US DEPARTMENT OF HEALTH AND HUMAN SERVICES

CENTERS FOR DISEASE CONROL AND PREVENTION

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

Division of Tuberculosis Elimination

IN-PERSON MEETING OF THE ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS

December 10th and 11th, 2019

RECORD OF THE PROCEEDINGS

Table of Contents

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ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
December 10th and 11th, 2019

Minutes of the In-Person Meeting

The United States (US) 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 10 and 11, 2019 beginning at 8:30 AM EST.

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 extent to which progress has been made toward TB elimination.

Information for the public to attend the ACET meeting 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*)

Day 1 Opening session

Carla Winston, PhD., M.A
Associate Director for Science, Division of Tuberculosis Elimination
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCCHHSTP) Centers for Disease Prevention and Control
ACET Designated Federal Officer (DFO)

Dr. Winston called the meeting to order at 8:30 AM EST, welcomed participants and conducted a roll call to confirm 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 proceedings are a matter of public record. She informed the ACET members to be mindful of their responsibility to disclose any potential public conflict of interest (COI), as identified by the CDC Committee Management Office and recuse themselves from voting or participating in discussions where they have a conflict.

Dr. Winston made announcements regarding the changes in ACET membership since the previous meeting in August 2019.

- Meeting participants were asked to welcome the following new ACET members:
  - Mr. Marc Gaudreau, who is the Manger for the TB Task Group, Public Health Agency of Canada. He is representing Dr. Howard Njoo who serves as ACET Liaison Representative.
  - New ex-officio member, Dr. Lawrence Kline of the US Section, US-Mexico Border Health Commission. He replaces Dr. Bruce San Filippo
  - CDC sent a letter to the Substance Abuse and Mental Health Services Administration (SAMHSA) with a request to identify a replacement, on August 16th, 2019
  - CDC sent a letter to the Office of Minority Health Substance Abuse and Mental Health Services Administration (SAMHSA) with a request to identify a replacement on April 24th, 2019
  - CDC sent a letter to the Agency for Health Care Research and Quality with a request on October 26th, 2019

ACET Voting Member (Institution/Organization)	Potential Conflict of Interest
Ana Alvarez, MD (University of Florida College of Medicine)	No conflicts disclosed
Robert Belknap, MD (Denver Metro Tuberculosis Control Program)	No conflicts disclosed

ACET Voting Member (Institution/Organization)	Potential Conflict of Interest
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)	No conflicts disclosed
Lixia Liu, PhD, MP, (ASCP), D(ABMM) (Indiana State Department of Health)	No conflicts disclosed
Kristine Steward-East (Advocate for Tuberculosis)	No conflicts disclosed
Zelalem Temesgen, MD (Mayo Clinic Center for Tuberculosis)	No conflicts disclosed

The roll call confirmed that the 19 voting members and ex-officio members in attendance constituted a quorum for ACET to conduct its business on December 10th, 2019.

DTBE Director's Update

Philip LoBue, MD, FACP, FCCP
Director, Division of Tuberculosis Elimination (DTBE), NCHHSTP

Dr. Philip LoBue, Director of DTBE, provided updates encompassing budget, guidelines updates, the Food and Drug Administration (FDA) Drug Shortages Task Force Report, a follow up on the National Institutes of Health and Centers for Disease Control and Prevention (NIH/CDC) TB Research meeting and selected DTBE accomplishments in 2019. He noted the budget for Fiscal Year 2020 was currently in its second Continuing Resolution. Level funding would be provided until December 20, 2019 based on the 2019 Fiscal Year budget, after which the onus would be on Congress and the Administration to decide on further budgetary determinations.

He went on to share successes regarding the publication of TB guidelines: the American Thoracic Society, Centers for Disease Control and Prevention, European Respiratory Society and the Infectious Diseases Society of America (ATS/CDC/ERS/IDSA) Drug-Resistant TB guidelines, published in the American Journal of Respiratory and Critical Care Medicine on

November 15, 2019, and the Latent TB Infection Treatment guidelines, accepted by the Morbidity and Mortality Weekly Report (MMWR). He noted that the authors of the Latent TB Infection Treatment guideline were currently responding to initial comments from MMWR editors. Following these revisions, a publication date would be generated, possibly in early 2020. He offered kudos to the contributing authors, particularly as publication seemed unlikely in recent years.

The FDA Drug Shortages Task Force Report was published in October 2019. The report identified three root causes of drug shortages, namely, (1) a lack of incentives for manufacturers to produce less profitable drugs; (2) a lack of recognitions and reward for manufacturers for "mature quality systems" that focus on continuous improvement and (3) early detection of supply chain issues, and logistical and regulatory challenges that make it difficult for the market to recover from a disruption and address the underlying issue. He mentioned that the full report was available on the FDA website and asked that colleagues at FDA correct any misrepresentation of the report's contents in his presentation. Dr. LoBue went on to highlight the Task Force's proposed solutions to the root causes identified. First, there is a need to create a shared understanding of the impact of drug shortages on patients and the contracting practices that may contribute to shortages. Secondly, there is the need to develop a rating system to incentivize drug manufactures to invest in quality management maturity for their facilities. He explained that this rating would evaluate the robustness of a manufacturing facility's quality system and reward facilities that achieve a high degree of quality management and system maturity. Thirdly, the report outlined the need to promote sustainable private sector contracts to make sure there is a reliable supply of medically important drugs. Dr. LoBue gave an example from the report regarding contracts between purchasers and manufacturers, whereby contracts currently include clauses that allow purchasers to break contracts if alternate manufactures offer lower cost medications. In such cases, manufacturers who have their contracts broken are left carrying inventory for which they have no purchaser. Such contracting practices make it difficult to manage supply and inventory.

Lastly, the FDA report proposed initiatives to help curb the drug shortage problem. These include improved data sharing and a risk management plan requirement. With improved data sharing, the Task Force suggested a legislative proposal that would expand the information required to be provided to the FDA when there is an interruption in manufacturing and authorize FDA to impose penalties for failing to provide timely and adequate notification. The risk management plan requirement would serve to provide FDA guidance for pharmaceutical stakeholders to develop, implement and maintain a risk management plan for the purpose of preventing and mitigating drug shortages. The FDA report also proposed a legislative lengthening of expiration dates for drugs. This would authorize FDA to require, when likely to prevent or mitigate a shortage, that an applicant evaluate, submit studies to FDA, and label a product with the longest possible expiration date (shelf life) that FDA agrees is scientifically justified. The FDA report also proposed the initiation of technical and regulatory considerations for pharmaceutical product lifecycle management in the form of the International Conference on Harmonisation (ICH) Guideline Q12. This Guideline has to do with the harmonization of regulations regarding drug production and approval internationally. Global implementation of this Guideline could facilitate the efforts of manufacturers who wish to modernize processes and

equipment, but have found the regulatory landscape, particularly in industrialized countries, financially burdensome.

Dr. LoBue provided a follow-up on the research meeting between the NIH and the CDC, held in July 2019. Dr. LoBue participated in a meeting at NIH held with the Chinese Academy of Medical Sciences which was, essentially, a tuberculosis research symposium, aimed at serving as a platform for researchers from both countries to share their works and look for areas for future collaboration. Also, the CDC held a webinar with NIH to discuss collaborative work on PZA resistance. He also mentioned that there would be a joint NIH/CDC webinar on December 13, 2019 discussing CDC novel bio-platform to identify pathogen and host directed therapies (HDT) against TB. He mentioned that there would be a more in-depth presentation on this to ACET later in the day.

Finally, Dr. LoBue presented selected 2019 DTBE accomplishments. The Division had a long list of accomplishments and those presented during the meeting were selected because they are relevant to issues discussed at ACET in the past or issues of interest to ACET. He presented accomplishments in categories as follows:

Epidemiology and Clinical Science

- DTBE completed analysis and drafted manuscript on the study of the accuracy of various LTBI tests, namely, QuantiFERON, T-SPOT, Tuberculin Skin Test (TST), in young children. He mentioned that the paper was currently going through the clearance process at CDC. Key among study results is that the findings support the expanded use of interferon-gamma release assays in children of all ages because in a number of cases of non-US born children, Interferon Gamma Release Assays (IGRAs) work even better than TST.
- The Division completed enrollment in a randomized non-inferiority clinical trial that compared electronic directly observed treatment (eDOT) with traditional in-person directly observed treatment (DOT). DTBE should have results early next year. There has been a lot of observational work in this area, which is highly supportive of the use of eDOT, and various economic studies have supported cost savings. Dr. LoBue mentioned that the randomized trial will help DTBE produce more rigorous reviews of eDOT.
- DTBE also began enrollment for the Tuberculosis Trials Consortium (TBTC) study 37, a phase 3 clinal trial which compares 6 weeks of daily rifapentine versus 3-4 months standard regimen of rifampin-based therapy for treatment of LTBI.

Laboratory Science and Services

- DTBE has started work on the development of a novel 3-D cell culture model which uses human monocytes and fluorescent protein-expressing Mycobacterium species to screen potential host directed therapy. Dr. LoBue mentioned that there would be a presentation on this later in the meeting.
- As part of the CRyPTIC Consortium and 100,000 Genomes Project, DTBE collaborated on a publication of a study assessing how well whole-genome sequencing performs for

the detection of susceptibility to first-line anti-tuberculosis drugs. Dr. LoBue mentioned that this was going to be important domestically as it will be in the future, in terms of looking for ways to consolidate whole genome sequencing for both molecular epidemiology and testing for drug resistance. He mentioned that research could move to a single pathway for molecular testing.

- DTBE received and tested almost 1000 samples from 43 jurisdictions for drug resistance testing.

Program and Policy

- DTBE finalized the 2020 Report of Verified Case of TB (RVCT) and the message mapping guide. Dr. LoBue mentioned that DTBE would be rolling these out in 2020, moving toward the new RVCT for updated case reporting.
- DTBE also published an evaluation showing that, over five years, the CDC-funded TB Centers of Excellence provided 14,586 expert medical consultation and training healthcare providers of TB patients.
- DTBE completed the Program to Expand Latent Tuberculosis Infection Testing and Treatment to High-Risk Communities in collaboration with Massachusetts Department of Health. The program screened 10, 000 patients, of whom 15% tested positive for TB. He mentioned that LTBI treatment and acceptance rates were quite high, with completion rates of approximately 80%.

Communication and Education

- DTBE's Communications and Education Branch has started developing and using personal stories (videos and content). Within the past year, four patients with either latent TB infection (LTBI) or TB disease have been invited to tell their story; one of the personal stories is in Spanish.
- A tremendous amount of work has been done around World TB day promotion and awareness activities. There have been over 50,000 visits to the webpages; resources on the webpages have been downloaded over 5,000 times and the videos viewed approximately 4,000 times.
- DTBE awarded funds via a new contract and cooperative agreement to develop a TB community engagement network and communication campaign to raise awareness of LTBI and increase testing and treatment among at-risk populations. Dr. LoBue mentioned that Dr. Nick DeLuca would provide ACET with a more in-depth presentation on the TB community engagement network and communication campaign during the meeting.

ACET Discussion: DTBE Director's Update

Shortages

Dr. Robert Horsburgh posed a question about FDA's proposal to maintain a supply of drugs that are not in great demand - for example drugs for multidrug-resistant Tuberculosis (MDR-TB). Dr. LoBue stated that he presented mainly highlights from the report but did not get a clear impression of a plan for an incentive mechanism for such drugs. Dr. LoBue did not note a

legislative proposal or recommendation in the FDA report regarding this concern. Dr. Robert Horsburgh indicated that there are special programs for orphan drugs but nothing similar that provides incentives to manufacturers for drugs with low demand, as far as he can tell. Dr. LoBue agreed and reiterated that the proposed incentives are meant to maintain a supply of drugs that are already in supply, and not necessarily incentivizing manufacturers to bring new drugs to the market or maintaining a drug that may not be profitable. Dr. LoBue asked Dr. Karen Elkins, US Food and Drug Administration, whether she had further insights. Dr. Elkins stated that Dr. LoBue's response is a fair summary of the current situation. Dr. Elkins clarified that the orphan drug program is intended for manufacturers already in the process of developing a drug or biologic for their own reasons, typically market driven, but this is not the same as inspiring a manufacturer to bring onboard a drug that does not exist or is still in the research process. This is a subset of the ongoing effort regarding drug shortages and targeting issues that are within the FDA's control. Dr. Robert Horsburgh stated that, for providers, the priority is keeping availability of drugs that are already approved and are in supply. Dr. Elkins answered that many of the drugs that are in shortage are typically older drugs in shortage; there is no reason for manufacturers to be inspired to change the process. This report focuses on drugs that are in FDA's wheelhouse.

In terms of Dr. Jennifer Flood's inquiry regarding FDA's response to CDC's letter to inquire about the process with which the FDA report was developed, Dr. LoBue stated that CDC can expect a specific response and responses to such specific inquiries would come from the "program". The letter sought clarification regarding gaps and solutions that were not addressed in the report. Dr. Flood hoped that ACET would discuss this further during the TB Drug Supply Workgroup presentation. Dr. LoBue added that he had brought up these issues during a meeting where the FDA Task Force was present; the Task Force operates within a specific scope of work and some of the issues may be beyond this scope and hence not addressed. Dr. Jennifer Flood mentioned that it would be nice to have FDA leadership attend an ACET meeting and provide further details regarding timelines for the proposed solutions, publishing proposed ratings for quality management, and lengthening expiry dates. Dr. LoBue stated that some of the proposed initiatives were legislative and FDA cannot predict timelines for these.

Dr. Karen Elkins agreed that progress against the proposed initiatives would depend on congressional action and increased funding. Dr. Elkins offered to act as a conduit and identify contact persons who can address the concerns expressed (offline). Ms. Cole asked who would be involved in this process, to which Dr. LoBue responded that this would be FDA's Legislative liaison. He reiterated that Dr. Elkins had offered to identify a point of contact to invite to ACET.

