MEETING OF THE BOARD OF SCIENTIFIC COUNSELORS, OFFICE OF INFECTIOUS DISEASES

Centers for Disease Control and Prevention
Tom Harkin Global Communications Center
Atlanta, Georgia

May 7–8, 2019

A one-and-a-half day, open public meeting of the Board of Scientific Counselors (BSC), Office of Infectious Diseases (OID),[1] was held on May 7–8, 2019, 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 and other members of the public (appendix).

The agenda included

- Updates from CDC Director Robert Redfield, the Center for Global Health (CGH), and the National Centers for Emerging and Zoonotic Infectious Diseases (NCEZID); HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP); and Immunization and Respiratory Diseases (NCIRD)
- Reports from the BSC/OID Acute Flaccid Myelitis (AFM) Task Force; the BSC/OID Food Safety Modernization Act Surveillance Working Group (FSMA SWG); and the Vector-borne Diseases (VBD) Workgroup of the BSC/OID and the BSC, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry (NCEH/ATSDR)
- Presentations and discussion on the following topics: infectious diseases associated with the opioid epidemic in the United States, One Health activities, the ongoing Ebola outbreak in the Democratic Republic of the Congo (DRC), and the CDC Surveillance Strategy and CDC Public Health Data Strategy

Following the NCEZID update on antimicrobial resistance, the BSC/OID approved a decision to send a letter supporting a Centers for Medicare and Medicaid Services (CMS) proposal to implement new antibiotic stewardship standards in acute care hospitals.[2]

Opening Remarks

BSC/OID Chair Ruth Lynfield, State Epidemiologist and Medical Director, Minnesota Department of Health, called the meeting to order and was joined in welcoming participants and facilitating introductions by Jay Butler, the new CDC Deputy Director for Infectious Diseases, and Sarah Wiley, the Designated Federal Official. Dr. Lynfield welcomed Dr. Butler, who is a former BSC member, and recognized the service of

- Andy Pavia, Guillermo Ruiz-Palacios, and Judy Wasserheit, who have rotated off the BSC
- Kristy Bradley, Mary Hayden, Jim Le Duc, Bonnie Maldonado, and Jill Taylor, who will complete their terms in September

[1] Name of BSC/OID reflects previous organizational unit. The Office of Infectious Diseases is now known as Deputy Director for Infectious Diseases.

[2] The BSC/OID letter, dated May 17, 2019, was sent to the Secretary of Health and Human Services.

Dr. Lynfield welcomed Jeanne Marrazzo and Jesse Goodman (former ex officio member from the Food and Drug Administration [FDA]) as new BSC members, and Hugo Lopez-Gatell as the new liaison representative from the Secretariat of Health of Mexico. No significant conflicts of interest were identified during the roll call.

NCHHSTP Update

Jonathan Mermin, NCHHSTP Director, provided updates on NCHHSTP activities and discussed two major issues: the infectious disease consequences of the opioid crisis and the initiative to end HIV in the United States.

NCHHSTP Updates

- **Leadership updates**
  - Carolyn Wester is the new Director, Division of Viral Hepatitis.
  - Michelle Van Handel is the new NCHHSTP Associate Director for Program and Performance Improvement.
- **President's Budget request.** The fiscal year (FY) 2020 President's Budget request for NCHHSTP is $1.318 billion. The Infectious Diseases and the Opioid Epidemic program includes a $53 million request for CDC, and the Initiative to End the HIV Epidemic in the United States includes a $140 million request for CDC.
- The **Division of HIV/AIDS Prevention** recently issued the following:
  - ***HIV Prevention Progress Report, 2019*****.** Eight out of 21 progress indicators have been met, and progress has been made in meeting 9 additional indicators.
  - **March 2019 *Vital Signs: Ending the HIV Epidemic. HIV Treatment Is Prevention*****.** In 2016, 80% of new HIV infections were transmitted from the nearly 40% of people with HIV who either did not know they were infected or had received a diagnosis but were not receiving HIV care.
- The **Division of Adolescent and School Health** continues to advance school-based primary prevention to improve health outcomes. Updates include the following:
  - From 2014 to 2018, CDC-funded school districts reported
    - Increased implementation of quality sexual health education curricula in middle schools and high schools; increased student access to youth-friendly sexual health services; and an increased number of safe and supportive school environments
    - Declines in the percentage of students who initiated sexual activity, were currently sexually active, and had four or more sexual partners in their lifetime
  - A 2017 health disparities survey in 19 states and large urban school districts found that transgender students are more likely than cisgender students to report substance abuse, suicide risk, and being victims of violence.

