A one-and-a-half day, open public meeting of the Board of Scientific Counselors (BSC), Office of Infectious Diseases (OID), was held on May 3-4, 2017, at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. In addition to Board members and CDC staff, the meeting was attended by representatives of several public health partner organizations.

The meeting included updates from the Center for Global Health (CGH) and CDC’s infectious disease national centers: the National Center for Immunization and Respiratory Diseases (NCIRD), the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), and the National Center for Emerging and Zoonotic Infectious Diseases (NCEZID). Reports were made from the BSC’s Food Safety Modernization Act Surveillance Working Group (FSMA SWG) and the Infectious Disease Laboratory Workgroup (IDLWG). The meeting also included focused discussions on H7N9 influenza, Middle East Respiratory Syndrome Coronavirus (MERS CoV), and vector-borne diseases, and presentations on progress towards the elimination of TB and viral hepatitis in the United States. The meeting also included a conversation with Acting CDC Director Anne Schuchat.

Following the discussion on vector-borne diseases, the BSC passed a unanimous motion to explore the establishment of a joint workgroup on vector-borne disease issues with the BSC of the National Center for Environmental Health (NCEH)/Agency for Toxic Substances and Diseases Registry. The BSC also suggested exploring the need for re-activation of the Board’s Antimicrobial Working Group, which has not been active since the establishment of the Presidential Advisory Council for Combating Antibiotic-Resistant Bacteria.

Opening Remarks

BSC Chair Dr. Ruth Berkelman, Rollins Professor, Emory University, called the meeting to order and was joined in welcoming participants and facilitating introductions by Dr. Rima Khabbaz, CDC Deputy Director for Infectious Diseases, and Robin Moseley, the BSC’s Designated Federal Official. Dr. Berkelman welcomed two new members, Mary Hayden, Rush University Medical Center, and Sheldon Campbell, the BSC’s new representative from the Clinical Laboratory Improvement Advisory Committee (CLIAC).

Dr. Khabbaz reported that HHS Secretary Thomas Price visited CDC last week and expressed his appreciation for CDC’s work. She noted that the federal budget has been extended through the end of FY2017 and that the budget proposed for FY18 (to be released later this month) is expected to call for a 20% cut to HHS agencies that may include specific (rather than across-the-board) decreases in funding. Dr. Khabbaz also provided an update on laboratory safety. OID is working with Steve Monroe,
Associate Director for Laboratory Science and Safety, to emphasize transparency and encourage reporting of any safety incidents.

**NCIRD Update**

Nancy Messonnier, Director, NCIRD, provided the following updates.

**Leadership Changes**

- Barbara Mahon is the new Director of the Division of Bacterial Diseases
- Carolyn Bridges, Associate Director of Adult Immunizations, is retiring at the end of May
- Recruitment is underway for Deputy Director, Division of Viral Diseases

**Vaccine Updates**

- **Human papillomavirus (HPV) Vaccine.** New developments include
  - The Advisory Committee on Immunization Practices (ACIP) recommendation for routine use of a 2-dose schedule for patients who start the HPV vaccination series before age 15. The corresponding HEDIS measure will be updated to reflect this recommendation.
  - Publication of the 2016 *NIS-Teen Data report*, which provides data on vaccine coverage of adolescents aged 13-17 years, is expected by the end of August. HPV vaccine trend data from 2012 through 2016 suggest increased distribution of vaccine.
  - CDC’s communication strategy involves tailoring HPV messages to doctors’ perceptions of their practice and the need for the vaccine (i.e., clinicians who think that HPV vaccination is 1) important, but current coverage rates are fine; 2) important for high-risk patients, but not for everyone; 3) not important enough to push parents to allow it; or 4) not important, because patients can be screened for HPV-related pre-cancers).

- **Mumps.** More than 40 outbreaks of mumps were reported in 2016, mostly at universities, with a few in community settings (e.g., in a group of Marshall Islanders living in northwest Arkansas). ACIP is creating a new workgroup to review data on the measles, mumps, rubella (MMR) vaccine and make policy recommendations. Studies are underway to
  - Characterize mumps cases and outbreaks in nine sites and identify disease risk factors
  - Evaluate the long-term effectiveness of the MMR vaccine in persons who have received two or three doses (conducted by the [Marshfield Clinic](https://www.marshfieldclinic.org)).
  - Evaluate mass vaccination with a third dose of MMR vaccine as an outbreak response strategy for mumps.
  - Evaluate the role of viral shedding from persons with asymptomatic infections in disease transmission during outbreaks of mumps.

- **Influenza Vaccine**
  - The overall efficacy of the 2016-17 seasonal flu vaccine is estimated to be 48%, with 43% efficacy against influenza A (H3N2) viruses and 73% efficacy against influenza B viruses.
  - A comparison of influenza vaccine coverage data from the past four flu seasons suggests that CDC’s decision in June 2016 to stop recommending the live attenuated influenza vaccine (LAIV) did not have a significant effect on overall vaccination rates.
Two EIS officers provided assistance to the NYC Department of Health and Mental Hygiene during an outbreak of H7N2 influenza among shelter cats. The investigation identified one human case—a veterinarian with prolonged exposure to sick animals.

A case-cohort analysis found that $\frac{3}{4}$ of pediatrics deaths due to influenza between 2000 and 2014 occurred in unvaccinated children.

**Adult Vaccination**

Although rates of adult vaccination are still lagging, the 2015 *National Health Interview Survey* reports increased use of the pneumococcal vaccine, the zoster (shingles) vaccine, and the tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap) between 2014 and 2015.

Overall, adult vaccination coverage is lower among those without health insurance and higher among U.S.-born respondents.

**Global Health Security Agenda (GHSA)**

NCIRD is working with ministries of health in 17 GHSA countries to build public health capacity, focusing on these areas: Laboratory, Workforce, Emergency Operations Center, Disease Surveillance, and Immunization. GHSA laboratory projects include trainings in packaging and shipping specimens during outbreaks and on laboratory-scale up during outbreaks. NCIRD has also expanded the *International Reagent Resource* (IRR) to include reagents and tests (including a multiplex RT-PCR assay) for additional respiratory pathogens, in addition to influenza. As of March 27, 2017, national laboratories in 14 GHSA countries have registered with the IRR and ordered reagents and tests.

**Laboratory Empowerment**

NCIRD has established a Laboratory Empowerment Workgroup to help foster workforce development, with a focus on training programs, career development, and staff promotion and retention. Laboratory Appreciation Week was held in April.

**Upcoming Events**

- The National Adult and Influenza Immunization Summit will be held May 9-11
- An updated HHS Pandemic Flu Preparedness plan will be released in 2017
- The June 2017 edition of *CDC Vital Signs* will describe the U.S. burden of health care-associated Legionnaires’ disease.

**Discussion**

Laboratory Empowerment. BSC members commented that

- Continued recruitment and retention of first-rate laboratory staff is critical to CDC’s work
- Keeping laboratorians engaged and knowledgeable of laboratory improvements while ensuring advancement potential is an issue for both public and private laboratories and requires innovative solutions. One possibility is to require laboratory administrators to rotate into the labs and work at the bench for short periods each year, similar to how medical epidemiologists are often required to complete rotations at medical clinics or hospitals.
• Meningitis Outbreaks. Dr. Messonnier reported that
  - The new Africa-CDC is not yet operational but in the future may join a WHO/AFRO project to enhance disease surveillance and response in the meningitis belt
  - Current outbreaks of non-A meningitis may be a new phenomenon or may have been present all along, masked by the past prevalence of group A strains that are now controlled through vaccination.
  - A low-cost multivalent vaccine is under development in India (by SAI Vaccines) that may be used for outbreak response or for preventive mass-vaccination of children.

• HPV
  - BSC members commended the new HEDIS measure on 2-dose HPV vaccination
  - In regard to whether 1-dose revaccination of teens with the 9-valent vaccine (for those previously vaccinated with the 4-valent vaccine) might be cost-effective, due to cross-protection, Dr. Messonnier noted that ACIP has taken multiple factors into account in making HPV recommendations. In addition to efficacy, safety, and potential cross-protective effects, these factors include parental concerns about frequent changes in HPV recommendations and the possible negative effects of shifting resources and attention from vaccination to re-vaccination.
  - In developing HPV messages, CDC considers information on provider perceptions and behavior, as reported by state health departments and documented by surveys, and research on factors that drive parents and clinicians to use or recommend vaccines

• Adult Vaccination
  - Although more people are insured, not all adults go to a doctor every year, and the number of vaccination clinics has decreased. Some adults regard vaccines as being primarily for children, and others may not perceive themselves to be at risk for vaccine-preventable diseases, even if they have underlying illnesses.
  - At the present time, adult vaccination occurs primarily at workplaces and at pharmacies. CDC is working with pharmacies and other private sector partners, providing tools and information, and exploring ways to ensure that vaccination information is recorded in electronic registries
  - CDC is also planning a half-day meeting at the National Adult and Influenza Summit to meet with Kaiser Permanente and other health provider organizations to consider how to improve and increase adult vaccination as well as reinforce vaccination across all levels of healthcare

• Global Health Security
  - To improve packaging and shipping of specimens, CDC might consider adopting innovations developed by high-volume private-sector shippers like Amazon that could allow for more rapid and efficient shipping.
  - The main issue for IRR is how to package samples and reagents safely and ensure they remain viable

• Outbreak of Acute Flaccid Myelitis
  - CDC has tested more than 1000 specimens since 2014, and many causes have been ruled out. An increase in cases of enterovirus D-68 has not been seen this year.

• Influenza/LAIV
  - CDC no longer recommends LAIV because its effectiveness decreased between 2013 and 2016.
- The National Institute of Allergy and Infectious Diseases (NIAID) is supporting studies to determine the cause of that decrease. One hypothesis is that the effectiveness of any vaccine in a given flu season depends on which strains are in circulation; another is that the vaccine’s use in successive influenza seasons has reduced its impact.
- NIAID also continues to support research to develop a universal (non-strain-specific) influenza vaccine

**Influenza A (H7N9)**

Dan Jernigan, Director, Influenza Division, reviewed the domestic and global impact of influenza and provided an overview of influenza viruses and how novel viruses emerge.

**Influenza Virus**

- The influenza virus has eight genetic segments that constantly mutate and can be exchanged with genes from influenza viruses in other species.
- The family of influenza A viruses—the type that gives rise to pandemics—includes 18 different subtypes of the hemagglutinin (H) protein and 11 different subtypes of the neuraminidase (N). There are three main reservoirs for influenza A. Birds are the largest reservoir with the most number of subtypes, humans and swine are the other two major reservoirs. Transmission between birds, humans, and swine can occur.
- Human-adapted pandemic viruses can evolve as a result of complex viral re-assortments involving avian and swine viruses. Reassortant viruses containing avian or swine genes have caused four human pandemics over the past 100 years: in 1918 (H1N1), 1957 (H2N2), 1968 (H3N2), and 2009 (H1N1).

**Novel Influenza Viruses**

- The world is increasingly crowded—due to explosive population growth in the last 50 years, connected—due to increases in global travel and trade, and converging—due to increasing exposure opportunities between the worlds of humans and animals. These factors contribute to the increasing number of human infections with novel influenza viruses.
- CDC has developed an Influenza Risk Assessment Tool (IRAT) that provides a risk assessment score for selected emerging novel influenza A viruses, based on factors related to viral genetics, population immunity, and ecology.
- The H7N9 virus that emerged in China in 2013 has maintained the highest IRAT score of any novel virus detected since it emerged in 2013, and has the highest risk score since the IRAT process was initiated.