Suzanne Marks offered additional DTBE updates, namely, the ATS/CDC/ERS/IDSA Drug-Resistant TB guidelines that CDC published. The guidelines have implications for practice. Secondly, TB- NCHHSTP Epidemiologic and Economic Modeling Agreement (NEEMA), a modeling consortium, has started a second (five-year) period of practice.

With regards to Dr. Julie Higashi's question about drug supply, clofazimine, and the possibility of future discussions between FDA and Novartis, Dr. LoBue responded by indicating that this would have to be between FDA and Novartis. Ultimately, the decision would belong to Novartis

and would have to go through the FDA regulatory process. Dr. Higashi stated that her concern stemmed from the substantial burden on jurisdictions and programs to get access to these drugs for drug-resistant TB. Dr. LoBue agreed with Dr. Higashi; however, he noted the current regulations and laws give manufacturers the prerogative in this regard.

Manuel, a participant on the telephone, questioned why the United States shares drug supply problems experienced globally, whereas Canada does not. Dr. LoBue responded by sharing that, within the TB realm, shortages are not always caused by manufacturers, but rather the middlemen in supply chain. Canada may operate differently.

CDC/NIH Meeting

With respect to Dr. Horne's question about whether TB vaccine testing was mentioned at the NIH/CDC meeting, Dr. LoBue indicated that this had been discussed at the meeting. Dr. LoBue added that the CDC is open to this kind of research, but it would need to have domestic relevance. CDC would be interested in looking at a post-infection vaccine that would prevent reactivation. For CDC to invest in a late phase 2 or phase 3 clinical trial, there would have to be a good proof of concept to show that the effectiveness of the vaccine would need to be comparable to the effectiveness of LTBI treatment. Dr. LoBue added that there has been discussion about a recent vaccine published in the *New England Journal of Medicine*. The vaccine was at ~54% efficacy, which CDC considered to be too low, especially considering that the vaccine requires 2 doses administered one month apart. This would mean that 100% of people may not complete the full dose, and therefore, the actual effectiveness would end up being in the high 40%s. This percentage is not very high when compared to current LTBI treatment. If a post-infection vaccine was developed that could replace 3HP (12-dose regimen of isoniazid-rifapentine) or 4R (4-month regimen of rifapentine), then CDC would consider that vaccine.

Dr. Mermin asked Dr. LoBue about his thoughts on conducting a study on short course dose treatment or something that could be combined with a vaccine, to which Dr. LoBue responded that in order to be competitive, a vaccine would need to be single dose. The treatment would require pre-clinical work to demonstrate effectiveness. One can make theoretical arguments that giving drugs and reducing the organism burden works, but the combination could have deleterious effect on the vaccine, since it requires immune response. CDC would need evidence from preclinical work of the efficacy of this treatment combination. Currently, there are no such trials; the limited research available does not provide enough evidence.

Mr. Saraj Madoori asked whether the NIH/CDC collaboration would continue in 2020 and what potential future agenda items would include. Secondly, he inquired whether the Biomedical Advanced Research and Development Authority (BARDA) would possibly be included in the ongoing collaboration. Dr. LoBue responded by pointing out that BARDA had been invited to similar discussion in the past, but no progress was made towards sustainable collaboration because the issues were outside of BARDA's scope. Another attempt could be made to initiate a collaboration, but Dr. LoBue stated that he would not be overly optimistic about this.

Guidelines

In terms of David Horne's question about whether the LTBI treatment guidelines included LTBI screening guidelines in addition to regimen guidelines, Dr. LoBue answered that the guidelines focus on regimen guidelines. There are existing guidelines on LTBI screening from the United States Preventive Services Task Force (USPSTF) pertaining to non-US born persons. The NTCA was also working on a companion document which would include answers to questions of broader scope.

NCHHSTP Director's Report

Jonathan Mermin, MD, MPH (RADM, USPHS)
Director, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCCHHSTP)

Dr. Jonathan Mermin opened his presentation with an overview of NCCHHSTP's 2018 TB Surveillance Report. The report showed that the absolute number of TB cases on record continues to slowly decrease, but not at the desired speed to meet elimination targets. The majority of cases still come from four states - California, Florida, Texas, and New York. Ultimately, the biggest challenge in domestic TB elimination was expanding LTBI diagnosis and treatment, which Dr. Mermin stressed would be the "job" of the next decade.

The STD Surveillance Report showed that the number of cases of sexually transmitted diseases (STDs) have increased for the 5th consecutive year. In 2018, the combined number of cases of syphilis, gonorrhea, and chlamydia were at an all-time high: approximately 1.8 million cases of chlamydia, 583,405 cases of gonorrhea, and 115,045 cases of syphilis. NCCHSTP has considered the factors that may have contributed to the increasing rates shown in the report. While no rigorous analysis has yet been conducted, a contributing factor may be the reduction in the number and hours of operation of publicly funded STD clinics which occurred during the economic downturn and have not been reinstated despite improvements in the economy in recent years. State and local health departments have not yet taken the opportunity afforded by the improvements in the economy to invest in STD clinics and get services to the people who need them. Other contributing factors may include: the increase in syphilis which started almost 10 years ago when serosorting among persons with HIV became more common; the decrease in condom use among vulnerable groups in the United States and youth in general; and increased injection drug use and outbreaks of several diseases (e.g., syphilis) among people injecting drugs. He mentioned that other countries are experiencing issues similar to the United States.

Unfortunately, congenital syphilis cases have increased 40% from 2017 to 2018; there were over 1,000 cases in 2018 with ~100 deaths. Congenital syphilis continues to be a major issue for mothers and infants, whose outcomes are quite severe. He mentioned that this situation can, potentially, be remedied with intervention and investigation into what has allowed this trend to occur. It is a failure of healthcare system and society not to be able to prevent congenital syphilis. There is an increase in syphilis among young women of childbearing age, who are not preventing themselves from getting syphilis or failing to obtain treatment in a timely fashion.

About 1/3 of women are coming to healthcare providers at the time of delivery, at which point it would be too late to diagnose and treat syphilis. A third of women are being diagnosed but not followed up with properly with treatment post diagnosis. Another third of women are not being tested. There are variations by community; however, a system has been put in place to support work related to congenital syphilis, including funding for the most severely impacted states.

The United States has a partial surveillance system for viral hepatitis, unlike TB. Many cases of viral hepatitis are not diagnosed and, of those diagnosed, many are not reported. Many states have no requirements to report cases of viral hepatitis or withdrew their requirements because of the overwhelming number of cases, particularly of hepatitis C virus (HCV). There has been an increase in the number of cases of hepatitis A virus (HAV) because of the massive multi-state outbreak of HAV. Hepatitis B virus (HBV) is consistently increasing among people who inject drugs, although it is not as transmittable as HCV. Dramatic increases have occurred in the incidence of HCV due to injection drug use, particularly in communities that either do not have access to needle programs or who are not aware of the risks associated with sharing needles. There has been a decrease in HCV mortality over the past three years due to access to highly effective medication. Incident cases of hepatitis C virus continues to be high, at ~ 40,000 new infections a year and is a major area of emphasis for the Division of Viral Hepatitis within NCCHSTP. An illustration of the multi-state hepatitis A virus outbreak showed outbreaks in Michigan and California in early 2017. While the two states were able to contain the outbreaks, it spread to other states in early 2018. Once several counties are affected, it is difficult to pass the critical point and start to improve. Kentucky and West Virginia have had thousands of cases costing a minimum of $14, 000 per hospitalization, which means millions of dollars for the nation. Some states have been able to prevent large increases by vaccinating people who are at risk, including persons who are homeless, inject drugs or use drugs. The solution is to bring vaccines to the communities rather than have people come to healthcare stations and providers. States that have successfully implemented this strategy are those that have obtained state funding, which helped to keep the situation from worsening. It is a challenge to obtain funding based on a theoretical, rather than a currently ongoing, risk. Therefore, most states have only been able to respond reactively, rather than preemptively. For this outbreak response, NCCHSTP has had its incident management system in place over the past two years. Every state would need to set up system to respond to the outbreak. Compared to vaccine programs for children (i.e., VFC), the adult vaccination program in the US is weak because we do not have similarly dedicated resources for adults.

The December 2019 CDC *Vital Signs* report highlighted the critical need to increase HIV testing, and treatment, particularly decreasing barriers to accessing pre-exposure prophylaxis (PrEP). *Vital Signs*, issued close to World AIDS day, reported 154,000 people with HIV (14%) are unaware of their status. Awareness of status has increased from 75% to 86% in the past 15-20 year; however, this is still not as high as needed, partially because these persons who are unaware of their HIV positive status are not taking advantage of life-saving medication, as well as continuing to inadvertently transmitting to others. Simply knowing one's HIV status decreases risk. To that end, CDC has implemented several measures to increase testing. The *Vital Signs* also reported an increase in viral suppression rates, that is two-thirds of people diagnosed have the virus under control. This has been the result of concerted efforts by programs, practitioners

and the community. For example, there is the *U=U* movement (Undetectable equals Untransmittable) which has mobilized the community to embrace prevention. About 50% of persons with HIV in the United States are supported by some form of Ryan White service. Viral suppression rates have increased dramatically to over 85% which has decreased disparities observed previously across racial and ethnical divides by focusing heavily on brining resources to communities where they are needed. *Vital Signs* also reported a doubling of the number of people taking PrEP medication. CDC has incorporated support for PrEP use in CDC's state and local health department funding announcements with communications about PrEP. The US Preventive Services Task Force has issued a grade A rating for PrEP which, hopefully, will deal with some of the largest barriers for PrEP (e.g., copays). HHS has started a PrEP program to provide coverage for the uninsured: up to 200,000 people fall in this category. There are major disparities in access to PrEP. A study conducted by the Center showed that almost 80% of men who have sex with men (MSM) are less likely to discuss PrEP with their healthcare provider and their clinicians are less likely to be prescribe PrEP for them. This is an area for major effort and mitigation by the CDC and other stakeholders, to increase prescribing of PrEP and increasing awareness among persons who are at risk. Several cities in the United States and other countries that prescribe PrEP have seen decreases in HIV incidence.

A new initiative has been announced by the Administration which has support for its first year's initial funding in both the House and the Senate budget bills. Using Minority AIDS Initiative funding, CDC issued $12 million to the 57 jurisdictions (50 local jurisdictions and 7 states) that are part of Phase One of the initiative. CDC does not want to wait until Fiscal Year 2020 to initiate planning as this would cause delays and hamper momentum. The funding will enable the communities to come together to plan. There are requirements about community membership (e.g., people with HIV) in the jurisdictional plan development. CDC has done this with the Health Resources and Services Administration (HRSA), whereby they have joint jurisdictional plans but, primarily, the state Health Departments with a few selected local jurisdictions. Most local jurisdictions are smaller and have not been involved in jurisdictional planning in the past. CDC is hopeful that this initiative will engage the local community and Health Departments to apply to HRSA and CDC, who will be the recipients of the initial funding.

CDC awarded $1.5 million to the National Alliance of State and Territorial AIDS Directors (NASTAD) for national capacity building. The Division of HIV/AIDS Prevention (DHAP) changed the name of the campaign from "Act Against AIDS" to "Let's Stop HIV together". The name lays the groundwork for purporting the idea of working against AIDS together. CDC has funded new partnerships and new resources and materials as part of the campaign.

CDC has new HIV web resources, including a new website, the *HIV Nexus*. HIV Nexus will help clinicians communicate with patients and caregivers about HIV prevention, screening and treatment. Tied with that is a new video, "Journey to Undetectable", which promotes keeping HIV viral loads undetectable for both practitioners and people with HIV and encourages people with HIV to stay in care. Funded via the Minority AIDS Initiative, the video promotes the benefits of HIV treatment adherence and viral suppression.

CDC published the *Social Determinants of Health among Adults with Diagnosed HIV Infection* report which focuses on social determinants and people with HIV. The report showed the highest HIV diagnosis rates were among those in geographic areas and census tracts where most residents either lived in poverty, had less than a high school diploma or did not have insurance coverage. The report also revealed that the lowest linkage to care rates were among people who lived in counties with lowest education achievement. These social determinants are driving the difficulties of lowering trends in HIV incidence and transmission.

Dr. Mermin closed with a staff update. Hazel Dean, the Deputy Director of NCHHSTP and former designated federal official for ACET has taken a new job, as of October 2019, as Editor-in-Chief of *Public Health Reports*. NCHHSTP will be advertising the position of Deputy Director shortly, and he asked those present to share this information widely.

ACET Discussion:

In response to Dr. Robert Belknap's question regarding how to protect funding for TB programs, defend against budget cuts, and identify threats, Dr. Mermin responded by pointing out that it behooves engaged, passionate pleas and thoughtful discussions with relevant leadership/decision makers at CDC and in DC. To counter the decline of the 'purchasing power' of TB, he advocated that, per practical public health, things can be done better. For example, HIV incidence reduced by 18% because the allocation of resources to states was shifted, and distributed per the disease epidemiology, rather than other designation. It is also important to focus on cost saving prevention. It is important to work with relevant partners, for example, NIH on game changing science, for example eDOT, 4R and 3HP. Secondly, it is important to make advancements with LTBI. One means to this, is to help other countries of interest to decrease their TB rates. Another means is to focus on more efficient screening of persons who migrate to America, encouraging screening prior to migrations.

With regard to Dr. Belknap's inquiry about how to improve access to LTBI treatments, using advancements with PrEP as a model to which Dr. Mermin responded that it is imperative to include LTBI testing in routine electronic health record prompts or if risk factors show the need for annual LTBI testing. This dramatically increases screening and testing.

