia Board of Health administered the 3HP treatment regimen to the study participants and served as the non-endemic site. The CDC/ Kenya Medical Research Institute (KEMRI) site in Kisumu, Kenya served as the endemic

site for the study. Emory recruited refugees who recently arrived in the United States and settled in the Atlanta area. The medical histories of the study participants included QuantiFERON (QFT)-positive, HIV-negative, no TB symptoms, and normal chest X-rays.

For the 60 antigens selected for the study, Emory aimed to assess the spectrum of antigen-specific responses in whole blood, evaluate the phenotypes and functions, and analyze the transcriptional profiles in more detail. A multiple antigen response spectrum assay (MARSA) was developed for the study and was performed by Emory and KEMRI at their respective sites using fresh blood. Emory acknowledged that as a screening assay, MARSA would be unable to provide definitive information on all of the research questions. However, Emory recognized that MARSA could serve as a starting point to simultaneously examine multiple antigens.

Prior to treatment, Emory observed a diverse spectrum of MTB-specific T-cell responses among the 100 participants in the DeKalb County LTBI cohort. After the initiation of treatment, the cohort was analyzed at three-month intervals, for a total of 12 months, to identify any changes in antigen-specific T-cell responses. Moreover, heat maps were generated for 48 study participants who had data for all five time points (i.e., baseline and months 3, 6, 9, and 12). Based on these results, Emory did not observe an obvious shift in the breadth of antigen-specific T-cell responses post-treatment, but qualitative shifts in magnitude were reported.

Emory also compared the findings between Myanmar and the Congo because these two countries accounted for the largest number of study participants from the endemic site. Beginning at month 3 post-treatment, the analysis showed tremendous differences in antigen-specific T-cell responses among individuals in Myanmar and the Congo. Emory engaged its biostatisticians to perform different types of data analyses. Most notably, individual peptide pools traditionally have not had distinctive patterns. However, the new analysis of the patterns of responses to peptide pools identified 14 different clusters among 48 study participants who had data for all five time points.

Emory changed the component of its study that was designed to determine the stability of MTB-specific T-cell responses in untreated individuals with LTBI. The original plan called for the inclusion of QFT-positive household contacts at the Kisumu, Kenya site as well as QFT-positive individuals at the DeKalb County site who declined LTBI treatment. The current plan includes 32 QFT-positive household contacts from the Kisumu, Kenya site who will be followed at three-month intervals for a total of 12 months as well as a QFT-positive cohort in the larger jurisdiction of metropolitan Atlanta who declined treatment.

Preliminary data from the study show that the overall stability of MTB-specific T-cell responses has been lower at the Kisumu site. Based on the three time points of baseline, month 6, and month 12, however, major differences have not been observed in the spectrum of antigen-specific responses over time. Data collection is ongoing to determine any changes in phenotypes. Moreover, the spectrum of MTB-specific T-cell responses between the cohorts at the DeKalb County and Kisumu sites has been relatively similar at baseline prior to treatment. However, the overall magnitude of the responses at the Kisumu site has been strikingly lower. Emory believes issues other than MARSA (e.g., parasite infections or factors that modulate immune responses) are the cause of this finding.

Emory reached several conclusions for Research Project 1 based on the preliminary findings. The spectrum of MTB-specific T-cell responses to LTBI in humans is broad. The magnitude of MTB-specific responses to untreated LTBI differs by the characteristics of cohorts and

geographical areas (e.g., the DeKalb County versus the Kisumu sites). MTB-specific T-cell responses expand and contract following the 3HP treatment regimen and fall into discernable patterns.

Based on MARSA, the spectrum of MTB-specific T-cell responses to untreated LTBI will remain fairly stable over time. Further analyses of the phenotypes of these responses might identify signatures of MTB persistence and clearance. To address more complex research questions, Emory's future studies will focus on phenotypic and transcriptional profiling, stimulation of peripheral blood mononuclear cells with specific peptide pools, metabolomics, and antibody responses.

EMORY RESEARCH PROJECT 2: ANIMAL STUDY

Emory and its partners launched this research project to administer the 3HP treatment regimen for LTBI to non-human primates (NHPs). Emory's hypothesis was that the NHP model might be better suited to identify recent infection, rather than LTBI, and control TB. Indian Rhesus macaques were selected as the NHP model for the animal study and were infected with a low MTB dose of the CDC1551 strain. The infected macaques typically converted to TST or IGRA positivity between weeks 3 to 7.

In Emory's NHP model, approximately 80 percent of the macaques were asymptomatic with controlled infection, while the remaining 20 percent progressed to primary, active TB infection. "Infection control" was based on chest x-ray and the lack of clinical symptoms. Similar to Emory's LTBI study in humans, one group of macaques received 3HP and the other group received no treatment.

The overarching objective of the animal study was to determine whether LTBI treatment actually cleared MTB (i.e., no reactivation) or if MTB persisted (i.e., reactivation to active TB). The findings showed a small spike in reactivation of MTB in the untreated macaque group, but only after co-infection of simian immunodeficiency virus. Moreover, pulmonary pathology specimens showed evidence of MTB clearance in the treated macaque group and persistence or reactivation of MTB in the untreated macaque group. Overall, the treated macaque group continued to survive and did not succumb to TB disease.

Emory reached several conclusions for Research Project 2 based on the preliminary findings. The 3HP treatment regimen for LTBI was successfully established in the NHP model. The NHPs with asymptomatic LTBI had persistent MTB infection, while the 3HP treatment regimen cleared MTB infection and resolved granulomas. The NHP model can be useful in investigating new drug regimens for LTBI, including those for drug resistant-TB (DR-TB). The NHP model also has utility in validating human biomarkers of MTB infection and clearance.

ACET DISCUSSION: IMMUNOLOGY STUDIES OF LTBI TREATMENT

Dr. Rengarajan provided additional details on the following topics in response to ACET's questions.

Animal Studies

- The possibility of Emory using its macaque model to advance research on vaccine development to prevent progression to TB disease or pursuing new studies that combine TB drugs for prevention.
- Emory's plans to design and implement additional research projects in the future, such as a study to pair its macaque model with positron emission tomography/computed tomography (PET/CT).

Human Studies

- The limited impact of health conditions or clinical variables of patients (e.g., smoking and alcohol use) on the LTBI research findings.
- The proteins that were recognized by a large number of people only after LTBI treatment and the potential usefulness of these proteins as biomarkers of LTBI treatment from a diagnostic perspective.
- Emory's strong interest in collaborating with research partners in the future to conduct additional LTBI studies by following patients over time, identifying signatures for the completion of active TB treatment, and determining the rates of relapse or recurrent TB.

Update on the *Guidelines for the Treatment of Latent TB Infection*

Timothy Sterling, MD
Director, Vanderbilt Tuberculosis Center and Professor, Adult Infectious Diseases
Vanderbilt University Medical Center

Dr. Sterling presented an update on the LTBI Treatment Guidelines. The most recent guidelines were published by the American Thoracic Society (ATS) and CDC in 2000 and focused on targeted tuberculin testing and LTBI treatment. Since that time, however, the 2RZ regimen has not been recommended due to the risk of severe hepatotoxicity. Data collected after 2000 demonstrated that compared to the 6H and 9H regimens, the 3HP, 4R, and 3HR regimens are as effective, more likely to be completed, and at least as safe.[2]

Most LTBI treatment regimens have not been compared head-to-head, but a network meta-analysis was published in 2014 (Stagg, *et al.*) and updated in 2017 (Zenner, *et al.*). To fill this data gap, ATS, the Infectious Diseases Society of America (IDSA), and CDC initiated the development of updated LTBI treatment guidelines in 2011. However, ATS and IDSA withdrew from this effort in December 2016. Most notably, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria are not well suited to address key areas, such as "who to treat for LTBI" or "how to ensure treatment." The GRADE criteria were found to be a more appropriate methodology for the new guidelines due to the focus of these recommendations on the specific regimens to use to treat LTBI.

NTCA and CDC recognized the importance of the LTBI guidelines for TB practitioners in the United States and other countries. In addition, neither the World Health Organization's (WHO) 2018 LTBI guidelines nor the 2014 and 2017 network meta-analyses included recent data on the safety and effectiveness of the 4R regimen.

[2] 2RZ=2 months rifampin + pyrazinamide; H=isoniazid; 3HP=3 months isoniazid + rifapentine; R=rifampin

The guidelines committee implemented a rigorous methodology to evaluate the recommendations and evidence for the new LTBI treatment guidelines. The population/intervention/comparator/ outcomes (PICO) format was used to write the clinical question, "Which regimens have the greatest effectiveness and least toxicity?" TB disease (as a marker of effectiveness) and hepatotoxicity (as a marker of toxicity) were selected as the two key outcomes. The importance of the outcomes was rated as "critical," "important," or "not important."

The sources for the systematic literature review included MEDLINE, the Cochrane Central Register of Controlled Trials, Google Scholar, and updated 4R data that eventually were published in July 2018. GRADE criteria were used as the standardized approach to assess the quality of the evidence. GRADEpro was used to develop evidence profiles that rated the quality of the evidence as "high," "moderate," "low," or "very low."