- The **Division of Tuberculosis Elimination** reports a 1% decrease in U.S. cases of TB from 2017 to 2018, to 9,029 cases (*2018 State and City TB Report*, preliminary data). Updates include the following:
  - Whole genome sequencing (WGS) of all *Mycobacterium tuberculosis* isolates from newly diagnosed patients is now routinely completed within 6 days of receipt. The WGS data are used to
    - Visualize TB transmission networks, by integrating sequencing data with clinical and epidemiologic data
    - Alert TB programs when a mutation associated with rifampin resistance is detected
  - Medscape issued an expert video commentary for healthcare professionals to highlight CDC's 2018 updated recommendations on treatment of latent TB infections. The video features Philip LoBue, Director of the Division of Tuberculosis Elimination.
- The **Division of STD Prevention** reports that the United States is experiencing steep increases in STDs, including gonorrhea, primary and secondary syphilis, and chlamydia. Moreover, cases of congenital syphilis (CS) have increased 270% since 2012. Missed opportunities to prevent CS occur when pregnant women
  - Do not receive prenatal care or do not receive prenatal screening as part of prenatal care
  - Receive inadequate treatment following a positive initial screening test for syphilis
  - Initially test negative for syphilis but are infected later, with infection detected at delivery

Infectious Disease Consequences of the Opioid Crisis

Linkages between Infectious Diseases and Drug Use

- **Syphilis**
  - Drug use among heterosexuals with syphilis has more than doubled in recent years
    - Between 2013 and 2017, the rate of primary and secondary syphilis increased 73% (from 5.5 cases to 9.5 cases per 100,000 persons).
    - During the same period, drug use involving methamphetamine, injection drugs, or heroin more than doubled among heterosexual men and women with syphilis.
  - These data suggest that the epidemics of heterosexual syphilis transmission and drug use are intersecting.
- **Hepatitis A**
  - A Health Alert Network update issued in March 2019 described widespread U.S. outbreaks of hepatitis A among people who use drugs and people who experience homelessness. The update recommends that healthcare providers consider homelessness as an indication for routine 2-dose hepatitis A vaccination.
- **Hepatitis C**
  - Hepatitis C virus infection in the United States varies widely by state, with the highest rates found in the West, in Appalachia, and in states disproportionately affected by the opioid crisis.

Budgets and Planning

- The FY 2020 President's Budget request for the Infectious Diseases and the Opioid Epidemic program focuses on three goals: reducing new infections of viral hepatitis and HIV, reducing morbidity and mortality due to viral hepatitis and HIV, and reducing overdose deaths.
- To advance implementation of those goals, CDC is making investments in
  - Screening and linking people to treatment in high-impact settings such as substance use treatment centers, permissible syringe services programs (SSPs), and correctional facilities
  - Ensuring that evidence-based and comprehensive preventive services are provided to people who use drugs
  - Increasing active surveillance capacity to monitor infectious disease clusters and guide a faster and more targeted response
- The Office of Infectious Disease and HIV/AIDS Policy (OIDP) in the Office of the Assistant Secretary for Health, U.S. Department of Health and Human Services (HHS), is coordinating the development of national action plans addressing HIV/AIDS, viral hepatitis, and STDs. All three will address the intersection between infectious diseases and drug use.