In terms of Dr. Flood's follow up question on how to galvanize the work of expanding LTBI testing and treatment to ensure funding, Dr. Mermin responded that it might be helpful for HRSA and CDC to constantly bring up the issue in the highest levels of Government, so that new resources can be created for this opportunity. Using the example of the HIV initiative, he mentioned that the CDC Director at the time has a keen interest in HIV and therefore began discussions with other agencies that were similarly interested. From there, the political support grew exponentially.

In terms of Dr. Horsburgh's question regarding the TB and HIV cascade of care, Dr. Mermin responded that the TB surveillance is outstanding. He added that there is a need to standardize the way the estimates are being produced.

Project ECHO's Support to TB Activities

Diana Fortune, BSN, RN
Former TB Program Manager
New Mexico Department of Health

Ms. Fortune presented on the use of project ECHO to support TB activities in New Mexico, United States. Globally, billions of people lack access to high quality healthcare. While healthcare exists, it is unevenly distributed. In 1950, the time to double the volume of medical and nursing knowledge was about 50 years. In the year 2020, it is estimated that it will only take 73 days for the volume of medical knowledge to double. There is no possible way for a single individual to keep up with this rate. Project ECHO's aspiration is to democratize medical knowledge. Knowledge is power and getting knowledge to the people that need it so that they can receive the treatment that they need and deserve is what project ECHO aspires to do. The goal is to touch 1 billion lives by 2025.

The ECHO model has four basic tenants: (1) Amplification and use of technology to leverage resources, as well as using video conferencing. Video conference enables participants to engage and look at actual persons as they make presentations. No one goes to a meeting in person with a shroud or bag over their head, and in the same vein, participants of project ECHO must turn their video on to facilitate physical and mental engagement in the session. Video technology is a significant part of the success of the ECHO project. The second tenant, (2) is sharing best practices. For example, with regards to finances, New Mexico has struggled to justify its TB budget and it is essential to continue to engage in best practices and not lower standards of care. The ECHO model enables sharing of such best practices. The third tenet, (3) is case based learning, which is essential. It involves presenting real cases to ECHO participants, monthly, in order to consider and correct possible mistakes in real-time versus learning retrospectively. The fourth tenet (4) is monitoring outcomes to determine whether progress is being made.

People use the terms ECHO and telemedicine interchangeably, but they are significantly different. In traditional telemedicine, there is one doctor who manages one patient remotely. On the other hand, ECHO exponentially pushes out medical knowledge. ECHO uses expert hub teams. It is important to maintain expert medical expertise in Health Departments who share knowledge with primary care teams, whether those are in a practice or local public health offices. Primary care teams provide care to persons who have either TB disease or LTBI. ECHO takes a few people with the required nursing knowledge and reaches many people. The difference between ECHO and a webinar is that, while webinars focus on a one-way flow of information, ECHO is participatory. People on both sides of the video conference share knowledge. Both the expert hub teams and the learners share knowledge, as learners may be experts in other relevant fields; ECHO is not a one-way flow of information.

There are eight reasons why the ECHO model works:

1. needs based learning addressing complex problems;
2. case-based learning;

3. collaborative learning;
4. low dose, high frequency learning;
5. interprofessional learning;
6. peer-to-peer learning via video conferencing;
7. mentorship with access to experts; and
8. quality improvement is implicit and increasingly explicit.

Among these eight, three were highlighted: case-based learning; low dose and high frequency, that is, keeping clinicals short, repetition during sessions; peer to peer learning, that is, taking advantage of technology to circumvent limitations of being unable to meet in person to increase the effectiveness of learning.

New Mexico has faced challenges in its TB programs. As background information, the state has seen a dramatic decrease in persons with TB, specifically a 66% decrease in cases since 1996. In 2018, New Mexico recorded 41 people with active TB. While this is not a large number, the complexity of cases is intense. Persons with TB typically have other medical needs which require a significant portion of resources to address. Medical care can last for as long as 6 to 9 months. Treatment would have to span the entire patient, whether pediatric or adult, as well as their families. In addition, the nursing workforce has decreased. In New Mexico alone, in the last year, three nurse consultants have either retired or transferred to a different job. When tallied, this statistic means over 100 years of nursing expertise lost. This is not only a trend in New Mexico, but also potentially in the United States and globally.

The first ECHO clinic in the US was held in April 2015. New Mexico was the first state to hold a TB ECHO clinic. The clinic focused on enabling nurses to develop skills and confidence in nursing case management. The expert hub team included physicians and nursing consultants. During the clinic, the expert hub team chose three points in time where patients with TB out to present to clinics: at the beginning of care, two months after care has been initiated, to ensure culture conversion, check chest X-rays etc., and finally, at the completion of treatment. Patients may have complications and would need to present to the clinic multiple times before treatment regimen is completed. As a centralized state, the Medical Director, in this example, Dr. Marcos Burgos, can give orders to nurses as they are presenting the patient during the clinic. All protected health information (PHI) remains confidential during the clinic. Tools used during the ECHO clinics include TB record forms, chest x-rays, follow-up chest x-rays, pictures of other forms of TB a patient may have. One challenge of the US TB ECHO clinic was obtaining support from health facilities management to allow nurses time to attend. Typically, one nurse is responsible for public health programs, so it is difficult for such persons to find time to attend ECHO. This is a significant problem that needs to be identified and addressed.

In New Mexico, there are four different ECHO clinics each month. The longest standing ECHO clinic is for TB disease and there have been 450 sessions with 1313 people in attendance and 669 case presentations. The newest ECHO clinic launched in June 2018 and focuses on TB infection. This ECHO clinic targets community providers who treat TB. Conducting the clinic is an ongoing challenge. So far, there have been 15 sessions on TB infection. Another of the clinics, is the Navajo Nation TB ECHO clinic. Ms. Fortune turned the presentation to Dr.

Jonathan Iralu, who is Medical Director for the Navajo TB ECHO Clinic to give ACET further insights. Dr. Iralu mentioned that the TB ECHO clinic has been a great boon for the Indian Health Service. Through the project, tribal health workers and primary care providers have been trained in the treatment of both LTBI and TB disease, as well as case management with plans to further expand the use of TB ECHO clinics. The Navajo Nation TB ECHO clinic has been incredibly effective and there plans to roll out a Hepatitis ECHO and a HIV ECHO, and in 2020, an HIV PrEP ECHO, which will start on Valentine's Day. Returning to her presentation, Ms. Fortune stated that the Navajo Nation ECHO is a wonderful illustration of collaboration between Arizona and New Mexico Departments of Health, Navajo Nation and the Indian Health Service, who meet monthly. The fourth ECHO clinic is the binational US/Mexico TB ECHO clinic. Launched in April 2017, the clinic has had 27 session with over 3,000 people in attendance and 21 case presentations. Participation from Mexico has skyrocketed in the past 6-9 months. Border states in the US have participated as well as non-border states. Taking migration into consideration, the objective of the clinic has been to increase bilateral understanding of resources and systems for TB care so that patients can receive adequate care regardless of which side of the border they reside. The clinic is held in Spanish and English simultaneously and the greatest challenge has been finding translators. Poll everywhere is used in both English and Spanish during the clinic, which has worked well.

Monthly didactics are conducted as part of the ECHO model. They are short (10-15 minutes) and didactics are archived for later viewing if requested. The University of New Mexico provides continuing education credits. Participants are issued a certificate if they complete the post evaluation link, which is shared after each clinic.

Project ECHO conducts monthly and periodic evaluations consisting of monthly pose-session evaluations, self-efficacy survey for nurses and focus groups conducted by the ECHO Institute. Per the evaluations, the biggest improvement in the ECHO clinic sessions has been timeliness. Previously, case presentations could take up to three hours, which have now been significantly shortened.

Members of the National Tuberculosis Controllers Association (NTCA) have been the latest users of project ECHO. ECHO is not only applicable in clinical settings; it may also be used as a community of practice, if different targets or sources of learning are identified. It was recently used for the NTCA Notice of Funding Opportunity (NOFO) in July 2019 and there was tremendous participation from TB program managers across the country. Jason Cummings provided a template that was used by a large percentage of participants to write their funding opportunity grants. Ms. Fortune asked Ms. Donna Wegener whether she would like to contribute to the topic at hand. Ms. Wegener highlighted the mentorship aspect of the ECHO model as one of the means to circumventing challenges caused by high turnover of TB program managers. Through ECHO, program manager throughout the US commented that for the first time they felt connected to a community. Ms. Wegener stated that there was going to be another ECHO session Thursday, December 12, 2019 to help TB program managers to prepare annual progress reports. Ms. Fortune reiterated that ECHO enables a constant communication with communities and helps to establishing real leadership. In closing, Ms. Fortune shared her

new contact information as she had recently resigned from the New Mexico Department of Health and was currently a TB nurse consultant with NTCA.

ACET Discussion: Project ECHO's Support to TB Activities

Dr. Horsburgh, Jr. commended Project ECHO, stating that it was a wonderful and very effective technique. He stated that there is a TB ECHO used in Massachusetts by providers to connect to local health centers to raise champions for LTBI screening and treatment. Ms. Fortune added that ECHO is also used in Colorado and Rhode Island and Washington State. She mentioned that although utilization of ECHO has grown in the US, it has been at a much slower rate compared to its use globally.

In response to Dr. Zelalem Temesgen's inquired about challenges of the TB ECHO model and how these may have been resolved, particularly in relation to situations where primary care providers seek immediate responses to questions regarding their patients. Ms. Fortune stated that there have been similar challenges elsewhere and unfortunately, no resounding resolution has emerged.

Update from TB Centers of Excellence

Dawn Tuckey, MPH
Project Officer
Field Services Branch
CDC Division of TB Elimination
TB Centers of Excellence Team

Allison Maiuri, MPH, CHES
Team Lead for Education, Training, and Behavioral Studies
Communication, Education, and Behavioral Studies Branch (CEBSB)
CDC Division of TB Elimination
TB Centers of Excellence Team

Neela Goswami, MD, MPH
Medical Officer
Field Services Branch
CDC Division of TB Elimination
TB Centers of Excellence Team

Dr. Neela Goswami, Ms. Allison Maiuri and Ms. Dawn Tuckey provided an update from the TB Centers of Excellence for Training, Education and Medical Consultation (COE), DTBE. Their presentation outlined the COE: training and education strategies and activities, including training sessions, mini-fellowships and technical assistance; activities in the US-affiliated Pacific Islands (USAPI), particularly regional trainings, conferences and an island-specific, culturally-appropriate educational product; and medical consultation strategies and activities. Through needs assessments, the COEs identified four main priorities for education and training, namely,

focus on key topics (complex medical issues, TB treatment, diagnostic tests, building partnerships with private providers and diverse populations), to tailor trainings (profession, setting, skill level or specialization, to keep people updated (new research and guidelines, keyed into right channels for updates) and provided mix of methods and formats (online, in-person and paper and digital). The COEs also provided medical consultation services for TB disease and LTBI, longitudinal consultation as requested by providers for complex clinical cases and collected, analyzed and shared medical consultation data with appropriate partners. In total, 14,586 consultations were addressed and entered in the COE Medical Consultation Database (MCD) from January 1, 2013 through December 31, 2017. A question was raised about a specific POC for medical consultations. It was agreed that a list of POC for medical consultations will be sent to Margie for dissemination to ACET for use as needed.

Advice requested from ACET

1. **What service should COEs prioritize if resources limited/some activities need to be limited during the rest of this or the next funding cycle?**
    - More face to face trainings for large groups of providers that are serving high risk populations; to support the scale up of LTBI testing and treatment. For example, civil surgeons, especially after the revisions to the TB Technical Instructions. Ms. Maiuri shared that the COEs supported the Division of Global Migration and Quarantine (DGMQ)-led training event for civil surgeons and panel physicians held in Florida, December 2019

2. **How can the COEs provide optimal coordination and support to TB programs beyond the current efforts?**
    - Have the COEs considered coordinating trainings using ECHO? There seems to be a lot of overlap between ECHO and the work done by COEs, in terms of longitudinal consultation, educational, and capacity building, for example the use of ECHO among the nursing force. Rather than brining people for large in-person training events, hold smaller scale, continuous sessions with providers to maintain and build capacity in TB programs.
3. **Are there any partners or stakeholders that the COEs should be working with beyond their current partnerships?**
    - Association of Public Health Laboratories (APHL) and the American Society for Microbiology could be a resource for laboratory consultations.
    - There is opportunity for further engagement with current partner, NTCA. ECHO is one of the ways COEs can engage with NTCA.
    - With regards to LTBI education, is it possible to reach out to organizations and associations involved in primary care such as the American Academy of Pediatrics Care and the American Academy of Family Physicians. The COEs have the education and knowledge resources but these organizations may not be aware of training available through the COEs. And if these people do not know; then how can they benefit?

4. **What populations or sectors in the US do you think are in need of, and may not be benefitting from COE services and how could we better target them?**

ACET Discussion:

In response to Dr. Lixia Liu's question about whether the COEs provide laboratory consultations, Ms. Tuckey answered by pointing out that during monthly COE all-calls, they have observed an increasing number of laboratory-related questions and therefore have recently brought relevant guest speakers experts to provide laboratory consultation.

Dr. Flood pointed out that it is important that COEs not replace the medical director in jurisdictions, as previously mentioned in the presentation. This situation is currently prevalent in California, where there are a lot of healthcare deserts: state health officers and nurses may play a significant role in providing care to persons with TB without an actual in-person visit. Additionally, these state health officers and nurses may not have extensive experience in treating TB disease. Dr. Flood expressed the desire for state Health Departments to work with the COEs to address this challenge. Dr. Goswami's agreed that this point cannot be overemphasized. In many cases, this situation impacts patient care. There is the need for additional resources is terms of TB expertise in the parts of the US where it is most needed.

In response to Ms. Nuala Moore's inquiry about whether there are pharmacists to provide consultations on the COE teams, Dr. Goswami responded that, yes, there is a need for pharmacists and one of the COE teams has a permanent pharmacist. Other COEs have access to pharmacy expertise, as needed.