The recommendations for a particular LTBI regimen were categorized into one of two groups. "Strong" recommendations were those in which the vast majority of patients would choose the regimen. These recommendations required at least moderate quality evidence and would be unlikely to change with further studies. "Conditional" recommendations were those in which it was uncertain if desirable consequences outweighed undesirable consequences, such as low-quality evidence for a critical outcome. Moreover, further studies might change the key findings and original intent of conditional recommendations.

GRADE evidence tables were developed to generate head-to-head comparisons of LTBI regimens evaluated in clinical trials according to the populations studied, such as HIV-positive or -negative adults and/or children. The GRADE evidence tables were prioritized based on the regimens, comparisons, and study populations that were deemed most clinically relevant to the United States, Canada, and other low TB incidence areas. The GRADE head-to-head comparisons also were prioritized over the results of the 2014 and 2017 network meta-analyses, but the guidelines committee reviewed both datasets.

Dr. Sterling presented the GRADE evidence tables that the guidelines committee developed to rank the "higher" and "lower" priority LTBI regimens.

HIGHER PRIORITY

Experimental Regimen	Comparator Regimen	Population	No. of Effectiveness Trials	No. of Toxicity Trials
3HP	9 Months INH	HIV-positive adults	1	1
3HP	9 Months INH	HIV-negative adults and children	1	1
3HP	9 Months INH	HIV-negative children	1	1
3HP	6 Months INH	HIV-positive adults	1	1
3HR	9 Months INH	HIV-negative adults	1	1
3HR	6 Months INH	HIV-negative adults and children	3	2
3HR	6 Months INH	HIV-positive adults	4	4
3HR	Placebo or no Treatment	HIV-positive adults	2	1
3HR	Placebo or no Treatment	HIV-negative adults and children	2	0
4R	9 Months INH	HIV-negative adults	1	2

Experimental Regimen	Comparator Regimen	Population	No. of Effectiveness Trials	No. of Toxicity Trials
4R	9 Months INH	HIV-negative children	1	1
4R	6 Months INH	HIV-negative children	1	0
6H	Placebo	HIV-negative adults and children	4	2
6H	Placebo or no Treatment	HIV-positive adults	5	3
9H	No Treatment	HIV-negative adults and children	2	0

LOWER PRIORITY

Experimental Regimen	Comparator Regimen	Population	No. of Effectiveness Trials	No. of Toxicity Trials
12 Months INH	No Treatment	HIV-positive adults	2	0
12 Months INH	Placebo	HIV-positive adults and children	5	3
12 Months INH	Placebo	HIV-positive children	3	1
12 Months INH	Placebo or no Treatment	HIV-negative adults and children	15	5
3HP	Continuous INH (up to 6 years)	HIV-positive adults	1	1
2RZ	6 Months INH, 12 Months INH	HIV-positive adults and children	4	2

The network meta-analysis did not include observational data, but the data were gathered from several sources, such as PubMed, Embase, Web of Science, and "gray" literature (e.g., abstracts from meetings). The study selection included RCTs of LTBI treatment that recorded at least one of the two pre-specified endpoints of prevention of active TB or hepatotoxicity. The network meta-analysis was updated to include effectiveness and safety data on 4R reported by the 2018 Menzies study and the 2018 Diallo study. The evaluation included 63 studies of 16 regimens.

The network meta-analysis compared TB risk to no treatment and showed the following results. The odds ratios in 2016 versus those in 2018 were the same or similar between no treatment and the treatment regimens of 3HP, 3-4R, 3HR, 6H, and 9H. The comparison of hepatotoxicity risk to no treatment also showed the same or similar odds ratios of these treatment regimens in 2016 and 2018. However, the finding of less hepatotoxicity from rifampin compared to no treatment was a surprising result that caused the guidelines committee to raise questions about the network meta-analysis.

Dr. Sterling concluded his update by presenting a table with the guidelines committee's draft recommendations and explaining the rationale for the priority ranking of the LTBI regimens. Treatment completion rates are higher with shorter regimens. Therefore, if two regimens have similar efficacy, the shorter regimen will be more effective in the clinical setting.

Priority Rank	Regimen	Recommendation	Evidence
Preferred	3HP	Strong	Moderate
Preferred	4R	Strong	Moderate (HIV-negative)*
Preferred	3HR	Conditional Conditional	Very Low (HIV-negative) Low (HIV-positive)
Alternative	6H	Strong Conditional	Moderate (HIV-negative) Moderate (HIV-positive)
Alternative	9H	Conditional	Moderate

*No evidence reported in HIV-positive patients.

ACET GUIDANCE

- The guidelines committee is commended for using understandable terminology, such as "preferred" to rank the priority of the recommendations and "strong" to characterize the recommendations. In addition to the table, however, this language also should be articulated in a clear, simple, and evidence-based statement: "The short-course regimens are the preferred treatment for LTBI." Because busy practitioners in the field likely will not read the document in its entirety, this statement should be repeated in the executive summary and conclusions section of the LTBI treatment guidelines as well as in CDC's communication messages and other companion materials.
- The guidelines committee should apply the evidence-based findings from its GRADE tables to encourage USPSTF to include LTBI treatment as a prevention modality that does not require cost-sharing.
- Several ACET members found some of the recommendations, including their priority rankings and level of evidence, to be confusing. The guidelines committee was advised to issue clear messaging in this regard to ensure that providers in the field comply with the recommendations. For example, TB control programs have prioritized nine months of INH over six months of INH for quite some time, but the 6H regimen has a stronger recommendation than the 9H regimen. Moreover, the 3HR regimen is a conditional recommendation with very low evidence for HIV-negative patients, but its priority ranking is preferred. However, the 6H regimen is a strong recommendation with moderate evidence for HIV-negative patients, but its priority ranking is alternative.

Dr. LoBue provided follow-up comments to one of ACET's suggestions. ACET's formal request to USPSTF two years ago and multiple public comments did not lead to USPSTF issuing a new recommendation on LTBI treatment as prevention. ACET's renewed request to USPSTF at this time, including the guidelines committee's new GRADE evidence tables, likely will not result in a different decision. Most notably, USPSTF has emphasized that its role is to make evidence-based recommendations on clinical preventive services for healthy people who might be at risk for, but have no signs or symptoms of a certain condition or disease. As a result, USPSTF will not issue a prevention recommendation for LTBI because the individual already has an infection that requires treatment.

Ms. Suzanne Marks, of DTBE, advised the guidelines committee to explore the possibility of conducting a network meta-analysis to show efficacy data among patients who completed their respective regimens across the clinical trials. This approach could be used to rank the efficacy of each regimen without being confounded by adherence issues.

Ms. Donna Wegener, Executive Director of NTCA, reiterated that the GRADE criteria do not address "who to treat for LTBI" or "how to ensure treatment." However, an NTCA workgroup is developing a companion document to specifically focus on this issue. NTCA intends to disseminate the companion document at approximately the same time as the release of the updated LTBI treatment guidelines.

Dr. Sterling thanked the ACET members for their helpful input. He explained that the next steps will be to compile ACET's comments into a written statement, submit the document to NTCA for consideration of any proposed revisions, and submit the final draft of the guidelines to CDC to initiate the clearance process. The cleared and approved version of the LTBI treatment guidelines will be submitted for publication in early 2019.

Update on the Draft Treatment of Drug-Resistant TB Guidelines

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

Payam Nahid, MD, MPH
Professor of Medicine, Pulmonary and Critical Care Medicine
University of California, San Francisco

Drs. Chorba and Nahid presented the background, methodology, and current status of the draft *Clinical Practice Guidelines for the Treatment of Drug-Resistant Tuberculosis* that will be published as joint recommendations by ATS, CDC, IDSA, and the European Respiratory Society (ERS). The new guidelines will serve as a companion document to the *2016 ATS/CDC/IDSA Treatment of Drug-Susceptible Tuberculosis Practice Guidelines*. The principals of the case management strategies, TB treatment in the presence of HIV infection, and treatment of extrapulmonary disease outlined in the 2016 drug-susceptible TB practice guidelines also apply to the new DR-TB treatment guidelines.

The writing committee implemented a rigorous methodology to develop the new DR-TB treatment guidelines. All 20 PICO questions that were addressed were relevant to the care of DR-TB patients. Evidence profiles to address the PICO questions were based on two meta-analyses at the individual patient level that were published in 2018 in *The Lancet* and *The Lancet Respiratory Medicine*. The GRADE approach was applied to measure the strength of the recommendations. Quality assessments were developed to categorize the evidence as "high," "moderate," "low," or "very low."

Evidence from RCTs versus observational trials had different levels of certainty. The strength of the evidence was lowered based on the inconsistency or heterogeneity of a specific trial or indirect evidence of a particular study population. "Strong" recommendations were those in which the benefits outweighed the harms (a higher degree of confidence). "Conditional" recommendations were those in which the benefits likely outweighed the harms (a lower degree of confidence).