**Emergence of H7N9 Influenza Viruses that Cause Illness in Humans**

- The first reported cases of human infection with H7N9 occurred in China in 2013 in the cities of Anhui and Shanghai. These cities are in an area of China with about 575 million people (45% of the population of China and 8% of the population of the world). This area also includes millions of domestic chickens, domestic ducks, and pigs.
- H7N9 virus apparently evolved through multiple genetic reassortments among viruses carried by domestic ducks (H7N9), wild birds (H7N9), and domestic poultry (multiple H9N2 viruses).
Outbreaks of H7N9 in China have occurred in five waves, starting with the 2012-13 winter season (about 135 cases), increasing during the 2013-14 season (about 320 cases), decreasing in 2014-15 and 2015-16 seasons (224 and 119 cases), and then rising abruptly and substantially in the 2016-17 season (755 cases). The geographic distribution of cases also increased during the fifth wave.

The number of human infections with H7N9 has surpassed the number of human cases of H5N1 (first detected in Hong Kong in 1997)

**Characteristics of H7N9 Viruses**

- About 85% of human cases of H7N9 influenza have been linked to exposure to live poultry. However, until 2017, the infected chickens had not exhibited signs of illness.
- The severity of the human infections is high, with 88%-90% of infected persons developing pneumonia and 68%-75% admitted to an intensive care unit. Forty percent of infected persons have died.
- Thirty-five clusters of H7N9 infection have been reported, with most occurring among family members and some occurring in healthcare settings. However, there is no evidence of tertiary transmission or of sustained and efficient transmission.
- The age distribution for H7N9 infection skews higher in older people, in contrast to the age distribution for H5N1 infection.
- A phylogenetic tree constructed from the sequences of 134 viruses isolated during the fifth wave includes:
  - A major clade of 129 viruses (the Yangtze lineage) that are genetically distinct from viruses isolated during the previous waves
  - 5 viruses (the Pearl lineage) that are more similar to viruses from the earlier waves and a better match than the Yangtze viruses to stockpiled vaccine
- Almost all of the 134 viruses have genetic markers associated with increased virulence, adaptation to humans, transmissibility, and pulmonary replication in mammals; 12 of 134 viruses also have genetic markers for resistance to neuraminidase inhibitor drugs (which may have arisen in response to treatment with oseltamivir)
- The Yangtze lineage includes a growing subset of viruses that (unlike the first detected H7N9 viruses) are highly pathogenic in poultry (classified by the U.S. Department of Agriculture [USDA] as Highly Pathogenic Avian Influenza [HPAI]). The emergence of an HPAI strain of H7N9 may impact the poultry industry; this strain might also cause more severe disease in humans.
- The clinical course of human infections with H7N9 virus is affected by underlying host factors such as age, immune function, and co-morbidities. It is also characterized by:
  - Increased binding to receptors in the lower and upper respiratory tracts as compared to H5N1, resulting in high respiratory tract viral load and prolonged viral replication
  - Induction of cytokines and chemokines, resulting in inflammatory tissue damage that can lead to acute respiratory distress syndrome, multi-organ failure, or sepsis

**Current Activities to Address H7N9 Influenza**

CDC continues to work with the Chinese Ministry of Health and other international partners to strengthen surveillance for human cases of H7N9 influenza, enhance capacity for laboratory diagnosis, and investigate outbreaks. CDC is also supporting research on antiviral drugs; assisting with surveillance for avian influenza in live-bird markets; and providing the Biomedical Advanced Research
and Development Authority (BARDA) with candidate viruses for vaccine production and stockpiling. As H7N9 viruses evolve, new vaccine candidates may be needed.

Discussion

- Surveillance for H7N9 Influenza
  - In China, there is a movement away from buying live chickens towards buying refrigerated chicken in stores, but at present live chicken markets are common in both urban and rural areas. Public health officials in Shanghai have instituted monthly closings and cleanings of chicken markets and do not permit chickens to be kept in markets overnight. Surveillance for H7N9 in poultry is difficult because infected chickens are not symptomatic, and poultry infections are typically detected only after a person falls ill.
  - Wide-scale, routine surveillance for H7N9 in bird markets has not been considered a priority by the Chinese Ministry of Agriculture. Therefore, adequate surveillance data for circulating avian influenza viruses in bird markets is not available. Small projects to monitor influenza in bird markets in China are supported by universities, USAID, and CDC. CDC is also working with Ministries of Health in Vietnam and Mongolia to conduct studies of influenza in wild birds.
  - In the United States, influenza surveillance is conducted in wild birds, poultry, and humans.
    - CDC has collaborated with the U.S. Geological Survey, Fisheries and Wildlife, and Department of the Interior to conduct some influenza surveillance projects in wild birds in Alaska. Ongoing testing by US Government agencies of wild birds submitted by hunters in the United States has not identified any Asian H7N9 in the country.
    - USDA tests for influenza in poultry in the United States to detect low pathogenic and highly pathogenic H5 and H7 viruses. This testing has not identified any Asian H7N9 in the U.S.
    - CDC has implementing a process of “right-sizing” domestic surveillance for influenza, to determine how many viruses must be collected from each state to monitor variant viruses, drug-resistant viruses, and viruses with pandemic potential.
    - The next step is to “right-size” global influenza surveillance, working in partnership with WHO, PAHO, and ministries of health. CDC is partnering with ministries of health to explore the development of regional hubs that will use next-generation, whole-genome sequencing to monitor influenza viruses globally.

- Development of Drugs, Diagnostics, and Vaccines. Pharmaceutical companies are conducting early-stage research into novel antiviral drugs, and NIH is supporting research into treatments involving monoclonal antibodies, with a few in clinical development. Past efforts in this area led to a limited number of treatments cleared by the U.S. Food and Drug Administration (FDA).

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

Susan Gerber, Acting Branch Chief, Respiratory Viruses Branch (proposed), NCIRD, briefly described the first two reported cases of MERS-CoV in 2012:

- A 60-year-old man in Saudi Arabia with acute respiratory distress syndrome and multi-organ dysfunction syndrome
- A 49-year-old man from Qatar admitted to a London intensive care unit with respiratory and renal failure

Genetic analysis indicated that these patients were infected with a coronavirus related to coronaviruses associated with bats.
Clinical Presentation of MERS-CoV

- Infection with MERS-CoV is associated with a wide spectrum of clinical manifestations, ranging from asymptomatic infection, to acute upper respiratory illness, to pneumonitis, respiratory failure, septic shock, and/or multi-organ failure resulting in death.
- Common signs and symptoms at illness onset include fever, chills, headache, non-productive cough, dyspnea, and myalgia. Other symptoms may include sore throat, coryza, sputum production, dizziness, nausea and vomiting, diarrhea, and abdominal pain. Atypical presentations include mild respiratory illness without fever and diarrheal illness preceding development of pneumonia.
- Clinical studies found that
  - High viral loads and weak antibody responses in patients with MERS are associated with severe pneumonia and mortality
  - The timing and intensity of respiratory viral shedding in patients with MERS closely matches that of patients with severe acute respiratory syndrome
  - MERS-CoV RNA can be detected in respiratory tract samples from asymptomatic and mildly ill persons, suggesting that these persons may shed virus
- A study of 70 adult patients found that most exhibited pneumonia and required intensive care. The median age was 62, and most had underlying comorbidities. Concomitant infections were a risk factor for severe disease, and age greater than 65 years was associated with increased risk of mortality.
- A study of laboratory-confirmed pediatric cases of MERS found that 9 out of 11 cases were asymptomatic. The two symptomatic children had underlying conditions (cystic fibrosis and Down syndrome; the child with cystic fibrosis died). The asymptomatic patients were detected during contact investigations of older patients.

Epidemiology of MERS-CoV

- To date, 1952 laboratory-confirmed human cases of MERS-CoV have been reported; 693 were fatal (36%). Among these cases
  - 642 were females and 1276 males (the gender of 34 patients is unknown)
  - The median age of cases was 53 years (range: 9 months to 109 years)
  - 16% of cases were healthcare personnel
- All cases are linked to nine countries: Saudi Arabia, Qatar, United Arab Emirates, Jordan, Yemen, Oman, Lebanon, Iran, and Kuwait. Forty-six cases involved persons who traveled to other countries.
- Person-to-person transmission of MERS-CoV is well documented, with 97 spatiotemporal clusters reported in household and healthcare settings
- The median incubation period is just over 5 days (range: 2-14 days)
- Routes of transmission are not fully known, and there is no evidence of sustained community transmission
- Epidemiologic studies found that
  - A rise in cases of MERS-CoV reported to the Saudi Ministry of Health in 2014 was largely due to secondary cases in persons who had visited a healthcare facility or been in contact with a healthcare worker or patient. About 3% of the cases did not report such contacts and might be primary cases. The investigators also found that most patients initially reported as asymptomatic had experienced at least one symptom consistent with a viral respiratory illness.
An outbreak of 38 cases of MERS in Taif, Saudi Arabia, was associated with four healthcare facilities, including a dialysis unit. Although viral genomic sequences obtained from specimens from 10 patients were closely related, not all of the 10 patients had received care at the same healthcare facility, suggesting that unrecognized transmission had occurred between facilities.

A 2015 outbreak of MERS in the Republic of Korea involved 186 cases that were linked to a single chain of transmission associated with several healthcare facilities. Thirty-eight of the cases were fatal.

### Household Transmission of MERS-CoV

- A study of 26 index patients and 280 household contacts identified 12 probable cases of secondary transmission, indicating a secondary household transmission rate of about 5%.
- A 2014 study identified sleeping in the room of an index patient, changing the patient’s clothes or sheets, and removing the patient’s waste as risk factors for MERS transmission. Casual contact and simple proximity were not associated with increased risk of transmission.

### Research Findings from Studies on MERS-CoV and Camels

- Risk factors for primary MERS-CoV illness in humans include direct exposure to dromedary camels during the 2 weeks before illness onset.
- Neutralizing antibodies to MERS-CoV are detected in persons in contact with dromedary camels.
- Dromedary camels are infected with MERS-CoV viruses that may match viruses isolated from human close contacts. This evidence supports transmission of MERS from dromedary camels to humans. A novel recombinant lineage that has been dominant since December 2014 led to the human outbreaks in 2015.

### CDC Activities

To detect and control cases of MERS-CoV infection, CDC has

- Developed guidance for testing patients with suspected cases of MERS-CoV, based on symptoms and travel history.
- Issued other guidelines, including
  - Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Patients Under Investigation (PUIs) for Middle East Respiratory Syndrome Coronavirus
  - Interim Infection Prevention and Control Recommendations for Hospitalized Patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Standard, contact, and airborne precautions are recommended, as they are for severe acute respiratory syndrome (SARS).
- Developed diagnostics, including
  - rRT-PCR MERS assays, which have been deployed to state health departments, USDA, and U.S. Department of Defense (DoD) laboratories, and national laboratories in countries in the Middle East, Africa, and South America.
  - Serologic assays for MERS-CoV, including enzyme-linked immunosorbent assays (ELISAs) that detect viral proteins.

### Where are We Now?

- Cases of MERS-CoV continue to be identified in the Arabian Peninsula.
- Small household and healthcare-associated clusters of MERS-CoV continue to occur.
- Infected camels that shed MERS-CoV are found in countries in the Arabian Peninsula and Africa.
• Strategies to address MERS-CoV include rigorous contact investigations and infection control
• Timely detection of imported cases of MERS-CoV is essential to prevent transmission in the United States

Questions for Consideration

• What should CDC be doing regarding domestic surveillance for MERS-CoV infections?
• What activities should CDC be involved in regarding international MERS-CoV epidemiology?