In terms of Dr. Ulana Bodnar's question about whether the COEs prefer for people to use a specific point of contact to receive consultations from the COEs, for the purposes of capturing this data, Dr. Goswami asked that people reach out to the relevant the COE per the patient's location. The COEs have both a hotline and a mailbox through which their services may be obtained. The COE team present will provide a list of COE points of contact that will be distributed to ACET members.

With regard to Dr. Julie Higashi's question about whether the COEs have people at the local level who have expertise in TB and are willing to engage with the COEs using a model akin to ECHO, Dr. Goswami answered by sharing that the COEs are in the process of testing an electronic system where an automatic email notification can be sent to a selected local point of contact whenever a person is a particular area seeks consultation from the COEs. This local point of contact or consultant can join the email thread and either observe or contribute to the conversation regarding the patient's care. This is based on the COEs traditional and older medical data base where a written report of each consultation is sent to both the caller and the state health department's TB program. The new electronic system is being piloted and currently only operational in one jurisdiction.

Ms. Tuckey added that the COEs are collecting data on the impact of medical consultations and making changes to their Funding Opportunity Announcement (FOA) based on the pilot test and asked for feedback from ACET.

Dr. Shama Ahuja added a comment regarding the need for more epidemiologic training. For example, the in New York, she receives a lot of questions pertaining to conducting a large contact investigation, how to conduct whole genome sequencing, or how to present data.

LTBI Communications Campaign Update

Nick DeLuca, PhD
Branch Chief
Communication, Education, and Behavioral Studies Branch (CEBSB)
CDC Division of TB Elimination

Dr. Nick DeLuca provided an overview of a newly funded Latent TB Infection Community Engagement Network and communications campaign. He opened his presentation with a video promotion of World TB Day, which highlighted personal stories from TB survivors. He acknowledged and thanked colleagues at the NTCA for the tremendous amount of work done in the last few years to create a community of survivors of both TB disease and LTBI.

The United States has been highly successful in reducing TB cases over the past two decades. There has been a slowing decline in TB incidents rates in the last few years. Majority (70%) of TB cases in the US occur in persons born outside of the US. Mexico, the Philippines, India, Vietnam, China, Guatemala, and Haiti are the countries of birth which account for majority of non-US born persons with TB and this trend has been consistent over the last several years.

NCHHSTP, as well as CEBSB, apply a dual approach to tackling TB elimination in the United States. Both have been continuing efforts to identify and cure persons with active TB disease while expanding capacity in high-burden jurisdictions for targeted testing and treatment of persons with LTBI. CDC's strategy for addressing LTBI is to accelerate screening and treatment, through expanded targeted LTBI testing and treatment, taking advantage of the TB blood test or Interferon Gamma Release Assays (IGRAs), as well as shorter course treatments such as 3HP or 4R. We need to think of novel ways to engage new partners as well as conduct outreach to engage with communities that are most affected and their primary healthcare providers. We need to target resources for the states with the highest disease burden: Florida, Texas, New York and California. Over 80% of active TB disease cases in the US are from long-standing LTBI. Up to 13 million people in US have LTBI. Also, LTBI treatment is 90% effective in preventing TB disease. The US Preventive Services Task Force and CDC recommend testing for TB as part of standard preventive care for certain at-risk groups, particularly people who were born in or frequently travel to countries with high TB prevalence, namely, Mexico, the Philippines, India, Vietnam, China, Guatemala, and Haiti.

Expanding LTBI testing and treatment is the final frontier of TB elimination in the US. By developing a targeted campaign(s) for LTBI and working with providers and community partners, we can increase awareness of LTBI and encourage testing and treatment among at-risk populations. CEBSB is creating such a campaign with a goal to develop targeted communication campaign to encourage testing and treatment among at-risk populations. The campaign will target consumers directly, that is, those directly at risk for TB, as well as primary

caregivers. In addition, the branch will develop a partner network, the TB Community Engagement Network, to engage at-risk communities to assist with outreach and other activities to encourage testing and treatment for LTBI.

The campaign will focus on Asians, and Hispanics/Latinos in the US, as well as healthcare providers who serve at-risk populations. In 2018, TB disease was reported in 3,190 Asians in the US, particularly Filipinos, Indians, Vietnamese and Chinese, accounting for nearly 35% of all people reported with TB nationally. If additional resources are available, the campaign can be expanded in several ways: working with additional Asian American audiences, Hispanic/Latino audiences, additional media markets and civil surgeons.

The objective of the LTBI communications campaign is to raise awareness about LTBI, risk and link between infection and disease, address misperceptions, decrease stigma and encourage testing and treatment. Moreover, the campaign will seek to increase awareness of treatment for LTBI, especially shorter regimens and encourage providers to testing and treat LTBI among at-risk populations. DTBE will develop the campaign and the community engagement network in parallel. Campaign messages will be influenced by recently conducted message testing research in addition to extensive formative research, which will begin in 2020. Campaign materials will be culturally and linguistically appropriate. The campaign will borrow from the Know your Hepatitis B Campaign, development by NCHHSTP's Viral Hepatitis branch, as a model. The know your Hepatitis B Campaign, a multilingual campaign developed by CDC and Hep United in 2013, also targeted Asian Americans, specifically Chinese American and Vietnamese. The campaign created a coalition, the Hep B United Coalition which is what the LTBI community engagement network will be modeled after. The Hep B United Coalition employed ongoing technical assistance and training, a mentoring program, and mini grants. Planned strategies for the LTBI community engagement network include, creating a network of community-based organizations, health centers, professional associations, and others. The LTBI community engagement network will also engage in capacity building and using the community network to implement the campaign. Some community partners have already been funded through CSTLTS's National Partnerships Cooperative Agreement. The lead community partner, the Asian and Pacific Islander American Health Forum (APIAHF), has subcontracts with the Association of Pacific Community Health Organizations (AAPCHO), the Hepatitis B Foundation (HBF) and STOP TB USA. The goals of the community engagement network are to engage at least 20 organizations interested in TB efforts and who are focused on Asian American, Native Hawaiian, and Pacific Islander (AANHPI) communities. Partners will be added to an electronic distribution list and there will be regular partnership calls or webinars. DTBE hopes to provide mini grants to these groups to conduct needs assessments within targeted communities. The CEBSB will also conduct formative assessments to inform development of the network and LTBI campaign. The culmination of these efforts will be to convene a two-day summit between new partners, as well as colleagues from Heb B United. The first TB summit will be held in Atlanta in 2020.

New partners for the LTBI Campaign include the group Weber Shandwick and subcontractors, IW Group and the Brunet-Garcia, each of which have expertise supporting Asian American and Hispanic/Latino communications, respectively. The development of the campaign itself will

follow a systematic process, beginning with formative research in 2020, development of campaign strategy and plan, creative development, initial campaign launch and dissemination, process evaluation and outcome evaluation. In terms of timelines, the base year (2019-2020) will be used for formative research, campaign development and pilot testing will take place in year 2 (2020-2021) and year 3 (2021- 2022) will be devoted to campaign implementation. Formative questions for the base year include (i) what factors influence decisions about whether to test and treat LTBI, (ii) what barriers and facilitators exist related to testing and treating LTBI, (iii) what are the trusted sources of health information and communication channels to reach populations of interest.

All these efforts will be couched in behavior change and communications theoretical framework. The social ecological model will be used to consider relevant factors at the individual level, the interpersonal level, healthcare setting level and larger societal level. During the first year, the branch will conduct focus groups in person, and in language with participants belonging to at-risk groups of Asian Americans and Hispanic/Latinos, as well as physicians, nurses, physician assistants, nurse practitioners and civil surgeons who serve these groups. Focus groups with communities will be health in Los Angeles, California, Houston Texas, New York, New York. The campaign itself will incorporate public service announcements, including print, digital and video formats; social media; partner coordination; and healthcare providers who serve at-risk populations.

In closing, Dr. DeLuca acknowledged the entire CEBSB for the team efforts toward the LTBI campaign and community engagement network.

Advice requested from ACET

1. **General comments in reaction to presentation**
    - All comments were relevant to advice requested and have been presented in the appropriate sections
2. **Any feedback on the proposed LTBI campaign and community engagement network?**
    - The general outline seems very well thought out and has all pertinent components. However, it is discouraging that it will take three years to arrive at a product
      Dr. DeLuca's response was that it will be a year before they get to start implementing and products may have been developed by the beginning of 2021. The project is currently looking for markets for implementation, where it would be most useful
    - It will be great if the methods and products can be made available prior to the above referenced implementation research.
      Dr. DeLuca's response was that the campaign is national, and all materials will be available nationally. Jurisdictions can adopt and use the campaign products developed
3. **Any suggestion for the provider component of the campaign?**

- A big missing piece of such initiatives is market research to understand what providers need

4. **Any suggestions for the evaluation component of the campaign?**
    - None was made
5. **Any suggestions of key partners to brief and include in this effort?**
    - The Chinese - American Physician Society, and Association of Physicians of Indian Origin Medical Professionals, National Healthcare for the Homeless Council
    - Dr. DeLuca responded by indicating that no associations have been contacted yet. However, there is an initial list of associations with whom CDC would like to collaborate on this project
    - A request was made for the list of associations that the CDC would like to engage moving forward
6. **Does ACET have any additional guidance on how they would like to engage with the TB Community Network in the future**
    - A representative from ACET could be assigned to participate in TB Community Network meetings, once established. ACET will review its rules to ensure this is allowed. To have a representative from the TB Community Network assigned to ACET in the same manner would require a change in ACET charter.
7. **The campaign and network have some initial funding; however, additional funding would allow us to include other populations (e.g. Hispanics) and expand the implementation pf planned efforts. Do ACET members have ides for resources?**
    - The issue of trying to leverage funding for public service announcements, advertisements is a struggle for all. One means to address this it to discuss within a community of practice, similar to ECHO. For example, in Los Angeles, Dr. Julie Higashi has sought contacts with local elected officials in the media field for potential in-kind support for health campaigns. Dr. DeLuca responded by pointing out that the Hep B Campaign received a lot of in-kind support which aided its success.

ACET LTBI Workgroup Update

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

Dr. Flood presented an update from ACET LTBI workgroup. She stated that Dr. Jeffrey Starke, who was the Chair of the LTBI Workgroup, has rotated off ACET, as of June 2019. In his presentation, Dr. Mermin articulated the heart of the LTBI Workgroup summary report, which is, “Expanding LTBI testing and treatment, making this happen, is the job of the next decade”, Dr. Jonathan Mermin, 2019. Dr. Flood acknowledged the membership of the LTBI Workgroup,

stating that it is one of the most engaged workgroups she has worked with. The workgroup considered evidence, literature, and experience in arriving at the contents of the summary report to be presented. In August 2019, Dr. Flood provided ACET with a preliminary view of summary report, on behalf of the LTBI Workgroup and it is yet to be finalized.

The LTBI report is entitled “Roadmap for Advancing TB Elimination in the United States through Scale Up of Testing and treatment of Latent TB Infection”. As a strategic document, the report is intentionally short, to allow for possible publication in the MMWR like past strategic plans produced by ACET. For this reason, it is not all-inclusive but rather gets to the main point regarding strategies and interventions. The report’s intention is to update the ACET 1989 strategic plan for the elimination by describing domestic actions needed to intensify LTBI testing and treatment. It has been 30 years since ACET had a strategic plan on TB elimination and the development of this updated report is timely, or even past time. Most of the presentation will focus on the report’s recommendations and accompanying rationale. The report’s audience is primarily CDC and HHS, which are ACET’s advisory capacity. However, it also considers a broader audience and secondary purpose, which is to increase the visibility and awareness about LTBI testing and treatment.

The focus on LTBI, while not a new concept, is because untreated LTBI now generates the newest TB cases in the US. Most of these long-standing LTBI cases occur among non-US born persons. These changes in the TB elimination terrain require a response. In 2016 the US Preventive Services Task Force called for routine LTBI testing and treatment of non-US born adults, given the effectiveness of this targeted testing. However, adoption of these recommendations across health centers in the US has been slow. The summary report produced by the LTBI workgroup seeks to further increase visibility of those same recommendations, that is, to increase targeted LTBI testing and treatment. The focus is a strategy document is to improve ability to conduct LTBI testing and treatment and measure LTBI outcomes in the US.

The report identifies reasons for the slow progression of LTBI testing and treatment in the US. These reasons are categorized into four sets of barriers:

Barriers for patients who may benefit from LTBI testing and treatment

- Individuals with LTBI feel well/unaware of risk of developing TB disease and benefit of testing and treatment, so there is little patient-driven demand
- Healthcare access is difficult for many who would benefit from TB prevention services
- Patients at risk for TB may not be in care or may have prohibitive out-of-pocket cost, for example co-pays.
- People who are at risk are not aware and may patients do not push for this.

Barriers for care providers

- Even if people were to ask for testing or want to know more about the risk, providers have not been equipped with necessary information about who is at risk, testing, and

treatment. Many healthcare providers are unaware of the USPSTF LTBI recommendations and are unfamiliar with newer tests and drug regimens. This is an important gap.
- LTBI risk assessment and testing are often overlooked by clinicians because of competing priorities.
- Systems for support adherence throughout treatment are typically undeveloped.

Health system barriers

- Few systems exist to help busy physicians with LTBI testing and treatment;
- Most electronic health records to no include TB risk factor question as part of routine.
- Changing electronic health records (EHRs) to include important elements (e.g. countries lived in) is difficult. It sounds easy to add, however, it is hard because electronic health records are part of a large business systems and one is required to make a business case to justify proposed additions. This has been a big problem that is difficult to resolve overnight.