The draft DR-TB treatment guidelines include the following sections.

Best Practices for Treating DR-TB

- Diagnosing TB and identification of drug resistance
- Treatment and monitoring of DR-TB
- Infection control and DR-TB
- Case management for DR-TB

Treatment of DR-TB

- Number of drugs in the regimen
- Duration of intensive and continuation phases
- Drugs and drug classes

Building a Treatment Regimen for DR-TB (With the exception of delamanid, all of the agents or classes of agents listed below have individual patient-level data.)

- Amoxicillin-clavulanate
- Bedaquiline
- Carbapenems with clavulanic acid
- Clofazimine
- Cycloserine
- Delamanid
- Ethambutol
- Ethionamide and Prothionamide
- Fluoroquinolones: Levofloxacin, Moxifloxacin, Ciprofloxacin, and Ofloxacin
- Injectables: Amikacin, Capreomycin, Kanamycin, and Streptomycin
- Linezolid
- Macrolides: Azithromycin and Clarithromycin
- P-Aminosalicylic Acid
- Pyrazinamide

Special Topics

- Standardized, shorter-course 9- to 12-month regimen
- Treatment of INH-resistant TB
- Role of surgery in DR-TB
- Treatment of DR- TB in special populations: HIV infection, children, and pregnant women
- Treatment of contacts exposed to DR-TB

The writing committee formulated six best practice statements to support the new DR-TB treatment guidelines.

1. Consultation with an expert in TB is recommended when there is suspicion for or confirmation of DR-TB. In the United States, DR-TB experts can be found through the CDC-supported TB Centers of Excellence for Training, Education, and Medical Consultation.

2. Molecular testing is recommended for rapid detection of mutations associated with resistance. Growth-based drug susceptibility testing (DST) for first-line drugs typically is performed concurrently with molecular methods. When mutations associated with

resistance are found, growth-based DST should be performed immediately for first-line drugs, fluoroquinolones, and aminoglycosides.

3. Regimens that only include drugs to which the patient's isolate has documented or a high likelihood of susceptibility are recommended. Drugs that known to be ineffective based on *in vitro* resistance or clinical and epidemiological information should NOT be used. This recommendation applies to all drugs and regimens discussed in this practice guideline.

4. Clinical, radiographical, and bacteriological monitoring of the treatment response, with cultures obtained at least monthly, is recommended. When cultures remain positive after three months of treatment, DST should be repeated. Clinical response and weight should be recorded monthly.

5. Asking patients about possible adverse effects at each visit is recommended. The toxicities and poor tolerability of drugs used to treat DR-TB are well established and all adverse effects should be thoroughly investigated and ameliorated.

6. Patient-centered case management is recommended to help patients understand their diagnosis; understand and participate in the selection of their treatment; and discuss potential barriers to completing treatment and achieving cure. The use of patient-centered strategies and interventions is recommended to address and minimize barriers to successful treatment, including the careful consideration of using techniques for observed therapy.

The writing committee's recommendations, qualified as strong or as conditional, for specific sections of the new DR-TB treatment guidelines are set forth below.

Selection of an effective duration of treatment for DR-TB

- The use of at least five drugs is suggested in the intensive phase of treatment and four drugs in the continuation phase of treatment of multi-drug resistant TB (MDR-TB) (conditional recommendation, very low certainty in the evidence).
- An intensive-phase treatment of between five and seven months after culture conversion is suggested (conditional recommendation, very low certainty in the evidence)
- A total treatment duration of between 12 and 21 months after culture conversion is suggested (conditional recommendation, very low certainty in the evidence). In patients with pre-extensively drug-resistant TB (XDR-TB) and XDR-TB, a total treatment duration of between 15 and 24 months after culture conversion is suggested (conditional recommendation, very low certainty in the evidence).

Selection of oral drugs with which to compose an effective regimen for DR-TB

- The inclusion of bedaquiline in a regimen for the treatment of patients with DR-TB is suggested (strong recommendation, very low certainty in the evidence).
- The inclusion of clofazimine in a regimen for the treatment of patients with DR-TB is suggested (conditional recommendation, very low certainty of evidence).
- The inclusion of cycloserine in a regimen for the treatment of patients with DR-TB is suggested (conditional recommendation, very low certainty in the evidence).
- A recommendation for or against the use of delamanid was unable to be made due to the absence of individual patient-level data for the meta-analyses that were conducted for this practice guideline. Based on expert opinion, however, agreement was reached

on WHO's recommendations on the use of delamanid in the treatment of DR-TB (expert opinion recommendation).

- The inclusion of ethambutol in a regimen for the treatment of patients with DR-TB is suggested only when more effective drugs cannot be assembled to achieve a total of five effective drugs in the regimen (conditional recommendation, very low certainty in the evidence).
- The inclusion of fluoroquinolones (e.g., levofloxacin or moxifloxacin) is suggested as part of multidrug regimens for patients with DR-TB (strong recommendation, low certainty of evidence).
- The inclusion of linezolid in a regimen for the treatment of patients with DR-TB is suggested (conditional recommendation, very low certainty in the evidence).
- The inclusion of pyrazinamide in a regimen for the treatment of patients with DR-TB is suggested (conditional recommendation, very low certainty in the evidence).

Selection of oral drugs previously included in regimens for the treatment of DR-TB

- The inclusion of amoxicillin-clavulanate in a regimen for the treatment of patients with DR-TB is NOT suggested, with the exception of when the patient is receiving a carbapenem and the inclusion of clavulanate is necessary (strong recommendation, very low certainty in the evidence).
- The inclusion of ethionamide/prothionamide in a regimen for the treatment of patients with DR-TB is NOT suggested if newer and more effective drugs are available to construct a regimen with at least five effective drugs (conditional recommendation, very low certainty in the evidence).
- The inclusion of p-aminosalicylic acid in a regimen for the treatment of patients with DR-TB is NOT suggested if newer and more effective drugs are available to construct a regimen with at least five effective drugs (conditional recommendation, very low certainty in the evidence).

Selection of TB drugs administered through injection

- The inclusion of a carbapenem (that is always to be used with amoxicillin-clavulanic acid) in a regimen for the treatment of patients with DR-TB is suggested (conditional recommendation, very low certainty of evidence).
- The inclusion of amikacin or streptomycin in a regimen for the treatment of patients with DR-TB is suggested when susceptibility to these drugs is confirmed (conditional recommendation, very low certainty of evidence).
- The inclusion of kanamycin or capreomycin for the treatment of patients with DR-TB is NOT recommended (conditional recommendation, very low certainty in the evidence).

Building a treatment regimen for DR-TB

- A clinical strategy tool for building a treatment regimen for DR-TB is proposed.
- The evidence-based review of the individual drugs should be used, with consideration of the balance of benefits and harms for each drug, as well as expert opinion.
- This clinical strategy tool encourages the building of all oral regimens with five effective drugs for the treatment of MDR-TB.
- The individual patient data meta-analyses showed favorable synergies with improved treatment success and reduced mortality when bedaquiline was used in combination with linezolid or clofazimine.
- Amikacin and streptomycin showed effectiveness in the treatment of DR-TB only when the patient's isolate was susceptible to these drugs. Because of their significant

toxicities, however, injectables should be reserved for when a more effective or less toxic regimen cannot otherwise be assembled.
- The final choice of drugs and drug classes is contingent upon multiple factors, such as patient preferences in terms of the harms and benefits associated with the agents; the capacity to appropriately monitor for significant adverse effects, and consideration of drug-drug interactions and patient comorbidities.

Use of the standardized, shorter course 9- to 12-month regimen for MDR-TB
- Based on the available evidence at the time of the writing of this guideline and the fact that this standardized, shorter-course regimen includes the use of drugs for which drug resistance may be present, a recommendation cannot be made for or against the shorter-course regimen as compared to individualized longer-course regimens.

Treatment of INH-resistant TB
- The addition of a later-generation fluoroquinolone to a six-month regimen of daily rifampin, ethambutol, and pyrazinamide is suggested for patients with INH-resistant TB (conditional recommendation, very low certainty in the evidence).
- In patients with INH-resistant TB who are treated with a daily regimen of a later-generation fluoroquinolone, rifampin, ethambutol, and pyrazinamide, shortening of the duration of pyrazinamide to two months is suggested in selected situations (e.g., non-cavitary and lower burden disease or concerns for or experience of toxicity from pyrazinamide) (conditional recommendation, very low certainty in the evidence).

Role of surgery in the treatment of DR-TB
- Elective partial lung resection (e.g. lobectomy or wedge resection) is suggested and can be used as an adjunctive therapeutic option in combination with a DR-TB regimen when clinical judgement is supported by bacteriological and radiographic data suggest a strong risk of relapse or treatment failure with the medical regimen alone (conditional recommendation, very low certainty in the evidence).

Management of contacts to patients with DR-TB
- Based on expert opinion, six to 12 months of treatment with a fluoroquinolone alone or with a second drug is suggested. The selection should be based on the DST of the isolate from the presumed source-case. Based on the evidence of increased toxicity, adverse events, and discontinuation of pyrazinamide, the expert opinion is that pyrazinamide should not be routinely used as the second drug (expert opinion recommendation).