Discussion

• The BSC discussion primarily focused on what CDC should be doing regarding domestic surveillance for MERS-CoV infections and what activities CDC should be involved in regarding international MERS-CoV epidemiology

• Collaboration
  – Good relationships have developed between Saudi and U.S. health officials over the course of many visits, and specimens have been shared regularly over the past few years
  – CDC has provided the Saudi Ministry of Health with assistance in disease surveillance, electronic reporting, and characterization of viruses

• Healthcare Transmission
  – Healthcare workers are at increased risk of MERS-CoV infection, likely due to worker-worker and patient-worker transmission. The possible contributions of fomite and airborne transmission to disease spread require further investigation.
  – During the outbreak in Korea, patient-to-patient transmission was associated with crowding in emergency rooms and dialysis units

• Exposure to Infected Camels
  – A primary case of MERS-CoV infection may sometimes be matched with the camel that is the source of infection by comparing the sequences of viruses isolated from the patient and from the camel
  – It is not known whether MERS-CoV is uniquely adapted to dromedary camels or spreads in camel markets and/or during movement of camels between North African and Middle Eastern countries. Thus far, no primary cases of MERS have been reported in Africa.
  – The reason why men are more often identified as cases is also unknown. One hypothesis is that men have more frequent contact with camels. Another is that infected men are more likely to visit physicians, so their cases are more likely to be reported.
  – Drinking pasteurized camel milk—which is popular in Europe—has not been identified as a risk factor for MERS-CoV infection

• Vaccines and Antivirals
  – A human vaccine against MERS-CoV is in a Phase 1 trial in the United States. Development of a camel vaccine is not a U.S. priority, because few camels are available in the US for study.
  – The Coalition for Epidemic Preparedness Innovations (CEPI) has prioritized development of a vaccine against MERS-CoV
No existing antivirals are effective against MERS-CoV, and prophylactic administration of anti-MERS-CoV antibodies is not feasible, because patient titers tend to be low. More studies are needed.

Marmosets are under study as a potential animal model for MERS-CoV.

**Diagnostics**
- CDC has posted guidance for clinical laboratories on detection of MERS-CoV. Current strains of MERS-CoV can be identified using whole genome sequencing (WGS) or the rT PCR assay (developed in 2013), which detects 3 viral gene segments.
- MERS-CoV RNA has been found in the urine of some patients. In patients with severe disease, virus is sometimes detected in both urine and blood.

**MERS-CoV Surveillance in the United States**
- PUIs are most often people who have been hospitalized within 14 days of returning from an affected country. Most likely, the number of PUIs is under-reported. It is important to
  - Test travelers who develop illness within 14 days of arrival, even if other diagnoses are more likely, because co-infections can occur
  - Encourage physicians to take a travel history of all persons with severe respiratory infection
- As demonstrated in Saudi hospitals, outbreaks of MERS can be controlled using standard infection control measures. Special hospitals with enhanced capacities (like those used to treat Ebola patients) are not required. The principal need is for timely recognition of primary and secondary cases.
- Transmission of MERS-CoV on airplanes—where people sit for hours in close proximity—has not

**NCHHSTP Update**
Jonathan Mermin, NCHHSTP Director, described the launch of AtlasPlus, a mobile-friendly online tool that provides access to data on HIV, viral hepatitis, STDs, and TB. He also reported on recent staffing changes, which include
- Kathleen Ethier as the new Director of the Division of Adolescent and School Health
- Michael Melneck as the new Deputy Director for Management and Operations

Dr. Mermin also provided updates from NCHHSTP divisions:
- **The Division of Tuberculosis Elimination.** Recent developments include
  - Publication of *Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children* by the American Thoracic Society, the Infectious Diseases Society of America, and CDC
  - TB Elimination Champions Project activities conducted on World TB Day (March 24), to highlight the stories of individuals and organizations across country who are working to end TB
- **The Division of HIV/AIDS Prevention.** The estimated annual number of HIV infections in the United States declined by 18% between 2008 and 2014. Progress is not uniform among all populations or areas, with case counts and death rates varying by state. Other developments include
  - A CDC Vital Signs on *HIV and Injection Drug Use* that reports declines in HIV diagnoses among people who inject drugs (PWID), including a 50% decline among black and Hispanic PWID and a 28% decline among white PWID, who have the highest rates of syringe-sharing.
Increased use of advanced molecular detection (AMD). Sequencing is routinely conducted to test for resistance to antiretroviral therapy (ART) when new cases of HIV are diagnosed to assist with selection of effective treatment. Efforts are underway to use these data to identify HIV clusters and outbreaks, which can enable more rapid response and disease control, rapid provision of testing, treatment, and prevention services to members of sexual or drug-using social networks. TB clusters are already identified in a similar way.

The Division of Viral Hepatitis. Developments include
- Publication of *A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report (2017)*, by the National Academies of Science, Engineering, and Medicine (NASEM) (see page 18).
- High rates of hepatitis C virus (HCV) reported in Appalachia and other rural areas since 2013, associated with the opioid epidemic.
- Increased testing for HCV infection among baby boomers, likely due to compliance with CDC and U.S. Preventive Services Task Force recommendations.

Division of STD Prevention. The *STD Surveillance 2015* report indicates that STDs are at a record high. Total cases of chlamydia, gonorrhea, and syphilis are the highest ever reported, with more than 1.5 million chlamydia cases; nearly 400,000 cases of gonorrhea; and nearly 24,000 cases of primary and secondary syphilis. Men who have sex with men (MSM) represented the majority of new primary and secondary syphilis cases. There was also an increase in congenital syphilis that parallels an increase in rates of syphilis among women.
- The *CDC Call to Action: Let’s Work Together to Stem the Tide of Rising Syphilis in the United States*—issued in April—calls for the development of new tools to detect and treat syphilis. CDC and partners are developing new laboratory guidelines, creating a specimen repository, evaluating new technologies, and developing novel diagnostic tools and better methods for molecular surveillance.
- CDC and partners held *STD Awareness Month* activities throughout the month of April.

Division of Adolescent and School Health. The Division’s re-designed website includes a new Health Services for Teens site and an Infobrief for Parents that recommends that teens have one-on-one time with their health providers.

Questions for Consideration

- What are the two most effective actions CDC should take to reduce gonorrhea, chlamydia, or syphilis in the United States?
- What lessons have been learned from FoodNet, rapid molecular detection of *Legionella*, and other AMD programs that can inform HIV rapid outbreak response?
- How should CDC balance the need for interventions with a substantial impact on disease incidence with those aimed at reducing disparities in relatively small populations, e.g., rural incidence of HCV, STD rates among American Indians and Alaska Natives, TB in Alaska.

Discussion

- Declines in the Annual Number of HIV Infections
  - The BSC members commended CDC for progress in addressing HIV/AIDS and TB in the United States.
- Raising the Alarm about STDs.
BSC members stated that it is imperative to raise the alarm about rising rates of STDs, including syphilis, congenital syphilis (which has increased by 50%), gonorrhea, and chlamydia. All of these infections are preventable and curable.

- Although the increases in national STD incidence started before PrEP was available, concerns have been raised that PrEP use could exacerbate the situation if associated with less frequent use of condoms and increased risk behavior. New modelling research suggests that if PrEP care is provided per CDC guidelines, it would result in reduced STD incidence in the community since it includes frequent screening and treatment for STDs as well as HIV infection,
- If not stopped, the rise in STD rates could reverse U.S. progress on HIV/AIDS and threaten maternal, child, and adolescent health
- Cases of congenital syphilis and HCV should be regarded as sentinel events that identify communities where basic public health functions are not working (e.g., communities affected by the opioid epidemic). Wider dissemination of data about the rise in congenital infections might stir the national social conscience.

CDC efforts to sound the alarm include the Call to Action on syphilis and activities conducted during STD Awareness Month. Gail Bolan, Director of NCHHSTP’s Division of STD Prevention, emphasized the magnitude of the problem and its association with the opioid epidemic. An adequate response requires public and private resources (from states, companies, community-based organizations, and universities) to address medical, social, and public health issues at the community level.

- **Syphilis**
  - The rise in syphilis—including congenital syphilis—is symptomatic of societal problems. Guillermo Ruiz-Palacios, National Institutes of Health and Tertiary Referral Hospitals, Mexico City, reported that clusters of syphilis investigated in Mexico have included a significant number of cases with central nervous system involvement, raising the possibility that a virulent strain of syphilis is in circulation.
  - Dr. Mermin mentioned the CDC guidelines for syphilis screening in pregnancy
  - Dr. Bolan reported that CDC continues to work with FDA and Pfizer to address shortages of the type of penicillin used to treat syphilis, including pregnant women with syphilis who can pass on congenital syphilis. CDC helps STD clinics track their drug inventories and arranges drop shipments from Pfizer as an emergency measure. Dr. Bolan also said that
    - Few scientists in the U.S conduct research on syphilis, and few resources go into development of diagnostics, drugs, or vaccines against syphilis
    - A typing study is underway in NYC that may determine whether a new strain is responsible for cases of invasive neurosyphilis
    - There is no evidence of antibiotic resistance associated with treatment of syphilis

- **Strategies for Stemming Rising Rates of STDs**
  - *Establishing SSPs.* In addition to providing sterile syringes, SSPs provide screening for HIV and HCV, link infected persons to care, and provide access to medical and substance abuse services. Any state, county, or tribe can apply for federal funds to establish SSPs; to date, 29 jurisdictions have applied.
  - *Responding to clusters of STDs.* Some states are using WGS to identify and control HIV clusters among injection drug users. The knowledge that HIV is spreading in a community can change behaviors, and identification of a circulating strain of HIV can help ascertain the origin of the initial contact. This approach, which is already used with TB clusters, might also be a cost-effective way to respond to clusters of syphilis.
Implementing Newborn Screening for HCV infections. Dr. Mermin reported that

- The CDC / HRSA Advisory Committee on HIV, Viral Hepatitis and STD Prevention and Treatment is considering how to address perinatal HCV infections. Feedback from states that conduct newborn screening for HCV in high-risk communities would be welcome.
- Medical partners are developing treatment guidelines for congenital HCV

Making the healthy choice the easy choice.

- An example of an STD intervention that does not require a change in patient behavior might involve providing clinicians who use electronic records with automatic recommendations for STD screenings, based on each patient's age and gender.
- A recent modeling study concluded that wider use of pre-exposure prophylaxis (PrEP) among MSM will lead to decreased rates of STDs, if it is associated with 6-month screenings and treatment for STDs, as recommended by CDC guidelines

STD Diagnostics and Service Integration. BSC members suggested

- Bundling diagnostic tests—or creating a multiplex test—to enable simultaneous testing for HIV, TB, HCV, and STDs for persons in high-risk groups
- Evaluating self-collection of samples as a cost-effective way to increase testing for chlamydia and gonorrhea. This approach might be a way to adapt to the closure of STD clinics.
- Encourage medical clinics to establish standing orders to test people under 25 and people in high-risk groups for STDs

Balancing Targeted and Wholesale Interventions

- In regard to balancing interventions likely to have a large national impact with interventions targeted to small, at-risk populations (e.g., rural towns with a high incidence of HCV), BSC members made the following comments:
  - The two approaches overlap. The existence of health disparities means that an effective intervention that should be implemented nationwide has not been adequately delivered to a subset of the community.
  - More data are needed to evaluate the effectiveness of targeting interventions to small populations.