Ending the HIV Epidemic

- Key findings about the use of pre-exposure prophylaxis (PrEP) were presented at the March 2019 National HIV Prevention Conference.
  - Between 2014 and 2017, the number of PrEP prescribers in the United States increased more than four-fold, from 9,143 to 40,027.
  - Fifty-four percent of persons with private health insurance who initiate the use of PrEP continue to use it for at least 1 year, with high adherence. Adherence and persistence rates were lower among Medicaid-insured users, particularly among African Americans.
- CDC's priority activities to end the HIV epidemic include
  - **Diagnose:** Bring HIV testing to everyone who needs it and diagnose infections as early as possible
  - **Treat:** Promote rapid comprehensive care and start treatment at the time of diagnosis
  - **Protect:** Protect people at risk with proven prevention interventions, including PrEP and SSPs
  - **Respond:** Accelerate deployment of effective cluster detection and response systems
  - **Workforce**: Support on-the-ground teams to help tailor and ensure effective implementation
- CDC uses surveillance data to target HIV resources to areas that need it most. More than 50% of new HIV diagnoses occur in 48 counties; Washington, DC; and San Juan, Puerto Rico. Seven states have a substantial rural disease burden.

Discussion

Congenital Syphilis

- The public health community should regard each case of CS as a sentinel occurrence. For each case, clinicians and public health officials need to ask this question: What did we not do that allowed this to happen? As with mother-to-child transmission of HIV, the public health community must figure out how to prevent congenital transmission of syphilis.

- Gail Bolan, Director, Division of STD Prevention, reported that CDC is working with health departments in seven states that experience 70% of CS cases. Priorities include linking case management and mother/child healthcare resources and implementing case reviews to identify missed opportunities for disease prevention. All activities must take into account the concerns of pregnant women who are homeless or incarcerated, or who avoid prenatal care because they fear that a positive result on a drug test could lead to removal of their children.
- An important message to healthcare providers is that new mothers should not leave the hospital until they know the results of testing for syphilis. However, for many clinicians, CS is "not on the radar screen." CDC is updating public health information on congenital syphilis and welcomes suggestions for reaching out to medical, academic, and community partners. Current partners include the March of Dimes and American Board of Obstetrics and Gynecology, which supports a CDC fellowship that offers training in prevention of STDs and other infectious diseases.

HIV Prevention and Safe Sex

- The term"safe sex" is no longer well defined, due to the evolution of antiretroviral therapies and the availability of PrEP. The most effective way to prevent the acquisition of HIV is to abstain from sex or adhere to HIV PrEP therapy. However, PrEP is not recommended for all persons at risk for HIV, and condom use remains important to prevent the transmission of HIV and STDs. HIV prevention also requires that most infected persons be virally suppressed.

STD Prevention and Screening

- Promotion of condom use is important in the prevention of chlamydia, syphilis, and other STDs.
- Because a significant proportion of STDs occur in people living with HIV, screening regularly for STDs in this population (e.g., at Ryan White programs) could be an effective way to reduce STDs. CDC is modeling this approach.
- As with HIV, it is necessary address co-conditions such as incarceration, substance abuse, and homelessness to reduce the incidence of STDs. STD screening might be improved by
    - Arranging once-a-year testing for HIV and STDs (like having an annual mammogram) for people with risk factors. This approach would end the need to take a sex history from each patient.
    - Implementing screening for STDs, as well as hepatitis C and HIV, at SSPs and correctional facilities
    - Making testing for gonorrhea and chlamydia easy and convenient (e.g., having patients take their own rectal swabs so that testing does not require a physician office visit)
    - Using electronic alerts to make clinicians aware that persons diagnosed with STDs require follow-up care (e.g., when a testing facility refers a patient to another clinic for treatment)
    - Exploring ways to ensure that patients who have gaps in insurance coverage receive STD screening and that those who test positive remain in care
    - Establishing a Ryan White–type program to address STDs and other infections of public health importance
- The Veterans Administration is using routine testing for hepatitis C, facilitated by the use of electronic reminders, to advance its plan to eliminate hepatitis C within its patient population. CDC is considering a similar approach for eliminating latent TB infections.