The co-sponsors (e.g., ATS, ERS, and IDSA) submitted the draft DR-TB treatment guidelines to reviewers in their respective professional societies in October 2018. This peer review is expected to be completed in three to four weeks. Input is now being solicited from ACET. The co-sponsoring societies will return comments from their reviewers to the ATS document editor for compilation into a single decision letter that will be forwarded to the authors. The co-sponsoring societies and CDC will be copied on this correspondence.

The guidelines task force will revise the manuscript, provide a point-by-point response to the reviewers' comments; and submit the revised draft to the ATS document editor. After the co-sponsoring societies complete the initial cycle of reviews and revisions, the formal clearance and approval process by DTBE, NCHHSTP, and the CDC Office of the Director will be initiated.

The DR-TB treatment guidelines are expected to be finalized and published in the first or second quarter of 2019.

ACET DISCUSSION: DRUG-RESISTANT TB GUIDELINES
Drs. Chorba and Nahid provided additional details on the following topics in response to ACET's questions.

- Potential strategies to leverage opportunities for programs to more easily access the recommended TB drugs.
- The rationale for not conducting a PICO evaluation of high-dose INH.

ACET GUIDANCE
- Best Practice Statement 1 provides a link to the CDC-funded TB COEs for clinicians to obtain DR-TB expertise. However, the MDR-TB consultation program in New York City, the California MDR-TB Service, and other state or local programs also should be referenced as additional resources.
- The use of host-directed therapy (HDT) in conjunction with the recommended TB drugs should be considered for inclusion in the DR-TB treatment guidelines. Preliminary studies indicate that HDT is promising in reducing the duration of treatment and decreasing side effects.
- ACET should raise two key points if the members vote to approve the submission of a letter to the HHS Secretary on TB drug shortages in the United States. First, the letter should emphasize the limited availability of anti-TB drugs both domestically and globally. Second, ACET should highlight its advocacy role, particularly for expensive drugs that are recommended for patients in the United States.

NCHHSTP Office of the Director's (OD) Report

Hazel Dean, ScD, DrPH (Hon), MPH, FACE
Deputy Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
ACET DFO

Dr. Dean covered several topics in the NCHHSTP OD report to ACET. NCHHSTP sponsored a special supplement in the *American Journal of Public Health*, "Monitoring Disparities in Prevention and Treatment of HIV, Viral Hepatitis, Sexually Transmitted Diseases, and Tuberculosis." The supplement presented emerging and the best available methods, metrics, and indicators for monitoring health disparities and preventing HIV, viral hepatitis, STDs, and TB.

NCHHSTP issued a call for abstracts for potential papers to be included in a supplement to be published in *Public Health Reports*. The supplement will focus on policy approaches to reduce the morbidity, mortality, and incidence of HIV, viral hepatitis, STDs, and TB in the United States. The deadline for abstracts is January 4, 2019.

DTBE's release of the *2017 TB Surveillance Report* in October 2018 documented that 9,105 TB disease cases were reported in the United States in 2017. The number of reported cases in 2018 was the lowest on record, but is still too high. The *2017 TB Surveillance Report*

emphasized the ongoing need to maintain and strengthen TB control priorities and increase efforts to identify and treat LTBI in high-risk populations.

The CDC Foundation hosted an event in conjunction with the UN HLM in September 2018, "Preventing TB to End TB," to focus on the fight against TB. Remarks were provided by Mr. Alex Azar II, HHS Secretary, and Dr. Robert Redfield, CDC Director.

The Division of STD Prevention (DSTDP) released the *2017 STD Surveillance Report* that documented a steep increase in STDs. Most notably, over 2.3 million cases of chlamydia, gonorrhea, and syphilis were reported to CDC. The total number of STD cases in 2017 exceeded the previous record in 2016 by more than 200,000 cases. Steep increases have been observed for the past four consecutive years.

The *2017 STD Surveillance Report* also showed that congenital syphilis cases reached a 20-year high. The number of reported cases of congenital syphilis more than doubled from 362 in 2013 to 918 in 2017. The report emphasized the critical importance of pregnant women visiting HCP early during pregnancy and being tested for syphilis. Moreover, women at high risk should be tested more often, including at the first visit, early in the third trimester, and at delivery.

DSTDP is continuing to be concerned about antibiotic-resistant gonorrhea. Since 2015, CDC has recommended a single shot of ceftriaxone and an oral dose of azithromycin to treat gonorrhea. Dual therapy helps to prevent the emergence of antimicrobial resistance, but no resistance to ceftriaxone has been reported since the implementation of dual therapy. However, new CDC findings show that emerging resistance to azithromycin has increased from 1 percent of laboratory samples in 2013 to more than 4 percent in 2017.

DSTDP announced a new five-year CoAg for health departments to strengthen STD prevention and control. Over the project period from January 1, 2019 to 2023, 59 health departments will be awarded approximately $95 million in total. The awards to individual health departments will range from $300,000 to more than $7 million. The grant recipients will use their awards to support various activities, such as conducting STD surveillance; responding to STD outbreaks; identifying and linking people with STDs and their partners to care and treatment; promoting screening, diagnosis, and treatment among providers; developing partnerships to support STD prevention and control; and analyzing data for program improvement.

DVH calculated new HCV prevalence estimates that showed more than 2.4 million Americans reported living with current HCV from 2013-2016. Of this population, approximately 4.1 million people had evidence of past or current infection. DVH analyzed blood test results from National Health and Nutrition Examination Survey (NHANES) data and groups that were not captured by NHANES. Of all people living with HCV, 90 percent can be cured. HCV screening and referral to treatment are top priorities for public health.

DVH is assisting with outbreaks of hepatitis A virus (HAV) that involve multiple states: Arkansas, California, Indiana, Kentucky, Massachusetts, Michigan, Missouri, North Carolina, Ohio, Tennessee, Utah, and West Virginia. As of November 14, 2018, the states reported more than 8,600 cases that have resulted in 81 deaths and 4,987 hospitalizations (or 58 percent). The HAV outbreaks primarily are affecting people who inject drugs and/or are experiencing homelessness.

DHAP released the *HIV Monitoring Report* that documented an increase in HIV viral suppression. However, youth and people who inject drugs are less likely to be suppressed. In 2015, 86 percent of people living with HIV knew their status. Of people who were newly diagnosed with HIV, 76 percent were linked to medical care. The *HIV Monitoring Report* includes data from 40 jurisdictions.

DHAP will award approximately $14.6 million to 20 health departments to enhance and expand high-impact HIV prevention demonstration projects and surveillance strategies. The grant recipients will include several activities in their demonstration projects, such as improving pre-exposure prophylaxis (PrEP) use and adherence for specific groups and geographic areas (e.g., African American and Hispanic men); implementing interventions to address social and structural factors; using innovative methods, such as molecular epidemiology, to limit HIV cluster growth; and expanding access to medical care through telemedicine.

DHAP launched the "Act Against AIDS" initiative to focus on PrEP and post-exposure prophylaxis (PEP). The rollout of a new component of the initiative, "Prescribe HIV Prevention," was targeted to HCP to focus on PrEP and PEP. USPSTF issued draft recommendations for clinicians to offer PrEP to people at high risk of acquiring HIV infection. USPSTF found "convincing evidence that PrEP is of substantial benefit in decreasing the risk of HIV infection in people at high risk." The public comment period on the draft recommendation will be open until December 26, 2018.

DASH recently released new "Whole School, Whole Community, Whole Child" (WSCC) products to provide more information on this model to educators and other school-based partners. DASH collaborates with these partners to ensure that programs, policies, practices, and research integrate components of the WSCC model. The new products include web pages, an animated video, and a flipbook.

Preparation for the ACET Business Session

Barbara Cole, RN, MSN, PHN, ACET Chair
TB Controller
Riverside County (California) Department of Public Health

Ms. Cole conducted a high-level summary of the updates and overviews that were presented on day 1 of the ACET meeting. During the discussions that followed each presentation, she noted that the ACET members provided extensive guidance to CDC/DTBE. However, she pointed out that two topics from Dr. LoBue's update will require ACET's request for a new agenda item or its formal action during the Business Session on the following day.

First, ACET will need to revisit the inclusion of new TB-specific questions in the 2021 YRBS during the April 2019 meeting to meet DASH's December 2019 deadline for this effort. Second, a suggestion was made for ACET to submit a letter to the HHS Secretary to express its support of long-term solutions that were proposed by the FDA Drug Shortages Task Force. As chair of the TB Drug Supply Workgroup, Dr. Flood offered to take leadership in presenting the draft letter on the following day for ACET's review, discussion, revisions, and formal vote. The Business Session also will include discussions on the Public Charge and the response to ACET's letter from the Office of the HHS Secretary.

With no further discussion or business brought before ACET, Ms. Cole recessed the meeting at 3:26 p.m. on December 11, 2018.