Dr. Mermin noted the following:

- The existence of health disparities for diseases such as STDs, HCV, and HIV, and the role of the opioid epidemic in fueling their spread continue to be troubling.
- Targeting a small population may not be as effective a use of public health resources as large-scale efforts. On the other hand, if small at-risk groups are not targeted, health disparities may increase.
- When highly active antiretroviral therapy was first introduced in the mid-1990s, mortality decreased for all racial and ethnic groups but relative differences increased

Overview of TB Surveillance Trends and Focus on New Tools and Approaches to Latent TB Infection

Phil LoBue, Director, Division of TB Elimination, NCHHSTP, provided an overview of TB trends in the United States and discussed the importance of addressing latent TB infection (LTBI).

TB Surveillance Data and Disease Trends in the United States

- A total of 9,287 new TB cases were reported in the United States in 2016—the lowest number on record. This represents a decrease of 2.7% from 2015, and a 65.2% decrease from 1992. TB case
counts vary widely from state to state, with the highest numbers in California, Florida, New York, and Texas.

- The resurgence of TB in U.S. cities in the mid-1980s was marked by years of increasing case counts until its peak in 1992. Then, between 1992 and 2008, the total number of TB cases decreased 2%–7% annually. An unprecedented decrease occurred in 2009, when the total number of TB cases decreased by more than 10% from 2008 to 2009.

- TB rates are highest in certain population groups. In 2016,
  - Approximately 86% of all reported TB cases occurred among racial/ethnic minorities ( Asians, Hispanics, non-Hispanic blacks/African Americans, American Indians/Alaska Natives, and Native Hawaiians/Other Pacific Islanders). Thirteen percent occurred among non-Hispanic whites.
  - Foreign-born persons accounted for 68% (6,307 of 9,287) of reported TB cases. 55% of TB cases involved persons born in five countries: Mexico, the Philippines, India, Vietnam, and China.
  - Case counts among those who arrived in the U.S. less than 1 year ago or 1-4 years ago have declined since 2003, with a slight increase over the past few years. In contrast, case counts among those who arrived 10 or more years ago have steadily risen. These numbers might reflect the improvements in overseas screening and treatment of immigrants and refugees implemented by CDC in 2007.

- The number of primary multidrug-resistant TB (MDR-TB) cases in the U.S. decreased steadily from 1993 (407 cases) to 2001 (115 cases), with a slight increase in 2002 (132 cases). Since then, the total annual number of primary MDR-TB cases has fluctuated between 69 and 103, with 73 cases reported in 2015.

- Challenges to TB elimination include
  - Maintaining political commitment. Because TB cases have decreased, TB prevention may not be considered a public health priority by the public or by policymakers.
  - Loss of clinical, laboratory, and public health expertise and experience related to TB
  - Shortages of TB drugs and biologics. The U.S. market for TB drugs is small, and regulatory requirements limit access to TB drugs manufactured in other countries.
  - TB cases, clusters, and outbreaks tend to occur in populations that may be difficult to reach (e.g., homeless persons and incarcerated persons).
  - Lack of consensus on how to address the large pool of persons with LTBI (see below).

**Addressing LTBI**

- Although the number of U.S. cases of active TB disease is fewer than a thousand, millions of people in the U.S. have latent TB. Recent studies report that

  - **Most U.S. cases of active TB disease are due to reactivation of LTBI.** A CDC study involving whole-genome sequencing of 26,586 TB isolates obtained between January 2011 and September 2014 found that 14% are attributable to recent transmission and 86% likely result from reactivation of LTBI.

- **TB will not be eliminated during this century, unless we address LTBI as well as active TB.** The threshold for TB elimination is less than 1 case per million, and the current U.S. number (though very low) is 3 per 100,000. A Harvard modeling study suggests that elimination will require targeted interventions such as LTBI testing and treatment for new immigrants, as well as improved LTBI testing and treatment for people already in the United States.
5.9 to 13.9 million people in the U.S. have LTBI. In 2011-2012, data from the National Health and Nutrition Examination Survey (NHANES) showed that
- 4.7% of the U.S. population (13.1 million people) test positive for LTBI by the tuberculin skin test (TST), and 5% (13.9 million) by the Quantiferon test. 2.1% (5.9 million people) are positive by both tests.
- Among foreign-born persons, 20.5% (8.2 million people) test positive for LTBI by TST, and 15.9% (6.4 million people) by the Quantiferon test; 9.3% (3.7 million people) are positive by both tests.

The Way Forward

- TB elimination efforts can take advantage of
- The current low burden of TB disease in the United States, as well as high treatment completion rates
  - Tests that are easier to use in key populations. The interferon-gamma release assays (IGRAs) require a single visit for a blood draw, with follow-up visits needed only when a test is positive, and do not cause false positives in foreign-born persons vaccinated with the BCG vaccine.
- Short-course regimens for LTBI with lower toxicity and higher completion rates. The U.S. Preventive Services Task Force (USPSTF) Grade B recommendation on screening for LTBI in populations at increased risk
- Progress towards TB elimination requires
  - Targeted testing and treatment of persons who have a high risk of exposure to TB (e.g., incarcerated persons) and persons with LTBI who have risk factors for progression to active TB (e.g., HIV infection, smoking, diabetes, and use of TNF antagonist drugs to treat autoimmune conditions).
  - Expansion of testing and treatment efforts beyond public health departments to the primary care community.

Questions for Consideration

- How can the public health community expand testing and treatment for LTBI with level or decreased funding, while also maintaining case management and contact-investigations for active TB?
- Are there other strategies to consider?

Discussion

- TB Elimination Projects. BSC members suggested that CDC consider
  - Creating “islands of elimination” in the U.S. by supporting community outreach comprehensive efforts to detect and treat TB, MDR-TB, and LTBI in high-risk areas. Components could include comprehensive screening for TB, hepatitis C, and other STDs, as well as testing and treatment of contacts of people with MDR-TB.
  - Piloting local elimination efforts in rural areas to drive down rates of LTBI as well as active TB disease. Medical-community partners (e.g., federally qualified health centers) could use electronic registries to track the results of diagnostic testing, as well as completion of treatment for TB, MDR-TB, and LTBI.
  - Making LTBI a reportable condition. Dr. LoBue said that LTBI is already reportable in some states, although the utility of this approach remains under discussion.
– Working with the medical community to improve TB detection and treatment (e.g., using electronic medical record systems to provide clinicians with information about high-risk populations and reminders about TB testing).
– Working with international partners to develop a single standard of care for people with TB, MDR-TB, and LBTI in the United States and globally.
– Ensuring that the discussion about TB elimination in the U.S. acknowledges the stigma that may be associated with TB infection

• Diagnostic Issues
– Regarding the use of IGRAs, Dr. LoBue reported that
  o The cost-effectiveness of IGRA testing is good, with fewer false positives than TST.
  o The Tuberculosis Epidemiologic Studies Consortium (TBESC) is conducting a longitudinal study that
    ▪ Compares test results from TST and two IGRAs
    ▪ Assesses whether IGRA can identify individuals with LTBI who are likely to develop active TB
    ▪ Evaluates the use of IGRAs and TST in testing immunocompromised persons.
– Dr. LoBue also noted that
  o The WGS genotyping method used in the TB transmission study has not been compared to earlier methods used to identify transmission routes (e.g., during the TB outbreak in NYC in the 1990s). Validation was accomplished using a dataset of TB cases with confirmed epidemiologic links that indicate likely routes of transmission.
  o Two FDA-approved PCR tests for TB are commercially available. The older one is not much used, and the newer one is the Xpert MTB/RIF Assay, which is used domestically to determine whether a patient requires hospital isolation. Although a cheaper and more sensitive PCR test would be welcome, the number of people with active TB in the U.S. is likely too small to drive diagnostic test development.
– BSC members suggested that:
  o The market for TB tests may grow, both domestically and overseas, if testing for LTBI becomes more common
  o In the future, a rapid automated test might be developed that probes for a range of respiratory infections (including TB) within a single sputum sample

• TB Among Incarcerated Persons. Dr. LoBue reported that
– The DTBE advisory board includes a representative from the Federal Bureau of Prisons, and CDC scientists have made presentations on TB at prison health conferences. A CDC pilot study that used the 12-week LTBI regimen to treat persons incarcerated in a federal prison reported a 90% completion rate.
– CDC provides guidance on TB to health departments and correctional authorities in states where prison health is a public health priority. However, many states and localities do not regard LTBI treatment of incarcerated persons as cost-effective, because most people with LTBI are unlikely to progress to active TB. If a predictive test were available, it would be possible to target treatment to persons who are at risk for active TB.
A National Strategy for the Elimination of Hepatitis B and C

John Ward, Director, Division of Viral Hepatitis, NCHHSTP, reviewed the national strategy for the elimination of hepatitis B and hepatitis C issued by the National Academies of Science, Engineering, and Medicine (NASEM). The strategy has two parts:

- **Eliminating the Public Health Problem of Hepatitis B and C in the United States: Phase One Report (2016),** which concludes that “the time is right” to hasten elimination of viral hepatitis in the U.S. and globally
- **A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report (2017),** which lays out goals and targets to achieve elimination by 2030

The NASEM reports, which were co-sponsored by CDC, are in good accord with the WHO Global Health Sector Strategy on Viral Hepatitis: 2016-2021, which envisions “a world where viral hepatitis transmission is halted and everyone living with viral hepatitis has access to safe, affordable and effective prevention, care and treatment services.” The Phase Two Report recommends a series of actions to eliminate hepatitis B virus (HBV) and HCV as public health threats:

- **HBV vaccination of vulnerable populations.** Vaccination of infants beginning at birth and vaccination of previously unvaccinated adults at risk for HBV infection are essential.
- **Prevention of HCV infection among persons who inject drugs.** The NASEM strategy recommends that states and federal agencies expand access to syringe exchange and opioid agonist therapy, aiming for a 70% reduction in transmission risk; prevention effectiveness can be increased with the addition of medication-assisted therapy and HCV testing and curative treatment. About 270 syringe services programs (SSPs) are currently in operation; approximately 2,200 are needed. Thus far, 29 states and counties have been approved to use CDC funds to support SSPs.
- **Improved access to testing, care, and, treatment.** The NASEM strategy recommends that CDC and the states work together to identify settings that are appropriate for enhanced viral hepatitis testing (e.g., emergency departments and correctional settings) and to screen and treat HBV and HCV in correctional facilities.
- **Improved disease surveillance and strategic data analysis.** The NASEM strategy recommends that CDC support case surveillance, cross-sectional studies, and cohort studies to measure HBV and HCV infection incidence and prevalence in high-risk populations. In May 2017, CDC funded core surveillance in 14 states to increase acute case-finding and establish case registries; these states have reported over 70% of new cases of HBV and HCV infection. Assuming that funds are available, other activities would include using clinical care data to monitor hepatitis care at the national and state levels and including questions about HBV and HCV in public health surveys of high-risk populations (e.g., the National HIV Behavioral Survey).
- **National coordination of elimination efforts.** Coordination and oversight might be provided by White House Office of National AIDS Policy, the Office of the Surgeon General, the HHS Office of HIV/AIDS and Infectious Disease Policy, and/or by a newly constituted White House office.

The 2030 targets of the NASEM strategy include

- **A 50% reduction in HBV mortality.** Performance measures include (1) diagnosing 90% of chronic hepatitis B cases and linking 90% of those cases to care and (2) treating 80% of cases for whom treatment is indicated
- **Reducing HBV incidence as close as possible to zero in children less than 5 years old.** Performance measures include (1) achieving 85% birth-dose coverage for hepatitis B vaccine and (2) ensuring that 75% of infected mothers receive perinatal case management.
• **65% reduction in HCV mortality and 90% reduction in HCV incidence.** Performance measures include (1) diagnosis and cure of 260,000 people per year, from 2015 to 2030, and (2) reduction of new infections from 30,240 per year (in 2015 and 2016), to 2,730 per year (by 2030).