Workforce Issues

- Workforce issues pose a major obstacle to HIV care, and addressing those issues is one of CDC's five priority activities for ending the HIV epidemic.
- One area of concern is that the number of African American men entering medical school has declined and the healthcare workforce has become less representative of the U.S. population.

Synergies

- CDC divisions are developing joint approaches to addressing HIV, viral hepatitis, and STDs that are synergistic and mutually beneficial.
- Tammy Beckham, Director of OIDP and Acting Director of the HHS National Vaccine Program Office, reported that national action plans to address HIV, viral hepatitis, and STDs will identify ways that states can leverage opportunities and best practices that apply to all three diseases.

Upcoming Publications

- CDC is drafting guidelines for hepatitis C screening in adults, including pregnant women. Questions remain about treatment for hepatitis C in pregnant women and children, and the National Institutes of Health (NIH) may decide to fund treatment research to fill these knowledge gaps.
- The *Journal of Infectious Diseases* and CDC are inviting submissions for a thematic supplement titled *Infectious Diseases and Injection Drug Use: Public Health Burden and Response*.

Focused Discussion: Increases in Bacterial and Fungal Infections Associated with the Opioid Crisis

Isaac See, Epidemiology Research and Innovations Branch, Division of Healthcare Quality Promotion (DHQP), NCEZID, reviewed recent increases in bacterial and fungal infections and syndromes in persons who inject drugs (PWID) and discussed the role of infectious disease experts in the public health community in advancing the response to the opioid crisis.

Background

- Bacterial/fungal infection syndromes associated with injection drug use (IDU) include but are not limited to endocarditis and epidural abscesses. CDC surveillance data show that infections caused by *Staphylococcus aureus*, *Candida* spp. and group A *Streptococcus* (GAS) are increasingly associated with IDU. Treatment for infective endocarditis in drug users raises special issues for clinicians.[3]
- Most harm reduction efforts for PWID focus on reducing the risk of transmission of bloodborne viruses like HIV and hepatitis C by distributing sterile equipment (e.g., needles). However, most bacterial and fungal complications related to IDU occur when pathogens on the skin are introduced during injection, and some PWID may be at increased risk due to poor skin hygiene.

[3] See the following: The Treatment Gap: Injecting Drugs Can Ruin a Heart. How Many Second Chances Should a User Get?; Rising Rates of Injection Drug Use Associated Infective Endocarditis in Virginia with Missed Opportunities for Addiction Treatment Referral: A Retrospective Cohort Study; and Hospitalizations for Endocarditis and Associated Health Care Costs Among Persons with Diagnosed Drug Dependence — North Carolina, 2010–2015.

- Potential strategies for preventing bacterial and fungal infections in PWID include
  - Primary prevention of drug use
  - Secondary prevention of drug use, through medication-assisted treatment (MAT), which combines behavioral therapy and medications to treat substance use disorders
  - Promotion of safer injection practices. This approach is largely accepted but has not been rigorously studied.
  - Secondary prevention activities to prevent new infections or recurrence of past infections
  - Improved wound management and other activities to limit transmission of pathogens of concern among PWID

Surveillance Findings

- A surveillance study of invasive methicillin-resistant *S. aureus* (MRSA) infections among PWID conducted at six U.S. sites found that
  - PWID are 16 times more likely to develop invasive MRSA infections than people who do not inject drugs.
  - The proportion of invasive MRSA infections associated with IDU increased from 4.1% to 9.2% between 2005 and 2016.
  - During 2017, 29% of invasive MRSA cases in Maryland and 25% in New York State were associated with IDU.
  - The study concluded that reducing the risk of infection requires prevention of drug misuse and IDU, education about safer injection practices, and information for the medical community about wound care and early signs of MRSA.
- Findings from other surveillance studies conducted by CDC and partners include the following:
  - Rates of IDU-associated invasive *S. aureus* in Monroe County, New York, have risen in people aged 18 to 49 years, and 45% of those infections involve endocarditis.[4]
  - Maryland and Oregon reported significant increases in the proportion of candidemia cases related to IDU between 2014 and 2017.
  - An increased percentage of GAS infections associated with IDU was documented in a review of hospital charts in 10 states. Cumulatively, the percentage rose from 4.6% in 2010 to 14% in 2017.
  - A 12-fold increase in hospital admissions for infective endocarditis associated with substance abuse disorder was reported in North Carolina between 2007 and 2017.
  - An increased incidence of infective endocarditis associated with substance use disorder in persons 19 to 44 years of age was documented in a review of patient data in the Premier Healthcare Database.