Opening Session: December 12, 2018

Hazel Dean, ScD, DrPH (Hon), MPH, FACE
Deputy Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
ACET DFO

Dr. Dean conducted a roll call to confirm the attendance of the ACET voting members, *ex-officio* members, and liaison representatives (or their alternates). 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 ACET 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 confirmed that the 17 voting members and *ex-officio* members in attendance (or their alternates) constituted a quorum for ACET to conduct its business on December 12, 2018. She reconvened the proceedings at 8:40 a.m. and welcomed the participants to day 2 of the ACET meeting.

Update by the Essential Components Workgroup

Barbara Cole, RN, MSN, PHN, ACET Chair
TB Controller
Riverside County (California) Department of Public Health

Ms. Cole reported that the workgroup completed the updated *Essential Components of a Public Health Tuberculosis Prevention, Control, and Elimination Program: Recommendations of the Advisory Council for the Elimination of Tuberculosis (ACET) and the National Tuberculosis Controllers Association (NTCA)* document. Because the document requires additional minor revisions, the workgroup will table its plan to call for ACET's formal vote during the current meeting. The workgroup will present the final draft of the document during the April 2019 meeting for ACET's review, discussion, and formal vote.

Update by the Congregate Settings Workgroup

Lisa Armitige, MD, PhD
Medical Consultant, Heartland National Tuberculosis Center
University of Texas Health Center at Tyler
ACET Member & Workgroup Chair

Dr. Armitige reported that ACET charged the Congregate Settings Workgroup with exploring health inequities and other concerns related to homeless and incarcerated populations and presenting its findings to the full ACET membership. To fulfill its charge, the workgroup obtained outstanding expertise and input by ACET liaison representatives and *ex-officio* members, including the Federal Bureau of Prisons, ICE, and U.S. Marshals Service. However, the workgroup is not meeting the FACA requirement for workgroups to have representation by two members of the parent committee. Dr. Armitige is the only ACET member who serves on the workgroup at this time.

Dr. Armitige explained that the workgroup has devoted an extensive amount of time to addressing two key issues. First, the roles and responsibilities for TB contact investigations of prisoners who are transferred between jurisdictions are uncertain and not clearly defined. The workgroup will present its findings on this issue to ACET during the April 2019 meeting. Second, representation by the corrections community has been lacking in some of CDC's new documents, such as the 2020 RVCT and the 2020 TB funding formula. However, the workgroup's position is that this issue has been addressed. Several workgroup members provided ongoing advice and guidance after DTBE presented these documents during ACET meetings.

Dr. Armitige pointed out that the workgroup was established approximately two years ago and has fulfilled its charge. If ACET has no additional issues for the workgroup to address, she and the other members have agreed that the workgroup should be dissolved at this time. Her closeout presentation to ACET during the April 2019 meeting is the workgroup's only remaining task.

Update by the Child and Adolescent Workgroup

Jeffrey Starke, MD
Professor of Pediatrics, Baylor College of Medicine
Texas Children's Hospital
ACET Member & Workgroup Chair

Dr. Starke reported that the Child and Adolescent Workgroup has fulfilled its charge of ensuring harmonization between the recommendations by CDC and the American Academy of Pediatrics on testing and treatment of TB infection in children and adolescents. The workgroup's reviews of the documents and presentations to ACET showed that the two sets of guidelines are nearly identical.

Dr. Starke proposed dissolving the workgroup at this time. Any remaining issues related to TB infection in children and adolescents have been incorporated into the charge of the LTBI Workgroup. His closeout presentation to ACET during the April 2019 meeting is the workgroup's only remaining task.

Update by the LTBI Workgroup

Jennifer Flood
Chief, Tuberculosis Control Branch
California Department of Health Services
ACET Member & Workgroup Co-Chair

Advice requested from ACET by the LTBI Workgroup:

1. What is ACET's reaction to the approach and preliminary findings of the LTBI Workgroup?

Dr. Flood reported that the LTBI Workgroup has convened three meetings since its establishment in December 2017. At that time, the workgroup initially was charged with drafting a scope of work for the membership. Since that time, the workgroup has more clearly defined its two-part charge. First, recommendations will be drafted for CDC to identify and implement strategies to scale-up LTBI testing and treatment in the United States. Second, a publication of these recommendations will be developed and disseminated. The workgroup's non-clinical recommendations will be separate and apart from CDC's LTBI Treatment Guidelines

Dr. Flood explained that in preparation for the workgroup's update, a comprehensive three-page summary was distributed to ACET for review and discussion. The following topics are covered in the summary.

- Background on LTBI in the United States
- Methodology and approach for the workgroup to draft the recommendations (e.g., evaluate the relevant literature and consult with experts in the field)
- Major topics that will be addressed in the recommendations
- Challenges and barriers to scaling up LTBI testing and treatment in the United States
- Preliminary/potential recommendations to CDC

Dr. Flood concluded her update by describing the workgroup's next steps. During the Business Session, the workgroup will call for ACET's vote to formally approve its new charge. Technical experts will be invited to future workgroup meetings to make presentations on the major topics that will be covered in the recommendations. During its routine updates, the workgroup will present drafts of the recommendations to ACET for review and comment.

Update by the TB Drug Supply Workgroup

Jennifer Flood
Chief, Tuberculosis Control Branch
California Department of Health Services
ACET Member & Workgroup Chair

Advice requested from ACET by the TB Drug Supply Workgroup:

1. Does ACET support the submission of a response to affirm the efforts of FDA and HHS to identify solutions for drug shortages? (See attached DRAFT ACET resolution and *Federal Register* notice.)

Dr. Flood reported that during the April 2018 meeting, ACET approved the revised charge of the TB Drug Supply Workgroup: (1) identify strategies to ensure an uninterrupted drug supply for treating TB disease and LTBI and (2) address barriers, such as drug pricing manufacturing issues and distribution shortages. Since that time, the workgroup has been reviewing the literature to fulfill its revised charge. The workgroup's first data source was two key recommendations in the previous version of ACET's Essential Components document: (1) ensure that patients who have TB receive appropriate treatment until cured and (2) treat patients without consideration of their ability to pay.

The workgroup's second data source was international standards issued by WHO. An uninterrupted supply of quality assured anti-TB drugs is fundamental to TB control. A reliable system of procurement and distribution of all essential drugs to all relevant health facilities should be available. Anti-TB drugs should be available and free of charge to all TB patients because (1) many patients are poor and might find these drugs difficult to afford and (2) treatment has benefits that extend to society as a whole (e.g., cure prevents transmission to others).

In addition to conducting a literature review, the workgroup also has focused its recent activities on several key areas. The workgroup developed a risk profile for anti-TB drugs, including their potential vulnerabilities and risk attributes. The workgroup targeted this effort to TB drugs with a single manufacturer, problems with raw ingredients, transfer of the company in the past year, new higher demand, increased cost in the past year, and recent shortages in the past year. The workgroup's risk profile is set forth below.

RISK PROFILE OF ESSENTIAL ANTI-TB DRUGS

TB Drug	Single Manufacturer	New Higher Demand	Shortage	Recent Challenges to TB Drug Access
Intravenous INH	✓			Interruptions in the supply
Rifapentine	✓	✓	✓	Shortage
Bedaquiline	✓	✓		High cost: • $40,000 for MDR-TB treatment • $30,000 under the 340B Drug Pricing Program
Moxifloxacin	✓			
Clofazimine	✓	✓		Investigational new drug (IND) process and procurement process that is complex, time-consuming, and difficult for TB programs to understand from a legal perspective.
Cycloserine	✓	✓	✓	Shortage
Intravenous Streptomycin	✓			

The workgroup thoroughly reviewed and discussed the specific challenges related to access to Clofazimine (CFZ). In addition to the Institutional Review Board (IRB) documents and the consent process, Novartis also requires TB programs to sign a non-negotiable letter of agreement to receive CFZ. The letter outlines strict terms and conditions.

- All adverse events, including non-serious events and beneficial effects, must be reported to the Novartis online system.
- Novartis reserves the right to access data and other work products relating to the use of CFZ as well as to utilize all data resulting from the use of its product for all purposes, including submission to regulatory agencies, marketing, and/or sales of any therapeutic agent or formulation.
- Results of the use of CFZ cannot be reported via conferences, publications, or presentations without prior review by Novartis.
- Novartis reserves the right to delete information and delay a CFZ publication or presentation for up to 45 days.
- TB programs must accept all liability stemming from the use of CFZ.

In addition to identifying the current challenges related to the TB drug supply, the workgroup also reviewed recent efforts and successes. CDC took action on ACET's recommendation and used the national TB drug stockpile to increase rapid access to Rifapentine. NTCA and the Treatment Action Group (TAG) initiated discussions with industry to remove barriers to access and reduce the cost of key TB drugs. TB programs and the TB COEs centralized some of the requirements in the IND and IRB processes to increase access to CFZ.