The CDC Foundation Summit and the Viral Hepatitis Action Coalition convened a **Viral Hepatitis Elimination Summit** in Atlanta on April 27-28 that could be accessed by webcast. Next steps for CDC include using input from the Summit to improve its strategic plan, partnership strategy, and communication and policy materials and to begin documenting progress toward the elimination of viral hepatitis in the United States.

**Questions for Consideration**

- What is CDC’s role in identifying strategies to increase the affordability of HCV therapies for use in marginalized market segments? (e.g., convening meetings, conducting modeling, demonstration projects)
- How can CDC promote broader leadership and commitment to implement interventions that prevent viral hepatitis and other bloodborne pathogens among substance users?

**Discussion**

BSC members noted that the elimination of viral hepatitis, as well as TB, requires strategic thinking about how to address the affordability of treatment and how to improve testing and treatment in high-risk populations, including people who inject drugs. BSC members suggested that

- CDC might support pilot projects that demonstrate how to reach elimination targets in a city or in a prison. Dr. Ward noted that the Cherokee Nation is implementing an **elimination project** in Oklahoma that demonstrates how to test and treat those living with hepatitis C. Elimination projects are also underway in San Francisco, and in development for New York City and the **State of New Mexico**.
- Improved HCV testing and treatment in jails could have a major impact, because jails serve as “revolving doors” that introduce and re-introduce viral hepatitis into communities. One idea is to make jails and prisons eligible for the **HHS 340B Drug Discount Program**, which provides discounts on outpatient drugs to safety-net health providers.
- CDC might work with the Substance Abuse and Mental Health Services Administration (SAMSHA), the Health Resources and Services Administration (HRSA), and other agencies to implement the Surgeon General’s report on **Facing Addiction in America**. Establishment of SSPs and substance abuse treatment programs will also reduce transmission of HCV and HIV.
- The response to the opioid crisis should include building a Ryan White-like infrastructure—as a collaboration between the medical and public health communities—that provides HCV screening for people at risk, as well as linkage to primary care providers. The Ryan White approach has helped slow HIV/AIDS epidemic; it could help eliminate HCV infection, which (unlike HIV/AIDS) is curable.
- The U.S. standard of care for viral hepatitis should become the global standard of care.

In regard to the **CDC recommendation** that all baby-boomers be tested for viral hepatitis:

- Susan Sharp, Regional Director, Microbiology and Infectious Disease Laboratories, Kaiser Permanente Northwest, reported that Kaiser is implementing this recommendation for all patients born between 1945 and 1965. Broader adoption by healthcare systems will speed progress toward achieving HCV elimination goals.
• Dr. Ward noted that the baby-boomer population was infected many years ago, through a variety of transmission routes, including not only injection drug use (as today) but also via healthcare and blood transfusion (which now rarely occur). Approximately 70% have moderate-to-severe liver disease and can benefit from curative HCV therapy.

Center for Global Health

Global Polio Eradication Initiative (GPEI)

• Polio has been eradicated in all but three countries: Afghanistan, Pakistan, and Nigeria. Worldwide, fewer than 40 children were paralyzed by polio in 2016.
  – Health officials in Pakistan and Afghanistan are working together to eradicate polio. In Pakistan, polio has been reduced by more than 90% since 2014. Most parts of Afghanistan remain polio-free, and the national polio program is using emergency resources and innovative strategies to immunize more children in hard-to-reach areas.
  – In Nigeria, 35 of 36 states have been free of wild polio virus since 2014. In 2016, the national polio eradication program was able to reach and immunize missed children in conflict-affected areas.

• Transition planning is underway in these three countries and in polio-free countries. Activities include sharing lessons learned from GPEI (e.g., about social mobilization and how to reach vulnerable populations) and integrating tools and infrastructure improvements (e.g., in vaccine delivery and laboratory-based disease surveillance) into ongoing health initiatives. Knowledge and tools built by GPEI have contributed, for example, to improved responses to Ebola and avian influenza in Nigeria; to outbreaks of Marburg fever in Angola; to outbreaks of measles in multiple countries; and to natural disasters in Nepal, Pakistan, and India.

GPEI Post-Certification Strategy

The purpose of the GPEI Post-Certification Strategy is to define how a polio-free world will be sustained. Goals include
1. Contain Polio Sources, by ensuring that potential sources of poliovirus are properly controlled or removed
2. Detect and Respond, by detecting any poliovirus introduction and rapidly responding to prevent transmission
3. Protect Populations, by immunizing populations against unanticipated polio events
4. Manage and Monitor, by ensuring that ongoing polio functions are embedded in existing or develop new approaches to sustain the goals of polio post-certification

Global Health Security

• Countries that participate in the Global Health Security Agenda have made progress in multiple areas, including
  – Laboratory and Disease Surveillance: 13 countries have detected dangerous pathogens using molecular diagnostics; 12 countries have trained community members to detect and report potential health threats; and 9 countries are using surveillance data to inform targeted immunization campaigns.
Workforce Development: All countries participate in Field Epidemiology Training Programs (FETPs); more than 2300 people have been trained in disease detection and response; and trainees have investigated more than 475 potential disease outbreaks.

Emergency Operations and Response: 71% of participating countries have activated emergency operations centers to address either emergencies or simulated emergencies; 88% have evaluated their health-emergency management capacity; and 88% have assessed baseline capacity for responding to biological threats.

- In 2016, the CDC Global Rapid Response Team (GRRT) mobilized more than 250 times, providing investigative support to 23 countries during outbreaks of cholera, polio, Zika, Ebola, yellow fever, and natural disasters.

Malaria

- CDC is using AMD tools—including WGS and Malaria Resistance Surveillance (MaRS) software—to track the spread of drug-resistance in malaria parasites. The AMD approach, which is being shared with U.S. laboratories, enables rapid detection of mutations for drug resistance (including uncommon mutations) and development of comprehensive drug-resistance profiles. This activity complements on-the-ground support for drug resistance studies in over 30 countries in which malaria is endemic.
- Nigerian health officials are working with CDC to improve collection and analysis of surveillance data to accelerate malaria control. Four surveillance modules have been developed, with five more planned; a baseline assessment of surveillance data has been completed; and state-level trainings have been held in Zamfara and Kano.

Global HIV

CDC is working with ministries of health in PEPFAR countries to conduct population-based HIV impact assessments (PHIAs) to evaluate the results of 10 years of HIV control efforts, including scaled-up provision of antiretroviral therapy (ART). The results will inform the development of a new blueprint for action. The PHIAs will provide up-to-date information on the prevalence of HIV infection in adult men and women and document progress toward achieving UNAIDS 90-90-90 HIV treatment targets.

Discussion

- Laboratory Capacity-Building. Dr. Martin reported that:
  - As national public health programs adopt AMD methods, the CDC Global Disease Detection Centers (GDDs) will continue to isolate new and re-emerging pathogens
  - All GHSA countries participate in FETPs or Field Epidemiology and Laboratory Programs (FELTPs). The FETPs and FELTPs are partners in the effort to improve packaging and shipping of specimens (see page 3).
  - The FELTPs are developing a Laboratory Leadership Service (LLS) program along the lines of the U.S. model.
- Global Health Partnerships
  - BSC members suggested several organizations as global health partners:
    o The Infectious Disease Society of America (IDSA) Global Health Committee (see committee descriptions)
    o The Consortium of Universities for Global Health
    o The American Society for Microbiology (ASM) Global Outreach Program
CDC might consider training and research in implementation science as an area for increased collaboration with academic partners.

- Communications and Information-Sharing. BSC members commented that
  - It is important to communicate the benefits to the United States of global health efforts to address emerging disease threats and antimicrobial resistance
  - Communicators should consider using infographics and other visuals to explain how global health issues affect U.S. health

Report from the Food Safety Modernization Act Surveillance Working Group

The Food Safety Modernization Act Surveillance Working Group (FSMA SWG), established in 2011, is charged with providing advice and recommendations to CDC and FDA (and through them to HHS) on criteria for the designation of Integrated Food Safety Centers of Excellence (submitted in 2012) and improvement of foodborne illness surveillance. The Working Group includes 21 members representing the BSC, CDC, USDA, FDA, academia, consumer groups, industry, and state and local health organizations.

Harry Chen, Chair of the FSMA SWG, reported on the group’s May 1-2 meeting, which included the following topics:

**FoodNet**

- The Foodborne Diseases Active Surveillance Network (FoodNet) is a collaboration among 10 state health departments, USDA’s Food Safety and Inspection Service (FSIS), FDA, and CDC to assess the burden of foodborne illness in the United States; monitor trends in burden of specific pathogens over time; attribute illness to specific foods or settings; and disseminate information to improve public health practice and guide development of intentions.
- New activities since 2009 have included collection of data on positive results from culture-independent diagnostic tests (CIDTs), collection of case exposure ascertainment (CEA) data, and surveys of clinical laboratories to learn about changing diagnostic testing practices. FoodNet has enhanced data transmission and dissemination and conducted studies to evaluate the burden of STEC non-0157; to expand collection of antimicrobial resistance data; and update national case definitions for enteric pathogens.

Impact of CIDTS on Evaluation of Disease Trends

The use of CIDTs has led to an increase in the number of reported cases of campylobacter and other enteric diseases. This increase might reflect test-related factors, such as a rise in the number of tests ordered by physicians; greater sensitivity of CIDTs, which may identify infections are culture-negative; and use of multi-pathogen syndromic panels that increase testing for pathogens not typically included in routine stool culture tests (e.g., *Vibrio* and *Yersinia*).

- In 2016, FoodNet began collecting data on both culture-confirmed and CIDT-positive cases of campylobacter, *Salmonella*, and STEC, and found that different tests provide significantly different numbers. These test-related differences make it difficult to assess disease trends by comparing numbers of cases detected over successive years.
• FoodNet will continue to monitor changing testing practices, including the use of reflex cultures when CIDT results are positive. Thus far, results from laboratory surveys suggest that few clinical laboratories are conducting reflex testing (which is expensive) and that the burden is likely to fall on state public health laboratories, which lack sufficient resources for this purpose.

**FoodNet Fast**

In November 2016, FoodNet launched an interactive online tool called [FoodNet Fast](#) that improves access to FoodNet data and allows users to calculate the incidence rates of disease due to nine foodborne pathogens.

• Guidance from the FSMA SWG included that FoodNET continue to
  – Evaluate the impact of CIDTs (including multiplex syndromic panels) on surveillance for foodborne illness
  – Evaluate and improve FoodNet Fast, as needed
  – Update incidence rates, accounting for the effects of CIDT use, to formulate goals for Healthy People 2030

**Case-Case Comparisons**

• Case-control studies are considered the gold standard for testing epidemiologic hypotheses. However, they are often expensive, difficult to replicate, and time-consuming. Moreover, their results may be subject to recall bias. Case-case comparisons are modified case-control studies in which cases of a disease of interest are compared with cases of another disease. The advantage of a case-case comparison is that case data are often readily available through routine surveillance interviewing. In addition, recall and selection bias are likely more similar between comparison groups.

• Case-case comparisons only identify differential risk (e.g., the difference in risk between cases and surrogate controls). Moreover, the surrogate controls may not be ideal, because they have also been ill, although not due to the disease of interest. These limitations can make the results challenging to interpret. Nevertheless, in some situations case-case comparisons are a valid and practical way to identify risk factors and guide development of prevention and control measures.