[4] Felsen CB, et al. Increasing Incidence of Invasive Methicillin-Resistant and Methicillin-Sensitive *S. aureus* Infections Among Persons Who Inject Drugs, 2014–2017. IDWeek 2018. Abstract #1211.

Prevention Research

- Recent Epi-Aid investigations involved
  - GAS among homeless PWID in New Mexico (2018)
  - *Candida* bloodstream infections and invasive GAS infections associated with IDU in Colorado (2017–2018)
  - Multiple bacterial and fungal infections among PWID in New York State (2018)
- The investigation in New York State involved 112 PWID over 3 months presenting with bacterial or fungal infections.
  - Eighty-two percent had skin and soft tissue infections, and 16% had infective endocarditis. *S. aureus* accounted for 79% of these infections.
  - Eighty percent of the patients were admitted to the hospital, and 4% died during the hospital stay. Eighteen percent were hospitalized for 30 days or more, and 29% left against medical advice.
- The investigators in New York State observed that
  - Provision of MAT was uncommon. At the index visit, only 40% of patients with bacterial or fungal infections were offered MAT. Of the 75% of patients who reported a prior emergency room visit or hospitalization, only 13% were offered MAT. Offers of hepatitis vaccination or naloxone were also uncommon.
  - Barriers to the provision of MAT, naloxone, and/or vaccination included
    - The idea that provision of these services was not part of the hospital's culture
    - Uncertainty about who should provide services
    - Lack of training and/or understanding about drug use disorders
    - Lack of reimbursement for services to treat drug use disorders
    - A shortage of outpatient MAT services
- Lessons learned about behaviors that predispose PWID to infection included the following:
  - Poor skin hygiene can increase the risk of having bacteria or fungi on the skin enter the bloodstream during injection. PWID may not sufficiently clean the injection site at the time of injection, and/or they may have unstable housing and may not bathe for extended periods.
  - PWID may use contaminated equipment. They may re-use supplies; use non-sterile equipment, such as cotton balls; and/or contaminate their equipment during preparations for injection (e.g., by licking needles or using non-sterile liquids like tap water).
  - Although PWID tend to avoid the healthcare system—perhaps because of stigma or fear of drug withdrawal—many are treated in emergency rooms, for infections, overdoses, mental health-related arrests, or physical injuries. Some attend SSPs, and many are aware of the need for clean needles but anecdotally they know little about prevention of bacterial infections that can cause skin abscesses and endocarditis.
- Interviews conducted at SSPs suggest that
  - Educational information on bacterial and fungal infections is needed.
  - Provision of wound care is variable.
  - Facilities to assist with hygiene are not usually available.

- Some PWID likely developed infections as a result of IV lines (e.g., peripherally inserted central catheter [PICC] lines) inserted for home use at a previous hospitalization for a different infection.

Public Health Communications

- The CDC website provides information about infections and IDU for clinicians and the public. Key messages include the following:
  - *Prevent bacterial and fungal infections in patients who inject drugs*
  - *Injecting drugs can give you deadly infections*