The workgroup noted that FDA published a *Federal Register* notice on September 10, 2018 to request comments on its public meeting, "Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions." The public comment period will be open until January 11, 2019. The workgroup acknowledged the importance of ACET going on record with its position on this important issue. In accordance with its charter, however, ACET's comments will need to be in the form of a letter to the HHS Secretary. To guide this effort, Dr. Flood drafted a letter that was distributed to ACET for review and comment. During the Business Session, she planned to call for ACET's vote to formally approve the letter.

Dr. Flood concluded her update by describing the workgroup's next steps. The workgroup will continue to review and update the risk profile of essential anti-TB drugs and identify any new problems with access to TB drugs. The workgroup will conduct research to propose potential solutions, such as the importation of TB drugs, use of the Global Drug Facility, development of a centralized supply, and ongoing efforts by NTCA and TAG with individual manufacturers. These discussions will focus on assisting patients in receiving drugs at no or a reduced cost and developing better formulations (e.g., the INH/Rifapentine regimen) to more effectively meet the needs of adult and pediatric TB patients. The workgroup will compile its findings and draft a report on the status of the anti-TB drug supply in the United States for ACET's review, comment, and formal approval.

CDC Office of Infectious Diseases Board of Scientific Counselors

Barbara Cole, RN, MSN, PHN, ACET Chair
TB Controller
Riverside County (California) Department of Public Health

Ms. Cole presented an update in her role as the ACET liaison to the CDC Office of Infectious Diseases, Board of Scientific Counselors (BSC). The BSC's two-day meeting on December 5, 2018 was rescheduled as a one-day meeting because the federal government declared this day as a "National Day of Mourning" to honor former President Bush.

Ms. Cole noted that none of the updates presented during the rescheduled BSC meeting focused on TB-specific issues, but she highlighted the key agenda topics for ACET's review.

- A discussion was held on establishing a new Acute Flaccid Myelitis Task Force to address this issue in the United States.
- The Food Safety Modernization Act Surveillance Workgroup approved the Annual Report to the HHS Secretary.
- The Vector-Borne Disease (VBD) Workgroup discussed funding awards to states to support surveillance, prevention, and control of VBDs.
- The Infectious Disease Workgroup discussed its future activities and issues related to culture-independent diagnostic tests.

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 facilitated a review of old and current business items that warrant ACET's formal action at this time, additional discussion, or requests for future agenda items.

Business Item 1: Approval of Previous ACET Meeting Minutes

A motion was properly placed on the floor by Dr. Ana Alvarez and seconded by Dr. Robert Belknap for ACET to approve the previous meeting minutes.

ACET approved the Draft August 21, 2018 Meeting Minutes with no changes or further discussion.

Business Item 2: ACET Vote on the New LTBI Workgroup Charge

Dr. Flood reminded ACET of the new two-part charge that has been proposed for the LTBI Workgroup. First, non-clinical recommendations will be drafted for CDC to identify and implement strategies to scale-up LTBI testing and treatment in the United States. Second, a publication of these recommendations will be developed and disseminated.

Action	Description
Chair's call for a vote	Dr. Jennifer Flood properly placed a motion on the floor for ACET to approve the new charge for the LTBI Workgroup as proposed above. Dr. Robert Horsburgh seconded the motion.
Outcome of the vote	**The motion was unanimously approved by 9 ACET voting members.**
Next steps	Drs. Jennifer Flood and Jeffrey Starke, co-chairs of the LTBI Workgroup, will continue to provide leadership to the members in fulfilling their official charge.

Business Item 3: Advice Requested from ACET

Ms. Cole presented a table with the advice that the presenters requested from ACET during the August 2018 meeting. She led ACET in a review of these topics to determine whether any further action is needed.

ADVICE REQUESTED FROM ACET

TB Prevention Research

Ms. Cole reviewed the guidance that ACET provided to DTBE during the August 2018 meeting on recently completed and upcoming TB prevention studies. **ACET agreed that no further action is needed.**

DTBE's Concept of Operations (ConOps) for LTBI Surveillance

Ms. Cole provided a high-level summary of ACET's extensive guidance to DTBE during the August 2018 meeting on the LTBI Surveillance ConOps. Based on the LTBI presentations that were made during the current meeting, several ACET members provided additional comments for DTBE to consider.

- MDPH is using the Epic EMR system in its demonstration project at LCHC to scale-up LTBI testing and treatment in a CHC environment. DTBE should take the following actions to promote a shift from voluntary reporting at state and local levels to electronic reporting and surveillance of LTBI cases at the national level: (1) include the core elements of DTBE's TB care cascade in the Epic EMR system; (2) develop and disseminate clear instructions to state and local partners to access these data without modifying their existing electronic systems; and (3) provide leadership in implementing a standardized process and/or best practices for Epic users in the field.
- The ability to measure LTBI testing and treatment rates in the United States will be a critical component of achieving the national TB elimination goal. However, CDC's Tuberculosis Latent Infection Surveillance System (TBLISS) might have limited capacity in extracting data from existing EMRs. As a result, Epic should be considered as an optional EMR system to capture and measure the core elements in the TB care cascade, such as the non-USBP denominator, country of origin, and completion of LTBI therapy in non-USBP. These core elements (e.g., the percent of non-USBP who were

tested for LTBI and the percent of non-USBP with positive LTBI test results who were treated) should be featured in the Epic EMR system to support quality assurance efforts.

- Further development and implementation of the LTBI Surveillance ConOps will require tremendous efforts, but DTBE should build on its recent successes in this regard.
  - DTBE's proposal of new and modified ICD-10 codes was officially approved and will be launched on October 1, 2019 to improve medical coding and reporting of LTBI cases in the United States.
  - DTBE's recently published paper reported successful LTBI therapy completion rates among Medicaid enrollees.
  - DTBE's STEMS platform was used to create TBLISS. The CDC-funded TBESC sites are exploring strategies to collect and integrate STEMS and TBLISS data and extract this information from the Epic EMR system. To support the development of this new platform, the TBESC sites have initiated discussions to broadly share best practices.
- DTBE should provide comprehensive TA to state and local TB programs on implementing new technologies. Due to severe budget cuts, for example, state and local TB programs have been unable to retain robust information technology expertise to support electronic reporting and surveillance of LTBI cases to CDC through an EMR system or the upcoming 2020 RVCT form. To inform this effort, DTBE should launch a pilot of the LTBI cascade of care in health departments and CHC patient populations.
- DTBE should conduct a pilot project of electronic reporting of LTBI cases. The ACET members proposed several suggestions to inform and advance this effort.
  - DTBE should apply DVH's lessons learned in electronically collecting data from reportable conditions (e.g., HBV and HCV). Most notably, DVH is gathering data from the Epic EMR system to electronically report HBV and HCV cases.
  - The Digital Bridge project was designed to implement electronic case reporting and currently is being piloted nationally in multiple states. The Epic platform is being used for the Digital Bridge pilot project to develop a simplified approach to electronically extract data from EMRs and incorporate this information into state registries. However, Dr. Flood noted that TB was not selected as one of the five infectious diseases for the Digital Bridge pilot project. She emphasized the critical need to include TB in this effort.

Dr. LoBue made several overarching and specific remarks in response to ACET's additional guidance. In general, he explained that DTBE's rollout of the LTBI Surveillance ConOps will be in incremental phases over time due to the complex nature, multiple components, and extensive resources required for this initiative. In particular, he acknowledged that the Epic platform is being used to extract data from the LCHC EMR system for the LTBI testing and treatment demonstration project in Lynn, Massachusetts. DTBE will promote the pilot as a model for other states and local jurisdictions, but he pointed out that this process has been extremely time-consuming and difficult. Most notably, additional efforts and costs will be required for other programs to replicate the MDPH/LCHC Epic system for electronic reporting and surveillance of LTBI cases.

ACET agreed that further action is needed. Based on ACET's extensive discussion of and additional guidance on DTBE's LTBI Surveillance ConOps, Ms. Cole confirmed that an agenda item will be scheduled for the April or August 2019 meeting. The presentation will cover the key

experiences and lessons learned from DVH and the Digital Bridge pilot project on electronic case reporting. ACET's discussion will include potential strategies to apply these lessons learned to LTBI.

Business Item 4: ACET Vote on the TB Drug Supply Letter

Dr. Flood reminded ACET that FDA published a *Federal Register* notice on September 10, 2018 to request comments on its public meeting, "Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions." She presented a draft letter to the HHS Secretary that would serve as ACET's response to the *Federal Register* notice.

Based on the suggestions and comments by the ACET members, Dr. Flood revised the draft letter in real-time during the meeting. The extensive discussion resulted in a call for ACET's vote on the revised draft letter as set forth below.

December 12, 2018

The Honorable Alex M. Azar II
Secretary, Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

RE: U.S. Food and Drug Administration (FDA), U.S. Department of Health and Human Services (HHS), Federal Register Notice 2018-N-3272 Request for Comments

Dear Mr. Secretary:

The Advisory Council for the Elimination of Tuberculosis (ACET) provides advice and recommendations regarding the elimination of tuberculosis (TB) in the United States to the Secretary of HHS; the Assistant Secretary of HHS; and the Director of the Centers for Disease Control and Prevention (CDC). The members of ACET are writing to you in response to the September 10, 2018 *Federal Register* notice, "Identifying Root Causes of Drug Shortages and Finding Enduring Solutions," to express their support for taking action to prevent and mitigate anti-TB drug shortages and to ensure an uninterrupted supply of these drugs.