• A case-case comparison was recently used to identify a particular brand of nut butter as the cause of an outbreak of *Salmonella*, by “Project Mercury,” which is led by the Oregon Integrated Food Safety Center of Excellence.

**Population Survey**

• The CDC Population Survey, which is conducted in the 10 FoodNet sites, collects information on food exposures, environmental exposures, gastrointestinal illness, healthcare-seeking behaviors, and other special topics. Its primary objectives are to estimate the burden of acute gastroenteritis in the U.S. and help generate hypotheses during cluster and outbreak investigations.

• Past surveys have involved landline phone interviews, using random digit dialing (RDD) to sample households and a “next-birthday” method to sample individuals by selecting a single participant from a given household. During the last survey cycle in 2006-07 more than 18,000 respondents were contacted over a 12 month period. Each FoodNet site had the opportunity to add questions of interest.

• The next survey will launch in June 2017 and include an increased sample size (about 36,000 respondents), and modernized methods, including cell phone surveys and online surveys. The questions will be updated to align with the National Hypothesis Generating Questionnaire (NHGQ),
CEA, the National Antimicrobial Resistance Monitoring System (NARMS), and the FDA Food Safety Survey

- Guidance from the FSMA SWG included that
  - The Population Survey be conducted continuously rather than periodically, to save costs and possibly allow expansion nationwide
  - As data are obtained during the 2017 survey cycle, it should be continuously evaluated to allow adjustments in the collection scheme, if needed
  - Preliminary data should be made available before the end of the 2-year cycle
  - The results of the Population Survey should be made available for use in case-case comparisons

**National Outbreak Reporting System (NORS)**

The purpose of NORS is to facilitate reporting of enteric and waterborne disease outbreaks by state, local, and territorial public health agencies. It collects information on pathogens, affected groups, and outbreak settings, and characterizes outbreaks by modes of transmission (food, water, animal contact, person-to-person, environmental exposure, or unknown). At the present time, NORS primarily addresses disease transmission via food, water, and animals; future plans include working with the National Center for Environmental Health to integrate the National Environmental Assessment Reporting System (NEARS) into NORS.

**Norovirus Surveillance**

Components of NORS include
- **NoroSTAT**, a partnership of 9 state health departments and CDC that establishes and maintains reporting standards for norovirus outbreaks
- **CaliciNet**, the national norovirus outbreak surveillance network, which has been expanded to include 38 state laboratories, 5 of which serve as regional laboratories
- **NORSDirect**, a reporting tool launched in 2015 that allows state, local, and territorial public health departments to upload electronic outbreak data into NORS to reduce double data entry

**Waterborne Disease Surveillance**

NORS is working with state health departments to collect information on waterborne disease outbreaks. It is also working with the CDC One Health Harmful Algal Bloom System (OHHABS) to share electronic platforms and reporting structures for monitoring outbreaks associated with harmful algal blooms.

**Future Directions for NORS**

- Exploring ways to integrate surveillance data from laboratory, epidemiology, and environmental sources and advance the identification of the root causes of food contamination
- Developing a Foodborne Outbreak Prevention Initiative that will use data from NORS and other surveillance systems to identify and address food safety problems that can lead to outbreaks.

**Topics for Future FSMA SWG Meetings**

Dr. Chen reviewed the topics covered by the FSMA SWG over the past 6 years and listed ideas for future meetings, including
- Periodic reviews of foodborne surveillance systems
- Integration of data systems within CDC and among CDC, FDA, and USDA
• Updates on interagency collaborations such as the Interagency Food Safety Analytics Collaboration (IFSAC), Interagency Foodborne Outbreak Response Collaboration (IFORC), and Interagency Collaboration on Genomics and Food Safety (Gen-FS)
• Public health challenges related to imported foods
• Orphan illnesses, such as toxoplasmosis, cryptosporidiosis, and hepatitis A
• The impact of FSMA
• Food allergies and anaphylaxis
• Root-cause identification and analyses of foodborne disease outbreaks
• Building state-level capacity to address foodborne disease

**Discussion**

**CIDTs**

- Use of CIDTs in clinical laboratories is widespread and growing, causing a loss of isolates for public health purposes. The short-term solution is to obtain as many isolates as possible through reflex culture testing. The long-term solution is to transition to metagenomics methods that do not require isolates.
- Discrepancies between CIDT and culture-based test results make it difficult to compare data from successive years. There is no gold standard for testing and no baseline for assessing disease trends. On the positive side, state-level data suggests that CIDTs can detect outbreaks much faster than older methods.
- At the present time, some state health laboratories preserve isolates and conduct reflex-culture testing (or send isolates to CDC) when CIDT results are positive, while others do not. APHL is surveying state health laboratories about CIDT use and developing recommendations on best practices. The CDC Public Health Law Program is assisting APHL by developing language that states may adopt in describing rules for CIDT use.
- It is important to assess the clinical significance of test results that
  - Test positive by CIDT but negative by culture
  - Test positive for multiple pathogens on a multiplex CIDT panel
- The need for this assessment is illustrated by confusion over how to comply with a state-level regulation that requires two negative STEC tests before an infected child can return to daycare. When CIDT tests are used in place of culture tests, the child may test “positive” (and be excluded from daycare) for a month or longer, even though the child is no longer symptomatic.
- A 2012 Johns Hopkins study to evaluate the use of molecular diagnostics in assessing the etiologies of cases of pneumonia concluded that molecular tests are more sensitive than culture tests and more likely to detect multiple pathogens. They concluded that these tests would be very useful for disease surveillance, but less so for clinical follow-up.
- CDC might consider inviting public and private sector partners to a summit on CIDTs, as in 2012. Other ways to bring attention to this issue were included in the presentation and discussion from the IDLWG (page 31).

**Metagenomics**

- Metagenomics involves sequencing all of the genetic material within a given clinical sample (e.g., human, bacterial, and viral DNA) and using computer algorithms to sort out and identify the source of each sequence. Within the next decade, metagenomics methods may be able to detect pathogens in stool and other clinical specimens.
Unlike WGS, diagnostic testing based on metagenomics does not require isolation of pathogens in culture. Unlike CIDTs, diagnostic testing based on metagenomics will satisfy many public health needs (e.g., by identifying genetic markers for resistance and strain-typing).

BSC members commented that
- CDC might consider working with diagnostics manufacturers to ensure that data obtained via metagenomics will be available for both clinical and public health purposes
- Cultures will always be needed to characterize newly detected pathogens, as well as to provide reference organisms for research and development of diagnostics, drugs, and vaccines

Conversation with CDC Acting Director Anne Schuchat
Anne Schuchat, CDC Acting Director, spoke about the importance of keeping the CDC workforce motivated, confident, and focused on mission during this interim period. She noted that HHS Secretary Thomas Price has expressed support for CDC’s work in defending the nation against emerging infectious threats and in addressing priority issues such as childhood obesity, mental illness, and the opioid epidemic.

Dr. Schuchat has briefed the White House on H7N9 influenza, Zika, and pandemic preparedness, and next week will give a presentation on antimicrobial resistance—an area of work that has broad bipartisan support. She reported that
- Zika continues to be a major concern
  - According to 2016 data, birth defects have been associated with one in ten U.S. cases of Zika infection in pregnant women; all cases were travel-associated
  - The CDC Emergency Operations Center remains activated and ready to address any surge in cases over the summer
  - CDC is working with partners in Florida and Texas to advance planning and preparedness over the long-term
- CDC is paying close attention to the H7N9 outbreak of influenza in China
- CDC is using its cross-agency Winnable Battle (WB) framework to address the spread of bloodborne diseases associated with the opioid epidemic. The WB framework identifies priority strategies, defines targets, and implements interventions in collaboration with public health partners.
- CDC is planning an open-house for state and local partners in the State of Georgia

Dr. Schuchat emphasized the need for consistent CDC messaging and requested feedback on an animated slide describing CDC’s work to Prevent, Detect, and Respond to public health threats. The slide features activities under these topics: Communications/Guidance, Epidemiology/Surveillance, Global Health, Innovation, Laboratory/Diagnostics, and State/Local Health.
BSC Feedback

- It is important that public health services be recognized as investments. Information on the economic impact of public health programs should be more widely disseminated. Economic information has been provided, for example, on childhood vaccination and on PulseNet.
- Public health efforts to prevent disease may be invisible to the public and therefore not appreciated. Examples include prevention of cancers due to HBV and HPV vaccination. In addition to saving lives, these efforts save medical costs, including costs paid by Medicare and Medicaid.
- The Ebola epidemic illustrates the importance of upfront investment in global disease surveillance and response.
- In regard to the Prevent, Detect, and Respond slide and videos, it was suggested that CDC
  - Continue to emphasize CDC’s 24/7 emergency response capacity
  - Continue to put laboratory activities front and center and to emphasize the number and diversity of infectious diseases
  - Consider
    - Replacing “Prevent” with “Protect”.
    - Explaining how public health investments benefit states, localities, and Congressional districts
    - Providing information on public health training, in areas such as epidemiology and laboratory
    - Illustrating the benefits of the AMD program by adding a picture of a molecule to the graphics on Laboratory/Diagnostics
    - Giving more emphasis to chronic disease prevention and to collaborations between the medical and public health systems

NCEZID Update

Chris Braden, NCEZID Deputy Director, provided the updates on the following topics.

Staffing Changes

- Beth Bell, former NCEZID Director, retired on Jan 7, 2017; Rima Khabbaz is serving as Acting Director
- Debra Lubar is the new Deputy Director for Management and Operations
- Nicki Pesik will become Associate Director for Infectious Disease Preparedness, following the retirement of Tracee Treadwell later this month

Recent Outbreak Investigations

- *Shiga Toxin-Producing E. coli (STEC) in Soy Nut Butter*. The investigation, which is ongoing, began with a cluster of 10 cases, including 4 children hospitalized with hemolytic uremic syndrome. The cases were identified in four states through recognition of new pulsed-field gel electrophoresis (PFGE) pattern by PulseNet. The source—soy nut butter—was identified and recalled within 8 days. As of March 21, there have been 29 cases in 12 states.
- *Multistate outbreak of Seoul Virus Infections*. CDC assisted health officials in 15 states and Canada in responding to an outbreak caused by a rodent-borne hantavirus. The outbreak, which involved 17 cases of human disease, was linked to infected rats in multiple rat-breeding facilities.
• *Monkeypox in the Democratic Republic of the Congo (DRC).* As of March 30, there have been a total of 32 cases and 5 deaths, with active transmission still ongoing.

• *Yellow Fever in Brazil, Colombia, Peru, and Bolivia.* Yellow fever cases have been reported since December 2016, including 2900 suspect cases and a case fatality rate of 34% among confirmed cases. CDC is providing assistance with outbreak response, vaccination needs, and plans for fractional dosing, to extend limited stocks of vaccine.

Large outbreaks and potential limited vaccine availability could occur if the risk of yellow fever spread to non-endemic countries. Although the likelihood of spread to the United States is low (based primarily on modeling studies), CDC is working with FDA and Pasteur Sanofi to develop a contingency plan to ensure vaccine availability.