Measuring outcomes for improvement

- No national requirement for quality improvement of LTBI testing and treatment or no required national LTBI performance metrics.
- The care cascade, identifying at-risk populations, testing the population, having TB treatment accepted, initiated and completed, has a lot of attrition and there are no uniform or simple systems to measure outcomes and performance metrics. There should be a system to capture metrics, particularly from healthcare providers who receive funds from the Medicare system and treat at-risk populations.
- Clear need for measuring LTBI burden and outcome over time with nationwide system.
- Further impediments include resources. Health Departments, whether local, state or federal need new resources to tackle LTBI. These Health Departments are unable to focus on LTBI because of absence of designated funding and need to prioritize attention on TB diseases, previously called first tier priorities. However, now there is a have the dual approach and helping decline of TB disease will require attention to LTBI.
- The return on investment and future savings incurred by LTBI testing and treatment is not well-known to decision-makers. CDC has been working hard to articulate the cost effectiveness of targeting LTBI treatment to decision-makers; however, it is really hard to make a case when you can't talk about the return on investment, whether you are talking to Kaiser Permanente or Government entities.
- Complementary roles of public health department and primary care providers in preventing TB is not well articulated. According to the USPSTF findings, primary care providers are charged with TB testing, which is not very well known among providers. What role do public Health Departments play? Public Health Departments tend to play role as champions of targeted TB campaigns and act as subject-matter experts.
- There is little synergy between HBV, HCV screening for activities even though many patients at risk for all. A lot of patients have dual or triple infection yet there are no

systems that make use of an approach that is more integrated. Understanding how to address this could lead to greater efficiency in TB elimination.

These are the barriers that the LTBI Workgroup sought to address through its report.

The LTBI Workgroup did not conduct a systematic review or meta-analysis in its approach to craft the report. There are very few relevant intervention trials or implementation science research. Rather, the group reviewed past strategic plans, published literature, where it existed, and their subject matter expertise to craft strategies that could possibly be implemented to address the impediments or barriers.

Some of the USPSTF findings were key to the LTBI Workgroup in detailing the evidence base for the summary report. The workgroup's findings and recommendations are presented in four-five buckets, along the lines of the stepwise cascade.

1. **Find and engage high- risk populations and their providers.**

   It is important to identify the providers that are more likely to serve high risk populations. There is currently no intervention, test or treatment that can be given to every US resident. It is important to identify the provider groups who are serving those at risk, or non-US born individuals. A lot of work has been done in this regard; however, it is still imperative to carve out a target audience. There is the need to identify the community groups that are most at-risk. Kudos to DTBE for taking such a systematic approach in their TB campaign, because identifying target audience is such a critical step. It is not enough to create posters and other materials in a vacuum, but rather do this in a data-driven manner.

   There is the need to launch evidence-based strategies (educational campaign, marketing campaign and academic detailing) to raise TB raise awareness, promote testing and treatment strategies and create demand for testing.

   There is the need to build on specific strategies that drive success of other campaigns such as the Hep B campaign and some interventions in the HIV arena.

2. **Use focused, effective testing and treatment strategies.**

   We need much better dissemination of simple risk assessments, testing and treatment provider tools that prompt use of the most effective treats and the short course treatments.

   How do we motivate healthcare providers and plans to adopt routine risk assessments? This could be done using automations and/or the use of electronic health records. Other ways to motivate healthcare providers, beyond education, could include the use of metrics, policies and protocols. The most ideal solution would be simple.

   Regarding adherence strategies, there are now more ways to virtually track patients, or follow up with patients that did not previously. We need to have a means of documenting

treatment completion. Currently most electronic health records only show the drugs prescribed, and drugs ordered. There needs to be a more streamlined way to capture and document treatment completion. This would be beneficial both for evaluation purposes and for continuity of care if patients change providers and/or migrate to other states within the US.

There is also the need to describe the roles of local, state and federal Health Departments and providers.

3. **Develop LTBI surveillance: monitor and evaluate outcomes to drive improvement**

   LTBI surveillance in this context would not only consist of setting up TB case registries at local or state Health Departments, but also monitoring and evaluating the outcomes in order to drive improvements at the local, state and national level. The relevant elements would need to be defined, as DTBE has previously done. These surveillance systems should respond to healthcare setting, local and state needs and feasibility constraints.

   There is the need to measure success and outcomes of LTBI testing and treatment scale up.

   There is the need to establish a national quality improvement and performance metrics for:
   - Percent of non-US born persons tested for LTBI
   - Percent of LTBI treatment completion for those who test positive.

   These are two simple metrics that could be promoted. There is an Adult and Child Core set, that is a Centers for Medicare and Medicaid Services (CMS) course set, that all Medicaid recipients could report to. Every year a new set of metrics is considered, and this would be a great place to have a metric. A lot of effort needs to go into determining a metric that would measure how many Medicaid recipients are tested and receive treatment. There is a lot of effort that goes into getting measures to become required by health systems. Dr. Flood has had a lot of feedback in California regarding this issue. Many health centers that have expanded in recent years have begun collecting metrics on various conditions including colorectal cancer, asthma, breast cancer. Having one measure on TB would help health centers focus on TB and get the relevant elements into their electronic health system. This is one concrete step to work on in order to understand the percentage of persons with LTBI who are left untreated.

4. **Secure new resource for LTBI activities**
   - One strategy that has benefitted TB elimination efforts in California is the ownership of plans by the state, one of which has been published. In addition, the TB elimination plans initiate a conversation pertaining to budget and securing funds for implementation. One of the first steps towards achieving such buy-in is to secure a budget for TB elimination once the plan is published.

- It is important for CDC to support US public health department led activities geared toward TB elimination.
- Ignite support to fund activities and entities outside Health Departments. Even when an entity cannot provide the support itself, it is possible to ignite it. We need to do better to establish private partnerships that include philanthropy industry and other non-governmental health organizations. The Heb B Coalition utilized this approach, whereby the campaign was not only funded by the government.
- The need for new funding streams is critical as we cannot let the financial burden of treatment fall on the patient. This will hinder patients from successfully completing the treatment.

5. **Support research to advance needed tools**

   Below are the research proprieties, as defined by the LTBI Workgroup:

   - Define the rate of progression to active TB among those with LTBI generally and for specific subgroups to inform the risk/benefit ratio of LTBI testing and treatment and aid in clinical decision making
   - Develop more predictive diagnostics to identify those with LTBI who will progress to TB disease
   - Conduct trials to assess effective shorter treatment options. DTBE has taken leadership in conducting such research and the LTBI Workgroup supports its continuation.
   - Identify interventions that promote treatment adherence. Again, another priority for DTBE.
   - Identify the most cost-effective approached and populations to conduct screening testing and treatment in our current healthcare system.

The LTBI testing and treatment scale-up roadmap graphic illustrates all the concepts that have been described previously in one page and shows how they are connected. Again, it shows the progression from barriers to the final outcomes. It also shows the domestic strategies in the 4 main groupings or buckets. The workgroup expects that the intermediate outcomes will yield the final outcomes in the roadmap. For example, patient-driven demand for testing and treatment, improved provider knowledge and use of newest testing/treatments and ability to measure and evaluate success of LTBI scale-up activities will yield substantial reduction of US TB cases.

The LTBI Workgroup's priority recommendations, in a nutshell, are:

1. Resource and commit to a national TB elimination plan
2. Outreach to high-risk populations
3. Engage and motive providers and health systems
4. Measure and improve outcomes
5. Create strategic national policy that drives and supports TB elimination
6. Conduct research to advance tools for LTBI testing and treatment

The LTBI Workgroup's top 10 tangible next steps it would like to communicate to CDC and partners are:

1. **Create a visible national TB prevention and elimination plan** focused on LTBI testing and treatment. This would be an update to the last ACET strategy document and to complement the workplan and roadmap the LTBI Workgroup has developed
2. **Secure funding** and partnerships for CDC and health department-led activated, even if not heavily funded initially, and stimulate support needed by community organizations and persons at risk and healthcare providers
3. **Launch marketing strategy**, as presented by Dr. DeLuca, targeted at public and community-based organizations to raise awareness of who is at risk for LTBI and TB disease and to create demand for testing in healthcare settings public and community-based organizations.
4. **Disseminate evidence-based strategies tailored to risk groups and settings to bring people at risk into care** for testing and treatment
5. **Disseminate efficient models and tools for LTBI risk-based testing and treatment in clinical settings** (e.g. workflows, protocols, EHR triggers)
6. **Facilitate outreach to and provide incentives for newcomers** (status adjusters and those with B-notification) who test positive to promote linkage to and completion of treatment.
7. **Establish and track simple national state and local quality improvement and performance metrics** to stimulate improvement
    - **Establish measure in CMS Child and Adult Core set** which will be required of federally funded providers/clinics (FQHCs, Medicaid, and Medicare healthcare providers)
    - Work with state and local Health Departments to **launch rigorous evaluation and improvement of newcomer testing and treatment** (e.g. status adjusters and TB B-notifications)
8. **Support prioritized LTBI research agenda** advancing 2-3 high impact studies in the next 5 years

The LTBI Workgroup outlined critical future steps:

9. **Create streamlined exchange of LTBI data** for monitoring and action across healthcare settings, local and state health department and CDC
10. **Initiate a program for adult pre-departure LTBI testing and treatment** building on the Vietnam pilot experience
11. **Implement new research findings** that can lead to faster adoption of best practices and speed TB decline

In summary, the LTBI Workgroup is recommending the following to ACET, (1) provide a report that describes the recommended actions to support expanded LTBI testing and treatment, (2) in collaboration with CDC, disseminate a publication on TB elimination roadmap centered on LTBI scale-up and (3) recommend commitment to major steps and concrete actions. The LTBI Workgroup asked for ACET's endorsement of the "Roadmap for Advancing TB Elimination in

the United States through Scale Up of Testing and treatment of Latent TB Infection" report during the meeting.

ACET Discussion: LTBI Workgroup

Ms. Cole inquired whether, as a body, ACET members agreed with the recommended next steps put forward by the LTBI Workgroup.

Dr. Robert Horsburgh Jr., of the LTBI Workgroup, indicated that he supported the recommended next steps; as did Dr. Belknap.

There were no further comments from ACET members.

Ms. Cole inquired whether Dr. Flood would like to propose a motion regarding the report. Dr. Flood proposed a motion for ACET to adopt the report for communicating recommendations to CDC and HHS, barring minor edits. Dr. Ana Alvarez seconded the motion. Ms. Cole again opened the discussion to comments or questions; none were raised. ACET voting members voted to accept.

Dr. Flood invited comments from ACET as to whether the report ought to be published:

- Dr. LoBue pointed out that the report will have to go through the CDC clearance process if a joint publication with CDC is desired. This may not be desired because ACET is an independent body and should be able to make recommendations without CDC influence
- Dr. Higashi encouraged that the document should be published, particularly for local Health Departments
- Dr. Elkins asked how the workgroup would define LTBI, to which Dr. Flood remarked that the report is not a clinical guideline and might not be the most suitable document to propose a definition for LTBI. Dr. Ahuja suggested the definition of LTBI used in surveillance could be referenced.
- Suzanne Marks, DTBE, suggested that a few things could be emphasized in the report, including, the need to collaborate more with HRSA. Another point she raised was the need for better LTBI tests, and tests which cost less to fund. Letha Healey, a HRSA representative, responded that she would follow up with her colleagues at the Bureau of Primary Health Care to coordinate discussion about how they collect data and potential collaboration. Dr. Horsburgh Jr. remarked that this step would be very welcome.

Host-Directed Approaches to TB Therapy

Suraj Sable, DVM, PhD
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention

Dr. Suraj Sable provided updates on a newly developed approach to investigating anti-TB therapeutics. The National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention recently developed a novel 3-dimensional (3-D) bioplatform to screen antimycobacterial and

host-directed therapy (HDT) compounds. This new research was in response to the pressing need for improved, shorter treatment regimens against TB. HDT is a novel approach that involves therapeutic modulation of the host immune responses to eliminate the offending pathogen from the hosts' body. Examples of HDT include humanized monoclonal antibodies, cytokines, FDA-approved drugs that can be repurposed, and the patient's own immune cells that are bioengineered in vitro both for the amelioration and clinical cure of disease. HDTs have several advantages. It can augment the efficacy of current antibiotics against TB and in the process shorten the duration of TB treatment. Since HDTs act on the host cells rather than on the pathogen directly, microbial resistance is less likely to occur. HDTs have potential to reduce immunopathology in the lungs, protect delicate anatomical structures, promote immunological memory, and prevent relapse of the disease.

One of the challenges that hampers the identification of HDTs against TB is a lack of fast, robust and widely applicable platforms for rapid screening of potential HDT compounds. Several animal models of TB are available. These animal models of TB are useful, but they do not represent human TB infection and disease faithfully. In addition, they present several challenges concerning safety, cost, throughput, and time to conduct these studies due to the requirement of ABSL-3 facilities. Traditional 2-D cell cultures, agar and liquid cultures are available, but they cannot mimic the environment within the TB granulomas.

To counter these challenges, Dr. Sable and colleagues undertook research to develop an in vitro bioplatform, analogous to the patient's granuloma lesion, using *Mycobacterium* species and human immune cells that can be used at the BSL-2 (biosafety level-2) for screening of new anti-TB modalities. They envisioned that this bioplatform would have several advantageous over traditional methods for reasons including reduced animal usage, costs and time, and increased efficiency of screening for potential HDT compounds. In addition, the platform would also potentially reduce the safety concerns of the staff performing these studies. To accomplish this goal Dr. Sable and colleagues used a 3-D cell culture approach. 3-D cell cultures have been used extensively in the cancer field and this system has enabled the development of an array of treatment options.