Adverse Consequences of TB Drug Shortages
TB is an airborne disease and treatment with a multi-drug regimen is needed to interrupt transmission and cure TB. Failure to successfully treat TB can cause death or permanent disability. In addition to causing harm to individuals, TB drug shortages have public health consequences. The drugs used for treatment are limited in number and when there are interruptions in the TB drug supply, persons with TB disease may worsen and TB can spread to others. A TB regimen that is interrupted or contains too few drugs can also create drug-resistant forms of TB that are more expensive to treat or forms that are incurable.

In the past four years, there have been protracted shortages of the two most potent anti-TB drugs (isoniazid and rifampin), causing persons with TB to go untreated or to experience significant treatment delays. Also of concern, three of the five core drugs

for multidrug-resistant TB (MDR-TB) (cycloserine, clofazimine, and bedaquiline) have single manufacturers, making the supply of these drugs extremely vulnerable to shortages. Today, the supply of two of the core MDR-TB drugs, cycloserine and clofazimine, is tenuous. At the present time, cycloserine is in acute shortage and clofazimine is available through time-consuming investigational new drug (IND) application only.

Measures to Provide Enduring Solutions
To address anti-TB drug shortages and better ensure a continuous drug supply, ACET makes the following recommendations based on the key issues noted in the *Federal Register* notice and the considerable experience of its membership.

- **Establish a list of essential medicines** for public health conditions that are life-threatening and contagious, such as TB. This list would need to undergo regular revision as the treatment recommendations change and new drugs become available.
- **Provide a temporary waiver for importation for drugs during a shortage.** When the supply is threatened, targeted use of import waivers or expedited processes (e.g., product registration and annual facility inspection fees) can be waived to allow for rapid FDA acceptance of global quality-assured products.
- **Allow other entities, such as the Global Drug Facility, to fill gaps in supply.** Quality-assured products that are available through the Global Drug Facility, for example, have already been approved by World Health Organization (WHO) pre-qualification/European Medicines Agency/Global Fund expert review panel.
- **Revise trade policies and authorities.** Specifically, allow federal purchasers to buy imported drugs or raw materials to prevent or mitigate a shortage.
- **Require the extension of expiration dates for drugs during a shortage or risk of a shortage when scientifically justified.**
- **Consider federal investments in production capacity for essential medicines for conditions that affect national security, emergency preparedness, and defense, including infectious TB.**
- **Support the necessary elements of an ongoing centralized national supply of anti-TB drugs.** This would allow centralized procurement, distribution, and monitoring of supply and demand. One option is to enable the use of existing mechanisms, such as the Global Drug Facility, that U.S. tax dollars currently support. A pooled procurement mechanism would be more efficient, provide an ongoing drug supply, and allow for a rotating reserve.

FDA has a key role to establish policies that support a continuous drug supply. The measures recommended above require increased funding to allow for time-sensitive responses during shortages and a more robust proactive program. For funding some of the TB-specific activities, congress should increase the level of funding to CDC through the Comprehensive TB Elimination Act with specific funding for addressing the TB drug supply in the United States.

TB is a threat to the United States as well as globally. All Americans need to be able to obtain critically important public health drugs to treat TB. As there is currently no centralized national supply for TB drugs, local and state health departments have the primary burden of addressing these drug availability issues. ACET commends the

efforts of HHS, FDA, and the new Task Force to find national solutions to prevent drug shortages. The United States should have an uninterrupted and continuous supply of critical drugs, especially for a serious infectious disease such as TB, that so easily spreads within a community.

Sincerely,

Barbara Cole, RN, PHN, MSN
Chair, Advisory Council for the Elimination of Tuberculosis
2015–2018

cc: Dr. Robert Redfield, Director, CDC
Dr. Jonathan Mermin, Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Dr. Hazel Dean, Deputy Director, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Dr. Philip LoBue, Director, Division of Tuberculosis Elimination
ACET Membership

Action	Description
Chair's call for a vote	Dr. Jennifer Flood properly placed a motion on the floor for ACET to approve the draft TB drug supply letter to the HHS Secretary as revised above. Dr. David Horne seconded the motion.
Outcome of the vote	**The motion was approved by a majority of 8 ACET voting members and 1 abstention (Starke).**
Next steps	The draft letter will be edited to make any grammatical and editorial changes. The revised draft will be distributed to the ACET members for review. The draft letter will be finalized, signed by Ms. Cole, and submitted to the HHS Secretary.

Business Item 5: Proposed Public Charge Rule

Ms. Cole announced that DHS published a proposed rule in the *Federal Register* in October 2018, "Inadmissibility on Public Charge Grounds." If approved, the proposed rule will require non-U.S. citizens who apply for an extension of stay in the United States or a change in their current immigration status to demonstrate that "they have not received, are not currently receiving, or are not likely to receive public benefits." The public comment period for the proposed rule closed on December 10, 2018.

Dr. Benjamin informed ACET that the proposed public charge rule already is having an impact at the local level. Most notably, documented immigrants have reported their reluctance to present for care and treatment of a number of conditions for fear of jeopardizing their legal status in the United States. Moreover, the proposed public charge rule could have serious public health implications for non-USBP who are living with undiagnosed, untreated TB infection and are at risk for spreading disease.

The ACET members engaged in an extensive discussion in response to Dr. Benjamin's request for ACET to formally go on the record regarding the proposed public charge rule. Based on the discussion, Ms. Cole, Dr. Benjamin, and Dr. Starke proposed the following resolution for inclusion in ACET's letter to the HHS Secretary.

> ACET expresses its concern about the U.S. Department of Homeland Security's (DHS) Proposed Rule, "Inadmissibility on Public Charge Grounds," because of its potentially negative impact on the public health of individuals who are concerned about this rule not presenting for tuberculosis care. Any action taken by the Federal Government that would prevent, hinder, or discourage people who are within the United States from seeking services for tuberculosis care would constitute a significant threat to the public health of the United States. Therefore, ACET requests the HHS Secretary to advise DHS and other relevant departments of this potential risk to public health.

Action	Description
Chair's call for a vote	**Ms. Cole confirmed that the nine ACET voting members in attendance accepted and approved the language in the draft resolution.**
Next steps	Ms. Cole will draft a letter to the HHS Secretary with the resolution and circulate the document to the ACET members for review. The draft letter will be finalized, signed by Ms. Cole, and submitted to the HHS Secretary.

Business Item 6: HHS Secretary's Response to ACET

Ms. Cole reminded the members that ACET's letter and report of key activities from 2016-2018 were submitted to the HHS Secretary in July 2018. The letter highlighted ACET's priorities, recommendations, and major accomplishments toward reaching the national TB elimination goal. HHS Deputy Secretary Eric Hargan sent a response letter, dated October 16, 2018, to Ms. Cole. The response letter was distributed to the ACET members for review.

Ms. Cole pointed out that the response letter did not include an invitation for the Office of the HHS Secretary to meet with ACET representatives. She confirmed that the request for a meeting will be repeated in ACET's 2019 report to the HHS Secretary.

Business Item 7: Future Agenda Items

Ms. Cole confirmed that the Agenda Setting Workgroup will convene a teleconference to draft an agenda based on the topics ACET proposed over the course of the meeting. The draft agenda will be circulated to ACET for review in advance of the April 2019 meeting.

Presenter	Agenda Item
Dr. Robert Redfield	Overview of the CDC Director's priorities and/or areas of interest for TB. [Ongoing request based on Dr. Redfield's schedule]
DTBE, DASH, and ACET Membership	Discussion on including new TB-specific questions in the 2021 YRBS.
NCHHSTP/DVH and Guest Presenter	Overview of "Digital Bridge," an innovative collaborative that convenes key decision-makers in health care, public health, and health information technology to solve information technology exchange challenges. ➢ This overview also should describe the key experiences and lessons learned from DVH and the Digital Bridge pilot project in electronic case reporting.
NCHHSTP/DHAP	Overview of the infrastructure and mechanisms to develop, update, and maintain the HIV Guidelines to determine whether these best practices, experiences, and lessons learned can be applied to the TB Guidelines. ➢ Dr. Flood was interested in NIH serving as a co-presenter for this agenda item to address pragmatic issues, particularly related to NIH's funding, resources, and support of the HIV Guidelines.
CDC/DGMQ and Guest Presenters: HHS Administration for Children & Families, Office of Refugee Resettlement U.S. Immigration and Customs Enforcement	Overview of migrant TB care (including issues related to adult migrant workers and their children who currently are detained for TB, such as the settings to screen, treat, and follow-up these populations for TB). ➢ Dr. Reves raised the possibility of using this agenda item to address and resolve the disconnect between DTBE and Division of Global Migration and Quarantine (DGMQ) surveillance data, particularly TB data collected for the Civil Surgeon's examination.
CDC/DGMQ and Guest Presenters	Overviews by select local health departments regarding their model practices or experiences in the field over the past few months in implementing the new LTBI notification policy and efforts to link status adjusters to TB care. ➢ Dr. Flood will provide the Agenda Setting Workgroup with potential representatives of local health departments who can serve as presenters for this agenda item.