**Examples of Epi-AID Investigations**

Examples of Epi-Aid Investigations. Since December 2016, NCEZID EIS Officers have investigated

• Carbapenem-resistant *Enterobacteriaceae* (CRE) infections in Kentucky
• Infections due to bacteria-contaminated organ preservation fluid in Iowa
• Zoonotic spread of leptospirosis from dogs to people in Arizona
• Increased numbers of laboratory reports of Lyme disease in Arkansas
• Invasive group A *Streptococcus* infection among homeless people in Alaska
• Possible cases of infection with *Candida auris* in healthcare facilities in New York and in Panama

**Containment of *C. auris*: Getting Ahead of an Emerging Outbreak Caused by Drug-Resistant Yeast**

*Candida auris*, which is highly transmissible from person to person and highly drug resistant, is the cause of an increasing number of healthcare-associated infections among hospitalized patients. CDC is working with state and local health departments and healthcare facilities to ensure rapid detection and containment of *C. auris* outbreaks; 93 cases have been reported and investigated since last fall. Investigators have identified potential epidemiologic links between cases and used WGS to assess them. Outbreaks have been contained through improved infection control and treatment and by preventing transmission between facilities.

**Recent Publications**

• *Incidence and Trends of Infections with Pathogens Transmitted Commonly Through Food and the Effect of Increasing Use of CIDTs on Surveillance.* This FoodNet study found that use of CIDTs by clinical laboratories has been steadily increasing, is leading to lack of pathogen isolates for disease surveillance, and is complicating the interpretation of surveillance data (see pages 22-23).

• *Community Mitigation Guidelines to Prevent Pandemic Influenza – United States, 2017.* Released on April 21, the updated guidelines encourage state and local officials to plan and prepare for implementing non-pharmaceutical interventions (NPIs) early in a pandemic in community settings. The guidelines summarizes key lessons learned from the 2009 H1N1 pandemic response, describes new or updated pandemic planning and assessment tools, and reviews the latest scientific findings on the use of NPIs.
• **Notes from the Field: Powassan Virus Disease in an Infant - Connecticut, 2016.** In early November 2016, a previously healthy male infant aged 5 months developed fever, vomiting, and neurologic symptoms, including facial twitching and seizures. The parents reported that the infant had been bitten by a tick 2 weeks earlier, most likely carried into the home on a family member’s clothing. A cerebrospinal fluid sample obtained on hospital admission (4 days after illness onset) was positive for Powassan virus.

• Health Alert Network (HAN) Health Advisory: [CDC Recommendations for Diagnosing and Managing Shigella Strains with Possible Reduced Susceptibility to Ciprofloxacin.](https://www.cdc.gov/shigella/no-cipro.html) CDC is providing data on *Shigella* strains to the FDA and the Clinical Laboratory Standards Institute, which may decide to change the minimum inhibitory concentration (MIC) values for ciprofloxacin for treating shigellosis.

**Antibiotic Resistance (AR)**

- **Call for Innovative Proposals to Combat AR.** CDC has posted a broad agency announcement for proposals to address the following topics: diagnostic, sequencing, and metagenomics tools for AR detection and improved antibiotic use; international transmission, colonization, and prevention of illness caused by AR pathogens; domestic transmission, colonization, and prevention of illness caused by AR pathogens and/or *C. difficile*; microbiome disruption; AR pathogens and genes in water systems and the environment and their contribution to human illness; and medication safety and antibiotic stewardship. Awards will be announced in late summer or early fall.

- **AR Isolate Bank.** Established by FDA and CDC in 2016, the Bank provides panels of resistant bacteria to industrial and academic researchers developing new drugs and diagnostics. The Bank, which currently includes 495 isolates on 14 curated panels, has shipped more than 37,000 isolates to 358 customers.

- **AR investment Map.** The Map’s website provides an interactive app (along with state- and city-specific fact sheets) that describes how implementation of the [National Action Plan for Combating Antibiotic-Resistant Bacteria](https://www.cdc.gov/drugresistance/index.html) is transforming the way the nation is responding to AR.

**Healthcare-Associated Infections (HAIs)**

The [2016 HAI Progress Report](https://www.cdc.gov/hai/pdfs/2016/2016-HAI-Progress-Report.pdf), to be released soon, will provide state and national information on HAIs, including HAI trends in acute care hospitals, including rural critical-access hospitals and inpatient rehabilitation facilities, based on data reported to the [National Healthcare Safety Network](https://www.nhhsnet.gov/).

**Advanced Molecular Detection**

The AMD program is currently in its fourth year. Current focus areas include:

- Completing the PulseNet transition from PFGE to WGS in all state and large local laboratories
- Adapting HIV-TRACE software for use in state health departments to identify transmission clusters
- Developing ways to use WGS to generate data on enteric pathogens that cannot be obtained by CIDTs (e.g., strain-typing data)
- Developing and deploying sequence-based diagnostics for parasitic pathogens
- Implementing WGS for TB, influenza, Legionella, and viral hepatitis in some state and local laboratories
Quarantine

• 2017 marks the 50th anniversary of the CDC Quarantine program, which maintains 20 Quarantine Stations at airports, land borders, and seaports.

• CDC has updated U.S. quarantine regulations for the first time in decades. The new regulations, which become effective on March 21, 2017, clarify CDC’s authority to implement public health measures at U.S. ports of entry and domestic travel hubs and require that aircraft and maritime vessel manifest information to CDC within 24 hours, for more timely contact investigations of infectious disease. The new regulations improve CDC’s ability to protect the public from the introduction, transmission, and spread of communicable diseases while providing strong due process protections for individuals subject to public health orders.

Questions for Consideration

• Are the AMD training investments to support states on target?

• How should we be thinking about measuring surveillance trends in the era of CIDTs?

Discussion

• AMD
  – BSC members commented that
    o As WGS techniques come into use with a wide range of pathogens, workforce development needs will grow, both for laboratorians who generate WGS data and for epidemiologists who use WGS data for disease surveillance and decision-making
    o Regional investment in bioinformatics is a good idea. So are CSTE workshops, peer-to-peer trainings, and webinars from the Integrated Foodborne Disease Centers of Excellence. In the long run, however, all large public health jurisdictions should employ bioinformaticians.
    o Collaboration among agencies is essential
  – AMD is developing analysis tools that use WGS data to identify pathogen characteristics (i.e., genotype, serotype, pathotype, and resistance pattern). Subtyping will be achieved via multiple-locus variable-number tandem-repeat analysis (MLVA), which is currently used by PulseNet laboratories to further characterize outbreak-causing bacterial strains identified by PFGE. As part of these efforts, AMD is working with NCBI/NIH to develop databases of pathogen alleles.

• CIDTs
  – It is important to understand and address the impact of CIDTs and to be transparent about how surveillance data is interpreted and how disease trends are measured. CDC should continue to
    o Model and compare the sensitivity and specificity of CIDTs and culture-based tests
    o Think out-of-the-box about how to set new baselines and assess disease trends

• Antimicrobial Resistance
  – The BSC is interested in examining the potential benefit from re-invigorating its Antimicrobial Resistance Working Group, to review progress, consider new threats such as Candida auris, and help CDC develop a vision for the coming years. CDC would like to update the BSC on the
plans of the interagency WG on AR at the next BSC meeting as part of the discussion on potentially restarting the BSC WG on AR.

- The AR Isolate Bank is an example of an interagency collaboration to develop common AR tools and resources. HHS agencies are also seeking ways to better coordinate support for AR research. For example, NIAID can help CDC evaluate responses to its Call for Innovative Proposals to Combat AR.
- NIAID is supporting research to assess use of bacteriophage to treat drug-resistant bacterial infections. However, an appropriate animal model for testing this idea has not yet been identified.

- **Outbreaks and Diagnostics**
  - In regard to the multistate outbreak of Seoul virus infection
    - WGS data linked human infections with Seoul virus to infected pet rats and determined that the causative strain of Seoul virus was the same strain associated with pet-rat outbreaks in Europe.
    - During the 1980s, researchers determined that rodent-borne hantaviruses are widespread in the rat populations of U.S. cities. However, no cases of human disease were detected.
    - The human cases of Seoul virus infection detected in 2017 might be regarded as “sentinel events” indicating a large outbreak in a rat population.
  - CDC has posted information on methods for distinguishing *Candida auris* from non-pathogenic candida on MicrobeNET. Conventional laboratory techniques may lead to misidentification, making it difficult to control the spread of *C. auris* in healthcare settings.
  - Cases of Powassan infection may be under-reported, due to lack of testing. CDC might consider making diagnostics more widely available for Seoul virus (in urban areas) and for Powassan virus (in areas with tick vectors). For example, diagnostic tests for Powassan might be made available at Regional Centers of Excellence for Vector-Borne Diseases.
  - Smallpox (vaccinia) vaccines may provide cross-protection during outbreaks of monkeypox. Inger Damon, Director, NCEZID Division of High Consequence Pathogens and Pathology, reported that a CDC team in the DRC is participating in a vaccine trial involving a highly attenuated vaccinia virus that can be used safely in a population that is likely to include immunocompromised persons, due to parasitic infections and HIV.

One Health. NCEZID was commended for its focus on One-Health issues.

**Report from the Infectious Disease Laboratory Working Group (IDLWG)**

IDLWG co-chairs Jill Taylor, Director of the Wadsworth Center, New York State Department of Health, and Susan Sharp, Director of Laboratories, Kaiser Permanente Northwest, reported on the IDLWG teleconference on April 6, which covered the following topics:

**AMD**

- Observations
  - AMD has made tremendous progress, with special credit due to Greg Armstrong, Duncan MacCannell, and OID leaders
Much remains to be done. If insufficient resources are provided in the future, earlier progress could be wasted.

**Recommendations**
- CDC should consider expanding the group of AMD leaders
- Each AMD request for proposals (RFP) should include a statement describing public health goals and impact
- The initial focus on laboratory aspects of AMD was necessary but is not sufficient. It is imperative to engage epidemiologists who can use AMD data to improve public health practice.
- Advancement of AMD will also require
  - Input from state and local partners and representatives from clinical laboratories
  - Continued synergies with partners in academia and industry
  - New or revised IT policies that facilitate data-sharing by bioinformaticians, both at CDC and with state, local, and other national partners

**CIDTs**
- CIDTs are replacing culture-based methods. The transition is most advanced for enteric and viral respiratory pathogens but will soon involve other areas of testing.
- Widespread use of CIDTs is changing testing practices at both clinical and public health laboratories and is raising public health questions about which diagnostic methods are most accurate and how to calculate disease trends (see also pages 22–23).
- If the BSC requests it, IDLWG is willing to review options for addressing these challenges

**Discussion**
- CIDTs
  - Only a few states have laws requiring reflex cultures when CIDTs results are positive, so reflex testing is not likely to compensate for loss of isolates as CIDTs become more widespread.
  - Lack of isolates has affected gonorrhea and chlamydia surveillance for nearly 20 years, and CDC has found ways to compensate (e.g., the Gonococcal Isolate Surveillance Project). As more pathogens are detected by CIDTs, it is important to identify short-term solutions to enable calculation of disease trends and strain-typing to detect disease clusters.

- IDLWG’s Scope of Work
  - A year and a half ago, IDLWG recommended greater AMD focus on transferring techniques to state health laboratories. CDC responded by increasing AMD training resources provided via ELC.
  - Today, IDLWG might consider reviewing long-term and gap issues for both AMD and CIDT. To address CIDTs, IDLWG might
    - Recruit new members with expertise in regulatory issues (e.g., CMS and CLIAC) and diagnostic development (e.g., test manufacturers).
    - Reach a consensus framework in which clinical laboratories work with health departments to preserve cultures for public health purposes until metagenomic techniques come into use.
    - Identify and communicate a consistent way to use CIDT results in disease surveillance and trend analysis.
Diagnostic issues related to detection of enteric pathogens in stool are among the most difficult to address. It was suggested that IDLWG might work through issues related to CIDTs, metagenomics, and bioinformatics for a simpler specimen type (e.g., blood or sputum, or stool samples for *Salmonella*) and use the results as a model for other pathogens. This approach might benefit from input from experts in microbiome research.