To explain this approach, Dr. Sable showed an illustration of the 3-D spheroid developed using tumor cells. 3-D cell cultures have numerous advantages over traditional 2-D cell cultures, in that 3-D cell cultures allow for physiologic cell-to-cell contact, the cells interact with extracellular matrix, there is a diffusion gradient with an increased carbon dioxide and waste and decreased oxygen and nutrients toward the center of the 3-D spheroid. All these features are absent in the traditional 2-D culture. Since a human TB granuloma is an organized 3-D collection of infected macrophages in the lung, the core of the research conducted was to answer a question of whether it would be possible to develop a 3-D spheroid using human immune cells infected with *Mycobacterium* species, which is a BSL-2 organism and that expresses fluorescent protein to aid in the imaging.

Results of the investigation showed that 3-D cell cultures of human immune cells and *Mycobacterium* species formed a "tubercle or spheroid" within 3 days of infection. In 2-D cell culture, researchers only observed a monolayer of infected immune cells. Researchers

observed the green, granulomatous foci formed by *Mycobacterium* strain expressing green fluorescent protein (GFP) in the bioplatform 10 to 12 days post-infection of the immune cells. In 2-D cell culture they observed only loose aggregates of infected cells. They again observed, virulent but not attenuated *Mycobacterium* strains could form the organized granulomatous foci. Like human TB granulomas, the researchers also observed increased hypoxia, necrosis, and cavity formation in the 3-D bioplatform. They also observed that the increased cell death in the center of the infected 3-D spiroid compared to uninfected control spheroid was due to necrosis rather than due to apoptosis. Thus, the key features of human TB granuloma were also seen in the 3-D bioplatform. Other key features of human granuloma that developed in the bioplatform include, epithelioid macrophage transformation, upregulation of vascularization and angiogenesis markers, collagen secretion and matrix metalloproteinase (MMP) activity, and acidosis. The next phase of the investigation was to determine whether it would be possible to use this 3-D bioplatform to screen known HDTs and antibiotics. The results of the tests conducted showed that the 3-D bioplatform could indeed be used to screen both host and pathogen-directed therapeutics because they observed significantly reduced bacterial burden and resolution of granulomatous lesions in the 3-D spheroids.

Screening of an array of FDA-approved drugs in the 3-D bioplatforms showed that 9% of drugs reduced the bacterial burden over 75%, 12% reduced the bacterial burden by 25-75%, and 62% of the drugs did not have any significant effect on the bacterial burden, but 8% increased the bacterial burden by over 25%. The drugs that significantly reduced the bacterial burden can be potentially repurposed for the treatment of TB. This bioplatform could potentially be used to screen HDT compounds and other small molecules at a much lower cost, higher efficiency, and faster than current methods.

In summary, *Mycobacterium* species infection in a 3-D cell system developed organized granulomatous lesions and permitted longitudinal analysis in situ. Key features of human TB granulomas developed in the tuberculoma model described. Lesions developed in the cell cultures were resolved following known antibiotic and HDT treatment.

Potential uses of the bioplatform beyond HDTs could span the development of treatment regimens against drug-susceptible and resistant TB, evaluation of vaccine efficacy in vitro in clinical trials using immune cells of vaccinated volunteers, study of immune mechanisms of protection, study of TB coinfections and co-morbidities in vitro and could also potentially serve as a platform for wide range of human diseases where cell-to-cell and cell-matrix interactions are important.

Future directions for this research include further improving the 3-D bioplatform by adding different cell types from human blood; further optimizing readouts to study emerging therapeutic interventions such as immunotherapy; estimating reduction in laboratorian house in the BSL-3, reduction in number of testing in animals in the ABSL-3 facility, and time and resources saved. Dr. Sable's team is currently screening a large library of compounds and small molecules to develop HDTs.

ACET discussion: Host-directed TB therapy

In response to Dr. Zelalem Temesgen's question regarding how standardizable the application of the bioplatforms are and whether the replicating the tests would yield the same response, Dr. Sable answered that screening tests were conducted in 3 experiments using 3 different spheroids and the bacterial burden was reduced to greater than 75% each time compared to control untreated spheroids. Dr. Sable and colleagues are investigating Z'-factor and Z-score for the test results.

In terms of Dr. Horne's inquiry about the specific species of bacteria, Dr. Sable mentioned that he was not at liberty to disclose this information, as the research was in the process of filling patent application by CDC. Dr. Horne also asked whether metformin was among the drugs that caused an increase in bacterial load, to which Dr. Sable responded in the negative.

Dr. Robert Belknap sought clarification regarding whether the model would be appropriate for testing different drug combinations of medicines, to which Dr. Sable responded in the affirmative.

In response to Dr. Elkins' question about how Dr. Sable's methods compare with other *in vitro* granuloma modeling methods used by others like Dr. Paul Elkington, in the field. Dr. Sable explained that most of the models used in the literature employ traditional 2-D cell culture. Although these models form loose granulomatous aggregates of monocytes, key features of the human granulomas do not develop in these 2-D cell culture models. In Paul Elkington's research, peripheral blood mononuclear cells (PBMCs) were encapsulated in the alginate microspheres developed by bio-electro-spraying to form aggregates of infected monocytes that resembles granulomatous structures. These PBMC encapsulating 3-D microsphere structures have been used for the screening of anti-TB modalities. But this method could be technologically demanding and require BSL-3 facility. Dr. Sable's team found that most of the organized lesions are formed toward the periphery of the 3-D bioplatform, due to likely requirement of oxygen and nutrient-rich microenvironment, which is difficult to develop in the artificially encapsulated environment like microspheres and the key features of human TB granulomas such as hypoxia and cavity formation formed in their bioplatform have not shown in other available models.

In terms of Dr. Liu's inquiry about how the minimum inhibitory concentration of the drugs currently being screened by Dr. Sable's research might change per the historic data available now, he responded that this model mimics the in vivo microenvironment to an extent and that the results might be comparable, although further research is required.

In this presentation, Dr. Sable did not disclose the intellectual property and methods critical for the 3-D spheroid formation, human immune cell type used, or the Mycobacterium species needed to develop this unique tuberculoma bioplatform, and the top 'hit' or 'miss' compounds identified in the throughput screen using this bioplatform.

Update from Division of Global Migration and Quarantine

Joanna Regan, MD, MPH FAAP
Division of Global Migration and Quarantine

Dr. Regan led the process of revising the Tuberculosis Technical Instructions (TB TIs), which were implemented October 1, 2018. She acknowledges others who provided significant support, including Sarah Gordon, Lisa Armitage, Jennifer Flood of the NTCA; Barbara Cole of the ACET, Randall Reves of Stop TB USA, Terry Chorba of CDC DTBE, and Drew Posey of CDC Division of Global Migration and Quarantine (DGMQ).

Per the revised TB Technical Instructions, civil surgeons must now use IGRA instead of TST in all applicants age 2 years and older. Previously, the TB Technical Instructions allowed the option of either using IGRA or TSTs, which cost relatively less. This is the biggest change in the revised TB Technical s and is based on current scientific evidence. In addition, civil surgeons are now required to order tests, not refer applicants to the health department to have tests. Civil surgeons should have been ordering these tests prior to the revisions; however, this was not the case. This revision has proven to be a bigger change than anticipated initially. Reporting cases of LTBI to Health Departments is now required instead of recommended. Class B0 is a new category for people who complete tuberculosis disease treatment during status adjustment process.

Panel physicians under the revised TB Technical Instructions, must now use IGRA instead of TST in all applicants age 2 through 14 years of age in TB high-burden countries, where the World Health Organization (WHO) estimated TB rate is ≥ 20 per 100, 000. Again, the Class B0 category has been introduced for people who complete tuberculosis disease treatment by means of Directly Observed Therapy (DOT) with the panel physician. This group of people were previously included in the B1 category. Therefore, now domestic Health Departments can differentiate between people who received DOT treatment to cure (B0) from people who were TB suspects with negative smear and culture results (B1) and those who received unsupervised TB treatment (B1).

IGRA tests used in the U.S. or outside of the US on behalf of the US must be approved by the US FDA, i.e., the Qiagen QuantiFERON® or Oxford Immunotec T-SPOT®.TB must be used. This is because some other tests were introduced that were not comparable to those approved by the FDA. The current version of QuantiFERON® being used is the QuantiFERON-TB Gold Plus (QFT-Plus). Oxford Immunotec T-SPOT®.TB is also allowed, although only used by a few countries currently.

The strategy for implementing the revised TB Technical Instructions centered on informing civil surgeons and panel physicians early and often. Civil surgeons were sent email blasts starting in February 2018; webinars were organized for them starting spring 2018. DGMQ organized presentations to the US tuberculosis community in spring 2018. In addition, DGMQ held three civil surgeon training events; one each in Washington, Atlanta and Miami, held in November 2018, December 2018 and December 3-5, 2019, respectively. During the training events, civil

surgeons received clarifications on DGMQ's technical instruction. There are over 5, 000 civil surgeons and trainings only captured a fraction of this number. Separate email boxes were set up for civil surgeons and panel physicians to serve to answer their questions and concerns.

Similarly, the implementation strategy for panel physicians also included email blasts, webinars, workshops and summits. A panel physician workshop was held in Tanzania in conjunction with the International Organization for Migration (IOM), in November 2017; summits were held in Kuala Lumpur, Ghana and Miami, in March 2018, March 2019 and December 2019, respectively. There were a lot of questions about T-Spot during the trainings. Currently, I-693 forms are printed out, mailed and stored in a warehouse. There is a need to make this process more electronic.

The current process for QuantiFERON® involves having applicant's blood drawn at a local laboratory. For some sites, specimen tubes are shipped to a different laboratory for testing. There are some panel physicians who have the QuantiFERON® ELISA Machine and can do the required testing on site.

DGMQ conducts Quality Assessment Program site visits. Last year, site visits were made in 46 countries. Preliminary, unpublished data provided by DGMQ (Zanju Wang) on IGRA implementation overseas among refugee children 2-14 years of age indicate majority of them arriving in the US between October 1, 2017 and September 30, 2018, received TST testing. After implementation, this preliminary data shows very little TST testing being done in the same populations. Additionally, lower percentages of positive tests are being observed using IGRA testing. There is now very widespread use of IGRA, globally.

All immigrant examinations were previously processed on paper, totaling 500, 000-600,000 per year; eMedical is making this process electronic. Only immigrant applications that required notifications to health department were being entered into CDC's Electronic Disease Notification (EDN) system by a domestic CDC data entry team and it was difficult to generate the overall denominator of immigrant applications for various analyses. With the eMedical system, data entry will be performed at the panel physician site and will include all immigrant applications. Each record must be reviewed and signed by the panel physician. Similarly, a radiologist must review the chest x-ray images and designate if findings are present for each applicant. Electronic quality checks are in place to ensure required information is entered before the panel physician can submit the report. For example, for abnormal chest x-rays, additional information would need to be entered in order to be accepted by the system. All x-rays will eventually be available through EDN. Over 7,000 x-rays have been entered already. Overall, EDN notification will not appear different for health department, rather, the new measure will allow data to be made available more quickly and with better quality. The eMedical roll-out is ongoing; three waves have already been completed between July and November 2019; three additional waves will take place between January and May 2020.

Several challenges have hampered DGMQ implementation of revised TB TIs. Among civil surgeon, the costs of IGRA, and the unknown outcome for LTBI reports, unlike the EDN and eMedical data which go directly to Health Departments. Among panel physicians, the costs of

IGRA, the continued practice of follow up retesting and low domestic follow-up rates currently 59-70%, depending on the condition.

Further plans to monitor implementation among civil surgeons include partnering with programs, including DTBE programs, to determine what is happening at local health department to estimate gain in LTBI treatment. Plans to monitor implementation among panel physicians include monitoring EDN and eMedical data to assess completion of implementation, that is, to ensure all designated countries are using IGRA. Again, monitoring EDN and eMedical data to assess the effect of new IGRA requirement on the rates of receiving post-arrival evaluation and rates of completing LTBI treatment stateside.

ACET Discussion: Update from Division of Global Migration and Quarantine

In response to Ms. Cole's question about the criteria for which retesting of people arriving in the US would not be required, Dr. Regan answered that there is a need to build people's confidence in the current screening and testing processes. One way is to monitor success of the IGRA and other TB testing. DGMQ also monitors positivity rates based on data from panel physicians.

In terms of Dr. Alvarez's inquiry about the indeterminate rates among children based on the preliminary data shown in the presentation, Dr. Regan responded that the determination had not yet been made and it would shortly be analyzed within the following weeks.

With regard to Dr. Flood's inquiry about whether the US has harmonized screening methods with Canada, Dr. Regan indicated that Canada uses eMedical as well. Dr. Drew Posey added that Australia has the closest screening system with the US, when compared to Canada, UK and Australia. Australia requires skin tests or IGRA tests in their children from high-burden areas, which is what the US used to do. Canada will start doing IGRA testing for people who already have certain existing conditions like HIV. In terms of Dr. Flood's question about whether DGMQ has access to the data from the I-693 forms to be used as a denominator for analysis, Dr. Regan shared that the division does not have access to this data.

Dr. Robert Benjamin asked whether there were recommendations on the requirement to repeat testing if test results are deemed indeterminate. Dr. Regan answered that indeterminate tests are not required to retest. Children under 14 years do not need to have a retest or a chest x-ray. People are counselled to retake the test but are not required to do so for immigration purposes.

Day 2 Opening session

Carla Winston, PhD., M.A.
Associate Director for Science, Division of Tuberculosis Elimination
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention

Dr. Winston called the meeting to order at 8:30 am EST, welcomed participants and conducted a roll call to confirm 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 proceedings are a matter of public record. She informed the ACET members to be mindful of their responsibility to disclose any potential public conflict of interest (COI), as identified by the CDC Committee Management Office, and recuse themselves from voting or participating in discussions where they have a conflict.

The roll call confirmed that the 19 voting members and ex-officio members in attendance constituted a quorum for ACET to conduct its business on December 11th, 2019.