Current Activities to Support the Response to the National Opioid Epidemic

- CDC efforts include
  - Characterizing the relationship between infectious diseases and IDU by analyzing
    - Administrative and electronic medical record (EMR) data from the Premier Healthcare Database, to develop national burden estimates for bacterial and fungal complications among PWID
    - Sepsis burden data, in partnership with the Harvard Prevention Epicenter, to compare health outcomes among PWID and people who do not inject drugs
    - Data collected during Epi-Aid investigations, to identify barriers to MAT initiation when patients are treated for bacterial or fungal infections, to describe health outcomes, and to evaluate opportunities to link PWID to treatment
  - Collaborating with hospitals and healthcare systems to improve care for PWID with bacterial and fungal infections, by providing MAT and linkage to care, screening for viral hepatitis and HIV, improving patient education, and strengthening hospital infection control[5]
  - Participating in a discussion at the annual conference of the Council of State and Territorial Epidemiologists (CSTE) about the role of public health departments in addressing bacterial and fungal infections in PWID
  - Working with professional and clinical organizations—including the Infectious Diseases Society of America—to identify and address issues related to treatment of infective endocarditis and other infections associated with drug use
  - Working with the National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance Project (NEISS-CADES) to expand national surveillance for nonfatal overdoses to include information on infections associated with drug misuse

Misuse of Drugs Used in MAT

- Buprenorphine—including formulations combined with naloxone—is the drug most often used in MAT, usually in pill form or as a sublingual tablet. However, data from emergency room visits indicate that buprenorphine is also the third most common prescription opioid associated with acute complications due to drug misuse.

[5] The collaboration is coordinated by the CDC Opioid Response Coordinating Unit and supported by the Safety and Healthcare Epidemiology Prevention Research Development (SHEPheRD) program and a cooperative agreement with the Emerging Infections Program and the Healthcare-Associated Infections Community Interface.

- Of emergency room visits involving nonmedical use of buprenorphine, over 20% involve infectious complications from injection of crushed buprenorphine pills or tablets.

Future Activities to Support the Response to the National Opioid Epidemic

- Additional CDC activities may focus on
  - Characterizing the epidemiology of bacterial and fungal infections among PWID by expanding surveillance conducted by the Emerging Infections Program (EIP) and the Healthcare-Associated Infections Community Interface to include
    - Data on non-invasive infections of skin and soft tissue
    - Management and outcome data on invasive *S. aureus* infections and candidemia
  - Developing national estimates and a tracking system for infective endocarditis, using EMRs
  - Developing and evaluating public health interventions to reduce bacterial and fungal infections among PWID
  - Evaluating the clinical and economic impact of treating IDU-related bacterial and fungal infections
  - Developing guidance on MAT and overdose prevention

Discussion

Surveillance for Invasive Bacterial and Fungal Infections and Syndromes among PWID

- Systematic surveillance is required to evaluate the apparent rise in complications due to bacterial and fungal infections, including epidural abscesses caused by gram-negative bacteremia. BSC/OID members suggested expanded roles for
  - EIP, which provided data for a six-site study of invasive MRSA infections among PWID
  - The National Healthcare Safety Network (NHSN)
  - Software vendors, who could modify EMR software to improve data collection about cases of endocarditis
  - The Antibiotic Resistance Laboratory Network, if causative strains exhibit new patterns of resistance
- It is difficult to determine how many people inject drugs and how many cases of endocarditis or candidemia are related to drug use. Denise Cardo, Director, DHQP, noted that
  - Evaluation of studies on IDU-related infections requires an understanding of data sources and their limitations. For example, administrative data may be incorrect or incomplete compared with data available in electronic health records.
  - It is important to link epidemiologic data and isolate information as done in the EIP network.
- CDC might consider
  - Using surveillance data to determine whether rates of endocarditis—which is most frequent in adults—are rising in children or teens who inject drugs
  - Exploring possibilities for adding an EMR code for IDU or adding multiple EMR codes for different modes of drug administration by people with substance use disorders

- Gathering data on antibiotic prescribing practices by dentists in parts of the country with high rates of opioid use

Prevention of IDU-Related Infections

- It is important to address gaps in our knowledge of the routes of transmission of IDU-associated infections. Use of non-sterile needles and contamination of drugs during drug preparation—as well as the presence of bacteria that colonize the skin—may be important factors in pathogen transmission.
- Using WGS to determine whether bacteria on a patient's skin is the source of the bacterial strain causing the patient's endocarditis would require access to patient isolates and associated epidemiologic data.
- Assuming that bacteria on the skin is an important source of contamination, interventional trials could be used to determine whether
  - Swabbing the skin with chlorhexidine before injection can reduce invasive infections and endocarditis.
  - Using disinfectants on a regular basis to decolonize the skin of PWID reduces their long-term risk of IDU-related infections. It will also be important to determine how this approach may affect the skin microbiome.
- In regard to providing public health education,
  - Peer counselors at SSPs might be effective in explaining the infection risk of injection practices such as sharing non-sterile cotton balls.
  - Advancing patient education and improving infection control is the goal of the CDC collaboration with hospitals and healthcare systems cited above.