Public Comment Session

No members of the public provided comments for ACET's consideration.

Closing Session

The published agenda listed the proposed dates of the next three ACET meetings: April 16, 2019 (webinar); August 20, 2019 (webinar); and December 10-11, 2019 (in-person meeting in Atlanta).

Ms. Margie Scott-Cseh, the ACET Committee Management Specialist, will poll the members via email to determine their availability and confirm the dates of the next three meetings.

With no further discussion or business brought before ACET, Ms. Cole adjourned the meeting at 12:11 p.m. on December 12, 2018.

CHAIR'S CERTIFICATION

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

Attachment 1: Participants' Directory

ACET Members Present

Ms. Barbara Cole, Chair
Dr. Ana Alvarez
Dr. Lisa Armitige
Dr. Robert Belknap
Dr. Jennifer Flood
Dr. David Horne
Dr. Robert Horsburgh, Jr.
Dr. Lixia Liu
Dr. Jeffrey Starke

ACET Member Absent

Dr. Zelalem Temesgen

ACET *Ex-Officio* Members Present

Dr. Naomi Aronson
U.S. Department of Defense

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

Dr. Ulana Bodnar
U.S. Department of Justice

Ms. Kali Crosby
Agency for Healthcare Research and Quality

Dr. Karen Elkins
U.S. Food and Drug Administration

Dr. Jonathan Iralu
Indian Health Service

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

Mr. Stephen Martin
National Institute for Occupational Safety and Health

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

CDR Geri Tagliaferri
U.S. Department of Homeland Security
Immigration and Customs Enforcement
(Alternate for Dr. Diana Elson)

Dr. Kevin Taylor
U.S. Department of Defense
(Alternate for Dr. Naomi Aronson)

ACET *Ex-Officio* Members Absent

Ms. Sarah Bur
Federal Bureau of Prisons

Dr. Anthony Campbell
Substance Abuse and Mental Health Services Administration

Dr. Matthew Lin
U.S. Department of Health and Human Services, Office of Minority Health

Dr. Thomas Nerad
U.S. Department of Labor/Occupational Safety and Health Administration

ACET Liaison Representatives Present

Dr. Shama Ahuja
Council of State and Territorial Epidemiologists

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

Mr. David Bryden
RESULTS

Ms. Diana Fortune
National Tuberculosis Controllers Association

Dr. John Hellerstedt
Association of State and Territorial Health Officials

Mr. Surajkumar Madoori
Treatment Action Group

Dr. Robert Morris
National Commission on Correctional Health

Dr. Howard Njoo
Public Health Agency of Canada

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. Susan Ruwe
Association for Professionals in Infection Control and Epidemiology

Mr. Bobby Watts
National Health Care for the Homeless Council

ACET Liaison Representatives Absent

Dr. Fran du Melle
American Thoracic Society

Dr. Mayleen Ekiek
Pacific Island Health Officers Association

Dr. Ilse Levin
American Medical Association

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

Ms. Susan Rappaport
American Lung Association

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

Dr. Andrey Borisov
Ms. Sloane Bowman
Dr. Terence Chorba
Ms. Ann Cronin
Dr. Tracy Dalton
Dr. Nikolas DeLuca
Dr. Anne Gaynor
Dr. Neela Goswami
Ms. Maryam Haddad
Ms. Carla Jeffries
Dr. Cynthia Jorgensen
Dr. Awal Khan
Ms. Kathryn Koski
Dr. Wen Li
Dr. Philip LoBue
Ms. Suzanne Marks
Mr. Mark Miner
Dr. Subhi Nandakumar
Dr. Thomas Navin

Mr. Gibril Njie
Dr. John Parmer
Dr. Jessica Ricaldi
Dr. Suraj Sable
Ms. Margie Scott-Cseh
Ms. Maria Sessions
Dr. Angela Starks
LT Rebekah Stewart
Dr. Thara Venkatappa
Dr. Andrew Vernon
Dr. William Walker
Dr. Carla Winston

Guest Presenters/ Members of the Public

Ms. Jennifer Cochran
Massachusetts Department of Public Health

Dr. Brent Gibson
National Commission on Correctional Health Care

Ms. Nuala Moore
American Thoracic Society

Dr. Payam Nahid
University of California, San Francisco

Dr. Diana Nilsen
National Tuberculosis Controllers Association

Dr. Jyothi Rengarajan
Emory University School of Medicine

Dr. Timothy Sterling
Vanderbilt University Medical Center

Ms. Judith Thigpen
California Tuberculosis Controllers Association

Ms. Clarisse Tsang
Arizona Department of Health Services

Ms. Donna Wegener
National Tuberculosis Controllers Association

Attachment 2: Glossary of Acronyms

Acronym	Definition
2RZ	Two Months of Rifampin/Pyrazinamide
3HP	Three Months of Isoniazid/Rifapentine
4R	Four Months of Rifampin
9H	Nine Months of Daily Isoniazid
AAPIs	Asian Americans/Pacific Islanders
ACET	Advisory Council for the Elimination of Tuberculosis
ATS	American Thoracic Society
BSC	Board of Scientific Counselors
CBOs	Community-Based Organizations
CDC	Centers for Disease Control and Prevention
CFZ	Clofazimine
CHCs	Community Health Centers
CHWs	Community Health Workers
CMS	Centers for Medicaid & Medicare Services
CoAg	Cooperative Agreement
COEs	Centers of Excellence
ConOps	Concept of Operations
DASH	Division of Adolescent and School Health
DFO	Designated Federal Officer
DGMQ	Division of Global Migration and Quarantine
DHAP	Division of HIV/AIDS Prevention
DHS	U.S. Department of Homeland Security
DOT	Directly Observed Therapy
DR-TB	Drug-Resistant Tuberculosis
DST	Drug Susceptibility Testing
DSTDP	Division of STD Prevention
DTBE	Division of Tuberculosis Elimination
DVH	Division of Viral Hepatitis
EMR	Electronic Medical Record

Acronym	Definition
ERS	European Respiratory Society
FACA	Federal Advisory Committee Act
FDA	U.S. Food and Drug Administration
FQHC	Federally Qualified Health Center
FY	Fiscal Year
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HAV	Hepatitis A Virus
HBU	Hep B United
HBV	Hepatitis B Virus
HCPs	Healthcare Providers
HCV	Hepatitis C Virus
HDT	Host-Directed Therapy
HHS	U.S. Department of Health and Human Services
HRSA	Health Resources and Services Administration
ICD	International Classification of Diseases
ICE	Immigration and Customs Enforcement
ICE	U.S. Immigration and Customs Enforcement
IDSA	Infectious Diseases Society of America
IGRA	Interferon Gamma Release Assay
IND	Investigational New Drug
INH	Isoniazid
IRB	Institutional Review Board
KEMRI	Kenya Medical Research Institute
LCHC	Lynn Community Health Center
LTBI	Latent Tuberculosis Infection
MARSA	Multiple Antigen Response Spectrum Assay
MDPH	Massachusetts Department of Public Health
MDR-TB	Multidrug-Resistant Tuberculosis
MMWR	*Morbidity and Mortality Weekly Report*
MTB	*Mycobacterium tuberculosis*
NCCHC	National Commission on Correctional Health Care
NCCHC	National Commission on Correctional Health Care
NCHHSTP	National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NHPs	Non-Human Primates
NIH	National Institutes of Health
NOFO	Notice of Funding Opportunity
NTCA	National Tuberculosis Controllers Association
OADS	Office of the Associate Director for Science

Acronym	Definition
OD	Office of the Director
OHIN	Oregon Community Health Information Network
OMB	Office of Management and Budget
PEP	Post-Exposure Prophylaxis
PET/CT	Positron Emission Tomography/Computed Tomography
PICIO	Population, Intervention, Comparator
PrEP	Pre-Exposure Prophylaxis
Q	Quarter
QFT	QuantiFERON
RCT	Randomized Controlled Trial
RCTs	Randomized Controlled Trials
RVCT	Report of Verified Case of Tuberculosis
SHDs	State Health Departments
STEMS	Surveillance for TB Elimination Management System
TA	Technical Assistance
TAG	Treatment Action Group
TB	Tuberculosis
TBESC	Tuberculosis Epidemiologic Studies Consortium
TBLISS	Tuberculosis Latent Infection Surveillance System
TBTC	Tuberculosis Trials Consortium
TST	Tuberculin Skin Test
UN HLM	United National General Assembly High-Level Meeting
USBP	U.S.-Born People/Populations
USPSTF	U.S. Preventive Services Task Force
VBD	Vector-Borne Disease
WHO	World Health Organization
WSCC	Whole School, Whole Community, Whole Child
YRBS	Youth Risk Behavior Survey