Essential Components Workgroup Updates

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

Ms. Cole announced that the 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) has been summitted to MMWR and the workgroup is awaiting a decision regarding publication. She thanked everyone who contributed to the document. The remain tasks will be to respond to feedback from MMWR editors once received. After this, the Essential Components Workgroup will be shelved.

LTBI Workgroup

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

Dr. Jennifer Flood provided ACET with an update of the LTBI Workgroup's progress. She shared that the Workgroup, tasked with updating ACET's 1989 publication, *A Strategic plan for the elimination of tuberculosis in the United States,* had revised and finalized the new report following the previous ACET meeting in August 2019. This new report, *A roadmap to TB elimination: focus on LTBI*, is formatted for possible publication in the *MMWR* and outlines four

major recommendations for scaling up LTBI testing and treatment in the United States, namely: (1) identify and engage individuals at-risk and their providers; (2) increase testing of at-risk individuals and increase treatment of infected individuals; (3) measure success and outcomes of LTBI testing and treatment scale-up; (4) secure funding for these activities. At the conclusion of the presentation, Barbara Cole, ACET Chair, asked for comments from ACET. Two members expressed their agreement with the recommendations outlined by the Workgroup. Dr. Flood proposed a motion to adopt the report for communicating recommendations to CDC and HHS, barring minor edits. Dr. Ana Alvarez seconded the motion. Ms. Cole again opened the discussion to comments or questions; none were raised. ACET voting members voted to accept the report.

TB Drug Supply Workgroup

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

Dr. Flood shared that the two current active items for the TB Drug Supply Workgroup were the NTCA drug supply survey, which Donna Wegener would provide more insights on, and a future exchange with FDA. The workgroup hopes to plan a meeting with FDA prior to the June 2020 ACET meeting and then invite FDA leadership to the ACET meeting in June 2020. The workgroup will present their full report at this June 2020 ACET meeting, as well as the final report from the NTCA drug supply survey.

The purpose of the NTCA drug supply survey was to describe challenges related to accessing TB drug and PPD solution, understanding the barriers related to drug costs for patients and TB programs and to provide information to inform the development of nationwide actions, with a goal to achieve a continuous and affordable drug supply for people with tuberculosis disease and LTBI, in the US. The survey will close on December 20, 2019 and the final report will be available in late January 2020.

Preliminary analysis show that respondents, totaling 67 so far, are from a state TB program (N=31, 46%), a city TB program (N=4, 6%), a county TB program (N=29, 43%), a territorial TB program (N=2, 3%) or other, that is, a publicly supported TB clinic within a private hospital (N=1, 2%). Most of the respondents were either TB controllers or TB program managers. In response to one of the survey questions, “In 2019, which of the TB drugs has your program had trouble accessing and/or affording”, rifapentine was at the top of the list for over half of respondents. For rifapentine access, the main challenge was that it was unavailable, out of stock, or available to order, but only in small quantities. These shortages caused delays in starting patients on treatment because there would be interruptions in treatment, which is a significant problem. Secondly, these shortages adversely impact patient outcomes, and adherence to treatment. Moreover, if TB programs are not able to get access to and spend all their time trying to access

drugs, then they do not have to time to make sure patients are finishing the course. In some cases, providers stopped prescribing drugs that are in short supply.

In terms of potential solutions to drug supply shortages, survey respondents recommended: a centralized national drug supply system in order to streamline ordering, pool procurement and maximize negotiated pricing and allow ability to monitor drug supply and provide early warning of shortages (60%); a national TB drug supply website with a list of all TB drugs, manufacturers and their contact information and specific ordering information (56%); flexibility to use portion of federal agreement funds for TB drugs (56%) and additional patient assistance programs (44%). There is an informal network through which information about drug shortages can be obtained but there is no streamlined, formal source of information.

In terms of next steps, a more comprehensive analysis of the drug supply survey data will be conducted by NTCA. The results of the analysis will be shared at the next ACET meeting in June 2020. Also, the TB Drug Supply Workgroup hopes to review issues outlined in their letter to the FDA with relevant FDA representatives.

Ms. Donna Wegener, of the National Tuberculosis Controllers Association, provided an update on the current status of TB drug supply challenges. She read an email aloud from a TB controller in Midwest state which provides treatment free of charge to TB patients, regardless of income or insurance status, which is not the case in every state. In summary, the email indicated that the TB Controller was currently facing an apparent TB drug shortage. They had been notified that their pharmacy distributor had only a limited stock and that the manufacturer was not producing additional supply. After email inquiries to the CDC and the NTCA, the NTCA confirmed that several states may be experiencing shortages. When the TB Controller checked the CDC stockpile, there was no INH in store. A supply of INH became available via another manufacturer, but at a higher cost, $1,327 per bottle. Following this, the state and pharmacy distributor decided to hold all new orders of TB drugs until normal drug supply could be resumed. Existing orders continued to be filled. This entire situation will affect more than a 100 patients per month. If not controlled, patients will have to be switched to alternate regimen, which will increase both the cost and the length of their regimen. Ms. Wegener shared that similar situations occur often, and it is difficult to determine whether the issue lies with drug supply or distribution and whether shortages are nationwide or localized.

Advice Requested from ACET: TB Drug Supply Workgroup Updates

1. Suggestions for how to address the challenges associated with distribution or drug supply shortages.

    a. ACET will invite the appropriate person(s) from FDA to discuss and address the issues related to drug supply.

ACET Discussion: TB Drug Supply Workgroup Updates

In terms to Kristine Steward-East's question about whether the survey inquired about challenges obtaining liquid formulations of drugs for infants, Dr. Flood remarked that this would have been a great addition to the survey but does not feature in the current survey.

Dr. Robert Horsburgh Jr. inquired why the CDC stockpile had not been helpful in the case of the TB Controller. Dr. Flood indicated that the INH in the CDC stockpile may have expired. Dr. LoBue responded that sometimes the CDC has difficulty buying drugs for the stockpile. CDC must work through a purchaser if they do not get the supply then the CDC cannot move forward as there is no flexibility find alternate sources. He added that the various states have the same issue where they may be in contract with one supplier or distributer and they are limited to the options that the companies provide. Dr. Flood suggested that might be beneficial to look at models like the Global Drug Facility (GDF) or Canada who have a centralized drug supply system. In this way, even when drugs are not available via the stockpile, there could be a rotating supply to protect from shortages. Ms. Wegener pointed out that TB programs have benefitted greatly from the CDC stockpile, particularly during a rifapentine shortage. With regards to Dr. Flood's suggestion, Mr. Surajkumar Madoori, of the Treatment Action Group, disclosed that the Global Drug Facility can sell to US systems, which could potentially resolve the issue of having a centralized system. The only hurdle would be that the US companies would need to supply GDF with FDA-approved packaging.

In response to Dr. Julie Higashi's question about whether there is a centralized way to coordinate information about TB drug shortages without lag, Dr. LoBue provided an example from a Tubersol shortage where the CDC had timely knowledge about the shortage but could not broadcast this information due to FDA and the manufacturer's restrictions. He added that it was difficult to determine how widespread a drug shortage may be. The problem begins with not having a way to determine whether there is really a shortage, which parts of the country are affected and whether the shortage is a supply issue or distribution issue.

Dr. Mamodikoe Makene added that the FDA has a Shortage Coordinator and it might be helpful to identify them for further clarification to which Dr. Elkins suggested that it might be more effective to use the general mailbox. Emails received there are directed to the appropriate expert. Dr. LoBue also added that the CDC is in contact with the FDA 'Shortage Team'. However, this group can only supply information when the shortage is caused by a manufacturer. When shortages are caused by suppliers, the FDA 'Shortage Team' does not have purview. Dr. Flood suggested that the drug shortages issue should be discussed further during the June 2020 meeting, specifically, how to have a well-coordinated response when a drug shortage alert is received.

Dr. Higashi asked that the end dates for common TB drugs in the CDC Stockpile be communicated to relevant stakeholders including the NTCA.

In response to Dr. David Horne's inquiry about whether there were any examples of drug supply streams nationally, Dr. Flood indicated that there are larger states that purchase large volume of drugs at a time and tend to have less shortage issues.

ACET Business Session

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

Ms. Barbara Cole, ACET Chair, opened the Business Session and facilitated a review of old and current business items that warranted ACET's formal action. Ms. Cole allowed time for additional discussion and/or requests for future agenda items.

Business Item 1: Approval of Previous ACET Meeting Minutes

Ms. Cole inquired whether there was a motion to accept the August 20, 2019 ACET meeting minutes; Dr. Ana Alvarez moved to accept the minutes, seconded by Dr. Robert Horsburgh Jr. With no further discussion or corrections, the motion to accept the minutes carried unanimously with no abstentions or oppositions.

Business Item 2: Advice Requested from ACET

Ms. Cole reminded the quorum that one of ACET's responsibilities is to provide advice to the Department of Human Health Services (HHS) and the CDC; hence, the dedicated segment within the meeting.

Topic	Discussion from Minutes	Action
I. What is ACET's response to the following questions about adding a TB question to the Youth Risk Behavior Survey (YRBS)? a. What would be the added value of a TB question? Can't say. b. What additional variables would be necessary to be able to capture meaning patterns? c. What states would be feasible and relevant candidates for a TB question? d. If the group decides to move forward with a TB question, should ACET create a workgroup to organize these efforts?	See page 11-13	ACET will suspend any additional work or discussion around adding a survey question to the YRBS. Reasons for action (1) cannot articulate the added value of including a question and (2) difficult to formulate a single question to capture useful information.

Topic		Discussion from Minutes	Action
II.	What is ACET's input on the critical next steps to ensure a continuous, affordable anti-TB drug supply?	See page 27	The key components of the recommendations discussed during the previous meeting have been included in the ACET report to the HHS Secretary.
III.	What is ACET's reaction to the approach and preliminary findings of the latent TB infection (LTBI) Workgroup?	See page 27	As outlined in the previous minutes, the workgroup presented a full final report and recommendations to the ACET. The report was approved during this meeting. A letter will be prepared to accompany the report.

Business Item 3: Report from the Board of Scientific Counselors, Office of Infectious Disease

Relevant highlights from the recent Board of Scientific Counselors meeting held on December 4-5, 2019 were shared. Highlights included: the threat of multidrug-resistant TB (MDR-TB); discussion around the Global Health Security Strategy; and Ending Global Tuberculosis as a rationale for TB Preventive Treatment (TPT).

Business Item 4: Public Charge Rule

The letter sent to the HHS Secretary to express ACET's concern regarding the potential negative impact of the Public Charge, outlined in the Federal Register, has not yet received a definite response. The order was expected to go into effect in October 2019 but ended up in court. Ms. Cole stated that she was not aware of an updated implementation date, and neither was Dr. Robert Benjamin. ACET could potentially put forth another letter but will continue to monitor and gather resources that could be shared if people choose to use them.

Business Item 5: Response from HHS

ACET has sent three letters to HHS: (1) ACET's recommendations on essential components, (2) a letter regarding drug supply (3) the letter regarding the Public Charge as noted previously. Responses are usually deferred to CDC and ACET has received responses pertaining to items (1) and (2) but nothing definite has been communicated pertaining to item (3).

Business Item 6: ACET's Semi-Annual Report to HHS Secretary

The semi-annual report by ACET to the HHS Secretary was drafted during the April 2019 meeting, and revised further during the August 2019 meeting. During the December 2019 meeting, the following edits were proposed in order to finalize the letter; new content has been made bold and italicized:

Background

- No further comments/edits to the order of the six concerns
- A suggestion was made to edit the 2nd paragraph to include "While" at the beginning of the sentence "Progress has been made in the fight against TB, with 9,029 new cases reported in the United States during 2018, compared to 9,094 reported in 2017"
- It was recommended that the statistics stated in the first paragraph be corrected from 10.4 million persons worldwide becoming ill with TB, and 1.8 million lives being lost to 10 million persons and 1.5 million lives respectively
- A request was made to include language highlighting LTBI treatment in the Background section. Upon further discussion, it was agreed that it would be most appropriate to include this language in the conclusion of the letter. Finally, it was agreed that the inclusion will be made in the Background section, 1st paragraph, to read, "Additionally, an estimated 1 in 4 persons are infected with latent TB infection (LTBI), which represents a reservoir for future cases ***that could be prevented by LTBI treatment."***

Six Concerns That Continue to be Paramount During ACET Deliberations

- It was recommended that the letter consistently mention both the Tuberculosis Epidemiology Studies Consortium (TBESC) and the Tuberculosis Trials Consortium (TBTC) together. Currently the TBESC is mentioned under the Six Concerns (TB Research) but the TBTC is not, and conversely, the TBTC is mentioned under the 'Assistance from the HHS Secretary' sections but the TBESC is not.
- Under point 3, a request was made to include the following opening sentence, ***"Over 80% of US TB cases result from the progression of untreated latent TB infection to active disease."***

Assistance from the HHS Secretary

- A suggestion was made to remove the phrase "if needed" from the bullet stating "strengthen HHS support for reducing TB in congregate setting, ensuring resources for IDGRA based testing, if needed…"
- A comment was made to revise the 8th bullet ("establish a focus on domestic TB elimination within the Executive Branch by forming a Presidential TB Elimination Initiative;") to read "establish ***and fund*** a focus on domestic TB elimination within the Executive Branch by forming a Presidential TB Elimination Initiative ***to support CDC and domestic TB programs***;"

- In the first sentence, “Your leadership as Secretary of HHS is crucial if we are to reach TB elimination in the United States…”, a suggestion was made to change the word “reach” to “accelerate progress toward”.
- A question was posed regarding moving the 8th bullet about the establishment of a Presidential TB Elimination Initiative to become the 1st bullet. Ms. Cole asked whether all agreed. There were no abstentions or oppositions.
- A suggestion was made to add to the 7th bullet regarding funding for the NIH so that the sentence reads “facilitate research to shorten TB disease and LTBI treatment by increasing basic ***and translational*** science funding for the National Institutes of Health…”
- A suggestion was made to include verbiage concerning the shortage of anti-TB drugs in the 2nd bullet regarding supporting access to TB treatments. The bullet could read “support access to all TB treatments by ensuring medication needed to treat TB are available to TB programs, including newer drugs such as Pretomanid are included in the medical formulary.
- A suggestion was made to include language that highlights the treatment of LTBI in the first concluding paragraph after the ‘Assistance from the HHS Secretary’ section.