Opioid Prescribing Practices

- The *CDC Guideline for Prescribing Opioids for Chronic Pain* aims to ensure that patients have access to safer, more effective chronic pain treatment while reducing the number of people who misuse or overdose from these drugs.
- Dan Budnitz, Director, Medication Safety Program, DHQP, reported that the National Center for Injury Prevention and Control (NCIPC) is continuing to investigate changes in drug use due to changes in prescription practices (e.g., moving from prescription drug use to illicit drug use). Dr. See noted that NCIPC has posted an advisory about the potential for misapplication of the *Guideline for Prescribing Opioids for Chronic Pain*.

Hospital Management Issues

- The clinical and economic impact of providing care for invasive bacterial and fungal infections among PWID requires assessment. Increasing hospitalizations of PWID for endocarditis and other serious infections is a huge drain on the hospital workforce, with some hospitals better equipped than others to serve this population.

NCIRD Update

Nancy Messonnier, Director, NCIRD, provided updates and discussed current goals and priorities.

NCIRD Updates

- **Leadership updates**
  - Kristin Pope is the Acting Director, NCIRD, while Dr. Messonnier is on detail as Acting Director, Center for Preparedness and Response.
  - Amanda Cohn is the Acting Chief Medical Officer for NCIRD and is leading the response to the ongoing outbreaks of measles.
  - NCIRD is actively recruiting for the position of Deputy Director, Influenza Division.
- **Advisory Committee on Immunization Practices (ACIP)**
  - In February, ACIP issued new recommendations on Japanese encephalitis vaccine and anthrax vaccine.
  - Issues to be addressed at the June ACIP meeting include
    - Expanded age determination for the administration of human papillomavirus (HPV) vaccine
    - Routine administration of pneumococcal conjugate vaccine (PCV13) to all immunocompetent adults aged ≥65 years
    - Hepatitis A catch-up vaccination for persons aged 1 year and older with HIV
    - Serogroup B meningococcal vaccine booster doses for persons at increased risk and during outbreaks
  - ACIP has a new website that is mobile accessible.
- **Program updates**
  - **Influenza**
    - Influenza activity continues to decrease as the 2018–2019 flu season winds down. Severity indicators (influenza-like illness and hospitalization rates) are consistent with a season of moderate severity.
    - H3N2 viruses were responsible for the season's second wave of influenza activity. Two out of the three H3N2 viruses in circulation (3C.2a and 3C.2a1) were similar to 2018–2019 cell-grown reference viruses, but a third virus (3C.3a) was not. The World Health Organization (WHO) and the FDA Vaccines and Related Biological Products Advisory Committee have selected the A/Kansas/14/2017 (H3N2)–like virus strain (which is a 3C.3a strain) for inclusion in next season's flu vaccine to better correspond to currently circulating viruses.
    - An HHS pandemic influenza exercise called Crimson Contagion involved tabletop exercises with a federal focus (in January) and a state/local focus (in April). Two additional events are scheduled: an interagency seminar on May 14–15 and a functional exercise on August 13–16.
    - CDC has posted the MedFinder website to help providers and the public locate pharmacies with supplies of influenza antiviral drugs, which work best when administered within 48 hours of symptom onset. MedFinder was developed in collaboration with Boston Children's Hospital, HealthMap, and Harvard Medical School.