**Vector-Borne Threats: The Path We’ve Walked and the Path Before Us**

NCEZID’s Division of Vector-Borne Diseases (DVBD) focuses on surveillance, prevention, and control of viral and bacterial diseases spread by mosquitoes, ticks, and fleas. DVBD—which operates reference laboratories for more than 100 pathogens—includes the Arboviral Diseases and Bacterial Disease Branches in Fort Collins, Colorado; a Rickettsial Zoonoses Branch in Atlanta; and a Dengue Branch in San Juan, Puerto Rico, which also addresses chikungunya and Zika.

Lyle Petersen, Director, DVBD, provided the following updates:

**Mosquito-borne Diseases: Accelerating Emergence and Increased Incidence in North America**

- **Zika**
  - Yellow fever virus and dengue virus came to Americas with infected slaves in the 1600s. West Nile virus arrived in 1999, Chikungunya in 2013, and Zika in 2015.
  - Before 2015, Zika outbreaks were reported in central Africa, Southeast Asia, and the Pacific Islands. Today, they are also occurring in many parts of the Americas, including Puerto Rico, the U.S. Virgin Islands, and Miami-Dade, Florida
  - As of May 2017, 61 countries and territories, including 50 countries and territories in the Americas, currently report active Zika virus transmission.

- **Chikungunya**
  - More than 2.3 million chikungunya infections have been reported throughout the Americas since its introduction in 2014
  - Serological studies conducted in the U.S. Virgin Islands and Puerto Rico after the first wave indicated incidences of about 25%
  - Since then, the number of cases of chikungunya has decreased each year, as population immunity has risen. This is likely to occur with Zika too.

- **Yellow Fever**
  - The urban cycle of yellow fever virus—like that of dengue, chikungunya, and Zika—involves person-mosquito-person transmission.
  - Starting in late 2015, increased virus circulation in areas of Africa and Latin America led to the largest yellow fever outbreaks since the 1980s, when thousands of people were infected in Nigeria. Recent outbreaks have occurred in
    - Angola and the Democratic Republic of the Congo (DRC) in 2015-2016. The outbreak in Angola (which spread to the DRC) included 4,306 suspect cases, 884 confirmed cases, and 376 deaths. The outbreak in the DRC included 2,987 suspected cases, 81 confirmed cases, and 16 deaths. The outbreak was controlled by vaccinating 30 million people.
Brazil, Colombia, Ecuador, Bolivia, beginning in December 2016. The outbreak in Brazil has thus far included 2,900 suspect cases and 681 confirmed cases. The case fatality among confirmed cases is 34%. Current transmission in Brazil is believed to be due to the sylvatic cycle or jungle cycle, in which the virus cycles between wild animals bitten by mosquito vectors, with humans as an incidental or dead-end host.

- Dengue. Dengue incidence in the Americas has steadily increased since 2000, carried by *Aedes aegypti* mosquitoes, which also spread chikungunya, yellow fever, and Zika. However, since the Zika outbreak, there have been fewer reported cases of dengue in Puerto Rico.

- West Nile. West Nile disease is now endemic in the United States, with 20,265 cases of neuro-invasive West Nile disease reported between its introduction in 1999 and 2015. For every case of neuro-invasive case of West Nile disease, there are 30 to 70 non-neuro-invasive cases and 150 to 300 mild or asymptomatic infections. The main vectors of West Nile virus are *Culex* mosquitoes.

Tickborne Diseases: New Diseases and Increased Geographical Range

- Many human pathogens identified since 1960 are associated with blacklegged ticks (*Ixodes scapularis*). The discovery of new tickborne diseases is likely due to improved diagnostics and clinical recognition, as well as expansion of tick habitats and increases in tick populations.

- The average number of Lyme disease cases approximately tripled between 1992 and 2014, and the number of reported cases of anaplasmosis, ehrlichiosis, and spotted fever group rickettsioses steadily increased between 2000 and 2014.

Challenges to Addressing Vector-Borne Diseases

- Technical capacities for vector control have eroded at all levels. The United States has a shrinking entomologic workforce, diminished capacity to conduct mosquito surveillance, and a patchwork of local vector control units that vary widely in resources and capacities. An assessment conducted by the National Association of County and City Health Officials (NACCHO) in 2016 found that of 190 local vector control units, 21% were “fully capable,” 9% were “competent,” and 68% “need improvement.”

- During the outbreak of West Nile disease in Dallas County in 2012, pesticide spraying was used only after the outbreak had passed its peak. Better mosquito surveillance likely would have led to earlier vector control measures, and many cases could have been prevented.

- There is no proven scalable measure to control
  - *Aedes aegypti* mosquitoes, which spread the viruses that cause dengue, yellow fever, chikungunya, and Zika infections
  - *Ixodes scapularis* ticks, which spread the viruses that cause Lyme disease, Powassan infections, anaplasmosis, babesiosis, and *Borrelia miyamotoi* infections

- Diagnostic tests for vector-borne diseases need improvement, and little is known about insecticide resistance, which may be widespread in some areas

A Coordinated Strategy for Vector-Borne Threats

- The proposed CDC strategy to address vector-borne diseases aims to
  - *Advance Innovation & Discovery*, by developing cutting-edge diagnostic tools for fast and accurate detection of vector-borne infections; identifying new and emerging vector-borne...
diseases and improving our understanding of existing threats; and supporting R&D to monitor and prevent insecticide resistance and foster new vector control technologies

- **Build Comprehensive Vector Programs**, by developing skilled workforce that can respond to the full variety of pathogens and pathogen vectors and robust state and local vector control programs.

- As part of this strategy, CDC has
  - Established four [Regional Centers of Excellence for Vector-Borne Diseases](#) to conduct research and development and work with partners to develop workforce training programs
  - Identified core competencies for a state or local vector-borne disease program, including
    - Laboratory ability to test for vector-borne disease infections in people, mosquitoes, and animals
    - Epidemiologic and medical capacity to investigate suspected or confirmed vector-borne disease outbreaks, contribute to national vector surveillance systems, and recognize symptoms of vector-borne diseases
    - Vector control capacity to conduct vector surveillance, test for insecticide resistance, and reduce mosquito populations

### Questions for Consideration

1. Do you have suggestions on DVBD’s overall plan to improve national resilience to respond to vector-borne diseases?
2. How can we best engage academia and other partners (including other centers at CDC) in this effort?
3. What is the optimal role of state and local health departments in this effort?

### Discussion

- **Workforce Capacity.** The need for information on disease vectors has increased, but the pool of experts in entomology and arboviral diseases has eroded. This issue requires special attention.

- **Zika**
  - Zika infection (like infection with chikungunya and West Nile) apparently confers immunity after one infection. This clinical observation is supported by animal studies in which a second infection with Zika produced little or no viremia.
  - Before the current outbreak, birth defects were not associated with Zika infections, perhaps because of inadequate disease surveillance, or because cross-reactions with dengue on serologic tests masked the association between Zika and birth defects. Another theory is that most women of child-bearing age who live in endemic areas are exposed to Zika during childhood.
  - It is difficult to predict what to expect as far as Zika cases in Texas and Florida this summer. Heat waves are a common denominator of past waves of certain mosquito-borne diseases, such as West Nile virus.

- **Vector Control**
  - Vector control is expensive and needs to be sustained. Some vector-control experts recommend passage of the “[Strengthening Mosquito Abatement for Safety and Health Act or the SMASH Act](#), which would support local vector control programs, provide vector-control training, and improve use of pesticides.
— CDC efforts include providing technical support to local vector control units and providing response support in places where local capacity is lacking
— State agricultural departments may be important vector control partners
— The Regional Centers of Excellence for Vector-Borne Diseases might provide guidance, as needed, to entomologists at local vector control units

**Consideration of a Joint Working Group on Vector-Borne Disease Issues**

The Board of Scientific Counselors of NCEH/ATSDR has proposed forming a working group to look at pesticide issues in response to vector control. Discussions have begun regarding formation of a broader joint working group on vector-borne diseases with the BSC/OID.

**Discussion**

- The OID BSC had discussed the potential for a WG on vector-borne diseases at earlier meetings and had proposed such a WG at its Dec 2016 BSC meeting. Now seems a good time to revisit that proposal and vote on its formation.
- A good way forward might involve bringing together subject matter experts from both Centers to draft a joint mission statement or charge.
- NIH, FDA, EPA, and BARDA should be represented
- A Joint Working Group could help advance implementation of CDC’s strategy to address vector-borne threats. It could engage state health departments, university researchers, and the Regional Centers of Excellence for Vector-Borne Diseases.
- The timing is right, in terms of public attention and public health need

A motion was passed unanimously to work with the NCEH/ATSDR BSC towards establishing a Joint Working Group on Vector-Borne Diseases

**Upcoming BSC/OID Meeting**

The BSC/OID will convene its next in-person meeting December 6-7, 2017.
APPENDIX: Meeting Participants

BSC Members

Ruth Berkelman  
Jack Bennett  
Nancy Bennett  
(by phone)  
Luciana Borio  
Kristy Bradley  
Mike Brady  
Sheldon Campbell  
Harry Chen  
Barbara Cole  
(by phone)  
Jeff Duchin  
Emily Erbelding  
Mary Hayden  
Tim Jones  
Salmaan Keshavjee  
Jim Le Duc  
Randall Levings  
(by representing USDA)  
Mike Loeffelholz  
Ruth Lynfield  
Jorge Mera  
(by representing CHAC)  
Andy Pavia  
Lee Riley  
Guillermo Ruiz-Palacios  
Susan Sharp  
Theresa Tam  
Jill Taylor  
Judy Wasserheit  
Debbie Yokoe

Partners and Public Visitors

Meredith Allen (Association of State and Territorial Health Officials)  
Jeff Engel (Council of State and Territorial Epidemiologists)  
Priscilla Golden (PLG Solutions LLC)  
Celia Hagan (Association of Public Health Laboratories)  
Lilly Kan (National Association of County and City Health Officials)  
Peter Kyriacopoulos (Association of Public Health Laboratories)  
Walt Orenstein (National Foundation for Infectious Diseases)  
Kathy Talkington (The Pew Charitable Trusts)

CDC Staff

Greg Armstrong  
Richard Batson  
Gail Bolan  
Chris Braden  
Evelyn Cater  
Bill Cibulas  
Allen Craig  
Kim Distel  
Aimee Geissler  
Tom Gomez  
Marta Gwinn  
Rebecca Hutchins  
Dan Jernigan  
Rima Khazzam  
Chris Langub  
Alexandra Levitt  
Gladys Lewellen  
Allison Maiuri  
Ellyn Marder  
Rebecca Martin  
Tonya Martin  
Jonathan Mermin  
Nancy Messonnier  
Steve Monroe  
Dale Morse  
Robin Moseley  
Atis Muehlenbachs  
Antonio Perkins  
Lyle Petersen  
Sam Posner  
Don Sharp  
Michael Shaw  
Sharon Slocumb
### CDC Staff (cont.)

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I hereby certify that to the best of my knowledge, the foregoing minutes of the proceedings of the meeting of the Board of Scientific Counselors, Office of Infectious Diseases, on May 3–4, 2017, are accurate and complete.

/S/
Ruth Berkelman, M.D.
Chair, BSC, OID

07/27/17
Date