Future Agenda Items

Ms. Cole, ACET Chair, noted the Agenda Setting Workgroup would further develop the initial suggestions presented herein. The following topics were suggested:

Presenter	Agenda Item
Representative from Food and Drug Administration (FDA)	Discussion/presentation on drug supply and drug shortage concerns
Representative from HRSA (Health Resources and Services Administration)	Discussion/presentation on securing funding for research
Leadership of Global TB Branch	Deliver update on their activities since last presentation at ACET meeting in 2018/2017
Dr. Nick DeLuca	Provide update on Latent TB Infection Community Engagement Network and communications campaign rollout
TBD; Anne Kasmar (Bill and Melinda Gates Foundation)	Current status of TB vaccines
TBD	Processes and measures that could help establish LTBI measures (adult and child course measures)
TBD	Updates from NEEMA Consortium
TBD	Pediatric TB: challenges in diagnosis, and treatment.
TBD	Update on rollout of Whole Genome Sequencing

Presenter	Agenda Item
TBD	Follow-up/update from Division of Global Migration and Quarantine
TBD	Results from NTCA survey
TBD	Updates from the Tuberculosis Epidemiology Studies Consortium (TBESC) and the Tuberculosis Trials Consortium (TBTC)

Public Comment Session

- Ms. Donna Wegener, of the National Tuberculosis Controllers Association, provided comments on the current status of the TB drug supply challenges. Her update is included below:
  - Ms. Wegener read an email aloud from a TB controller in Midwest state which provides treatment free of charge to TB patients, regardless of income or insurance status, which is not the case in every state. In summary, the email indicated that the TB Controller was currently facing an apparent TB drug shortage. They had been notified that their pharmacy distributor had only a limited stock and that the manufacturer was not producing additional supply. After email inquiries to the CDC and the NTCA, the NTCA confirmed that several states may be experiencing shortages. When the TB Controller checked the CDC stockpile, there was no INH in store. A supply of INH became available via another manufacturer, but at a higher cost, $1,327 per bottle. Following this, the state and pharmacy distributor decided to hold all new orders of TB drugs until normal drug supply could be resumed. Existing orders continued to be filled. This entire situation will affect more than a 100 patients per month. If not controlled, patients will have to be switched to alternate regimen, which will increase both the cost and the length of their regimen. Ms. Wegener shared that similar situations occur often, and it is difficult to determine whether the issue lies with drug supply or distribution and whether shortages are nationwide or localized.

- The proposed meeting dates for the next in-person ACET meeting, June 16-17, 2020, were accepted as final, with no alternate dates suggested.
- December 8-9, 2020 were proposed as the meeting dates following the June 2020 meeting. Ms. Cole announced that there would be no virtual meetings in the interim between in-person meetings.

Closing Session

The next ACET meeting will be convened on June 16-17, 2020 in-person in Atlanta, Georgia.

With no further discussion or business brought before ACET, Ms. Cole adjourned the meeting at 10:46 am on December 11, 2019.

Attachment 1: Day 1 Participants' Directory

ACET Members Present

Ms. Barbara Cole, Chair
Dr. Ana Alvarez
Dr. Robert Belknap
Dr. Jennifer Flood
Dr. David Horne
Dr. Robert Horsburgh, Jr.
Dr. Lixia Liu
Ms. Kristine Stewart-East
Dr. Zelalem Temesgen

ACET Members Absent

Dr. Lisa Armitige

ACET *Ex-Officio* Members Present

Kevin Taylor for Dr. Naomi Aronson
US Department of Defense

Dr. Ulana Bodnar
US Department of Justice

Ms. Sarah Bur
Federal Bureau of Prisons

Dr. Karen Elkins
US Food and Drug Administration

Dr. Diana Elson
US Department of Homeland Security
US Immigration and Customs Enforcement

Dr. Letha Healey
Health Resources and Services Administration, HIV/AIDS Bureau

Dr. Jonathan Iralu
Indian Health Service

Dr. Steve Weissman for Mr. Stephen Martin
National Institute for Occupational Safety and Health

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

Dr. Lawrence Kline
US Section, US-Mexico Border Health Commission

Dr. Robert Benjamin
STOP TB USA

ACET *Ex-Officio* Members Absent

Dr. Thomas Nerard
US Department of Labor/Occupational Safety and Health Administration

Dr. Gary Roselle
US Department of Veteran Affairs

ACET Liaison Representatives Present

Dr. Shama Ahuja
Council State and Territorial Epidemiologists

Dr. Julie Higashi
National Tuberculosis Controllers Association Treatment Action

Mr. Surajkumar Madoori
Treatment Action Group

Ms. Nuala Moore
American Thoracic Society

Dr. Robert Morris
National Commission on Correctional Health

Dr. Randall Reves
International Union Against TB and Lung Disease

Dr. Kathleen Ritger
National Association of County and City Health Officials

Ms. Susan Ruwe
Association for Professionals in Infection Control and Epidemiology

Dr. Daphne Ware
Association of Public Health Laboratories

Mr. Bobby Watts
National Health Care for the Homeless Council

Mr. Marc Gaudreau for Dr. Howard Njoo
Public Health Agency of Canada

Dr. Amee Patrawalla
American College of Chest Physicians

Mayleen Ekiek
Pacific Island Health Officers Association

ACET Liaison Representatives Absent

Mr. David Bryden
RESULTS

Dr. Charles Daley
American Thoracic Society

Dr. John Hellerstedt
Association of State and Territorial Health Officials

Dr. Ilse Levin
American Medical Association

Dr. Gudelia Rangel
Mexico Section, US-Mexico Border Health Commission

Ms. Susan Ray
Infectious Disease Society of America

Ms. Susan Rappaport
American Lung Association

Dr. Michael Tapper
Society for Healthcare Epidemiology of America

Dr. Lornel Tompkins
National Medical Association

CDC Representatives

Dr. Terence Chorba
Mr. Justin Davis
Ms. Kathryn Koski
Dr. Philip LoBue
Ms. Allison Maiuri
Ms. Suzanne Marks
Ms. Margie Scott-Cseh
Ms. Rebekah Stewart
Dr. Andrew Vernon
Dr. Carla Winston
D. Thomas Navin
Dr. Jonathan Mermin
Dr. Drew Posey
Dr. Suraj Sable
Ms. Dawn Tuckey
Dr. Neela Goswami
Dr. Joanna Regan
Dr. Nick DeLuca
Ms. Annie Rossetti
Mr. Scott Nabiry
Dr. Bob Pratt
Ms. Sarah Segerlind
Ms. Allison Kline

Guest Presenters

Ms. Diana Fortune
New Mexico Department of Health (former)

Members of the Public

Ms. Donna Wegener
National Tuberculosis Controllers Association

Wen Li
DTBE Laboratory Branch

Attachment 2: Day 2 Participants' Directory

ACET Members Present

Ms. Barbara Cole, Chair
Dr. Ana Alvarez
Dr. Robert Belknap
Dr. Jennifer Flood
Dr. David Horne
Dr. Robert Horsburgh, Jr.
Dr. Lixia Liu
Dr. Zelalem Temesgen
Ms. Kristine Steward-East

ACET Members Absent

Dr. Lisa Armitige

ACET *Ex-Officio* Members Present

Kevin Taylor
US Department of Defense

Dr. Naomi Aronson
US Department of Defense

Ms. Sarah Bur
Federal Bureau of Prisons

Dr. Ulana Bodnar
US Department of Justice

Dr. Karen Elkins
US Food and Drug Administration

Dr. Diana Elson
US Department of Homeland Security
US Immigration and Customs Enforcement

Dr. Letha Healey
Health Resources and Services Administration, HIV/AIDS Bureau

Dr. Jonathan Iralu
Indian Health Service

Dr. Steve Weissman for Mr. Stephen Martin
National Institute for Occupational Safety and Health

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

Dr. Lawrence Kline
US Section, US-Mexico Border Health Commission

Dr. Robert Benjamin
STOP TB USA

ACET *Ex-Officio* Members Absent

Dr. Thomas Nerard
US Department of Labor/Occupational Safety and Health Administration

Dr. Gary Roselle
US Department of Veteran Affairs

ACET Liaison Representatives Present

Dr. Shama Ahuja
Council State and Territorial Epidemiologists

Dr. Julie Higashi
National Tuberculosis Controllers Association Treatment Action

Mr. Surajkumar Madoori
Treatment Action Group

Ms. Nuala Moore
American Thoracic Society

Dr. Robert Morris
National Commission on Correctional Health

Dr. Randall Reves
International Union Against TB and Lung Disease

Dr. Kathleen Ritger
National Association of County and City Health Officials

Ms. Susan Ruwe
Association for Professionals in Infection Control and Epidemiology

Dr. Daphne Ware
Association of Public Health Laboratories

Mr. Bobby Watts
National Health Care for the Homeless Council

Mr. Marc Gaudreau for Dr. Howard Njoo
Public Health Agency of Canada

Dr. Amee Patrawalla
American College of Chest Physicians

Mayleen Ekiek
Pacific Island Health Officers Association

ACET Liaison Representatives Absent

Mr. David Bryden
RESULTS

Dr. Charles Daley
American Thoracic Society

Dr. John Hellerstedt
Association of State and Territorial Health Officials

Dr. Ilse Levin
American Medical Association

Dr. Gudelia Rangel
Mexico Section, US-Mexico Border Health Commission

Ms. Susan Ray
Infectious Disease Society of America

Ms. Susan Rappaport
American Lung Association

Dr. Michael Tapper
Society for Healthcare Epidemiology of America

Dr. Lornel Tompkins
National Medical Association

CDC Representatives

Ms. Kathryn Koski
Dr. Philip LoBue
Ms. Suzanne Marks
Ms. Margie Scott-Cseh
Dr. Carla Winston
Dr. Suraj Sable

Members of the Public

Ms. Donna Wegener
National Tuberculosis Controllers Association

Attachment 3: Glossary of Acronyms

Acronym	Definition
AANHPI	Asian American, Native Hawaiian, and Pacific Islander
ACET	Advisory Council for the Elimination of Tuberculosis
ATS	American Thoracic Society
APHL	Association of Public Health Laboratories
AAPCHO	Association of Pacific Community Health Organizations
APHL	Association of Public Health Laboratories
APIAHF	Asian and Pacific Islander American Health Forum
BARDA	Biomedical Advanced Research and Development Authority
BSL	Biosafety Level
CBA	Capacity-Building Assistance
CBOs	Community-Based Organizations
CDC	Centers for Disease Control and Prevention
CEBSB	Communication, Education, and Behavioral Studies Branch
CfZ	Clofazimine
CMS	Centers for Medicare and Medicaid Services
COI	Conflict of Interest
COE	Centers of Excellence
DFO	Designated Federal Officer
DGMQ	Division of Global Migration and Quarantine
DHAP	Division of HIV/AIDS Prevention
DTBE	Division of Tuberculosis Elimination
eDOT	Electronic Directly Observed Treatment
EDN	Electronic Disease Notification
ERS	European Respiratory Society
FACA	Federal Advisory Committee Act
FDA	(United States) Food and Drug Administration
FQHC	Federally Qualified Health Centers
GDF	Global Drug Facility
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HBF	Hepatitis B Foundation
HCV	Hepatitis C Virus
HDT	Host Directed Therapy
HHS	(United States) Department of Health and Human Services
HRSA	Health Resources and Services Administration
ICE	(United States) Immigration and Customs Enforcement
ICH	International Counsel for Harmonization
IDSA	Infectious Disease Society of America
IGRA	Interferon Gamma Release Assay
IOM	International Organization for Migration
LHD	Local Health Department
LTBI	Latent Tuberculosis Infection
MCD	Medical Consultation Database

Acronym	Definition
MDR-TB	Multidrug-Resistant Tuberculosis
MMWR	Morbidity and Mortality Weekly Report
MSM	Men Who Have Sex with Men
NACCHO	National Association of County and City Health Officials
NASTAD	National Alliance of State and Territorial AIDS Directors
NCHHSTP	National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
NEDSS	National Electronic Disease Surveillance System
NEEMA	NCHHSTP Epidemiologic and Economic Modeling Agreement
NHANES	National Health and Nutrition Examination Survey
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NOFO	Notice of Funding Opportunity
NTCA	National Tuberculosis Controllers Association
NTM	Non-Tuberculous Mycobacterium
OMH	(HHS) Office of Minority Health
OSH	Office of Smoking and Health
PBMC	Peripheral Blood Mononuclear Cells
PEPFAR	A President's Emergency Plan for AIDS Relief
PHI	Protected Health Information
PrEP	Pre-exposure Prophylaxis
PZA	Pyrazinamide
RVBT	Report of Verified Case of TB
SAMHSA	Substance Abuse and Mental Health Services Administration
SME	Subject-Matter Expert
SSP	Syringe Services Program
STD	Sexually Transmitted Disease
TA	Technical Assistance
TB	Tuberculosis
TBESC	Tuberculosis Epidemiologic Studies Consortium
TBTC	Tuberculosis Trials Consortium
TB TI	Tuberculosis Technical Instructions
TST	Tuberculin Skin Test
USAPI	United States-Affiliated Pacific Islands
CBP	US Customs and Border Protection
USMBHC	US-Mexico Border Health Commission
USPSTF	US Preventive Services Task Force
WG	Working Group
WHO	World Health Organization
3HP	12-dose Regimen of Isoniazid-Rifapentine
4R	4-month Regimen of Rifapentine