- **Legionnaires' disease (LD)**
  - CSTE plans to issue a revised Position Statement this summer that will clarify clinical definitions for LD and allow cases that meet clinical criteria and are diagnosed by PCR to count as confirmed (rather than suspect) cases.
  - LD experts at CDC are
    - Establishing Water Matters, a collaborative effort to promote the prevention of disease caused by opportunistic pathogens in engineered water systems
    - Participating in a CSTE-led effort to develop a toolkit for risk communications about LD and to identify best practices for LD surveillance, cluster identification, and outbreak response
    - Drafting a 2-page white paper for hotels on the importance of water management
    - Preparing a talk on *Engineering a Plan for Legionnaires' Disease Prevention in Long-Term Care Settings* to be presented at the annual meeting of The Society for Healthcare Epidemiology of America (SHEA)
- **Immunization coverage**
  - Updated and redesigned Childhood and Adult Immunization Schedules were issued in February 2019.
  - Ongoing efforts to improve the efficiency of data collection for the 2019 National Immunization Survey (NIS) include
    - Increasing the number of calls to parents of young children
    - Evaluating the completeness of population and vaccination data obtained from healthcare providers and Immunization Information Systems
    - Augmenting data from vaccine coverage surveys with health system data, including insurance claims data and data from pharmacies

- **Update on measles in the United States**
  - The United States currently has the highest annual number of measles cases since measles was eliminated in 2000 (704 cases in 23 states). The rise is due to
    - A global increase in measles. WHO data indicate that cases of measles rose by 300% during the first 3 months of 2019, as compared with the same period in 2018.
    - Imported cases of measles. Outbreaks in New York City, Upstate New York, and Washington State began with imported cases.
    - Pockets of unvaccinated communities in the United States. Six of 13 outbreaks were associated with under-immunized, close-knit U.S. communities.
  - To provide state and local partners with technical support, CDC has
    - Deployed Epi-Aid teams to Washington State and New York State
    - Posted measles outbreak toolkits for state and local health departments and for healthcare providers
    - Conducted an increased number of air contact investigations for measles and scheduled a call with state immunization programs later in May

- Other communication activities include
  - Deploying health communicators to New York State to help identify opportunities for community engagement, taking into account the profiles and concerns of affected communities
  - Answering more than 500 media inquiries, participating in more than 25 media interviews, and posting travel notices and alerts for 26 countries
  - Providing information to travel clinicians and travelers through GovDelivery
  - Reviewing guidance on measles prepared by the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, the Federal Bureau of Prisons, and the U.S. Department of Defense (DoD)
- Ongoing work on measles includes
  - Hosting a stakeholder engagement meeting to discuss potential travel restrictions for preventing the spread of measles
  - Holding a Clinician Outreach and Communication Activity (COCA) call for providers
  - Recording a video for clinicians describing the clinical presentation of measles
  - Developing guidance to prevent the spread of measles in hospital settings; protect infants traveling to domestic outbreak settings; inform healthcare providers and the public about adult vaccination against measles; and facilitate outreach to vulnerable groups

- **Vaccine hesitancy**
  - CDC has developed a three-part strategy to address key drivers of low vaccination:
    - **Reducing barriers to vaccine access.** Barriers may include lack of medical insurance and lack of access to vaccines in rural areas.
    - **Finding and focusing on communities with low rates of vaccination.** CDC is working with the states to determine the reasons for vaccine hesitancy in these communities.
    - **Countering misinformation.** Strategies include
      - Working with Facebook to improve access to vaccine information from CDC, as part of a larger social media strategy to expand outreach to parents
      - Revising the *Parents' Guide to Childhood Immunizations*

NCIRD Goals and Priorities

- NCIRD goals include the following:
  - Strengthen the domestic immunization program
  - Accelerate development and introduction of new vaccines
  - Innovate through improved use of technology and systems
  - Protect Americans from influenza threats
  - Improve prevention, detection, and response of respiratory diseases
  - Nourish a culture that makes NCIRD the Healthiest Organization

- Dr. Messonnier highlighted priority activities to advance the second and sixth goals:
  - Accelerate development and introduction of new vaccines by
    - Implementing and evaluating the new zoster vaccine
    - Developing the evidence base to support decision-making about priority vaccines under development
    - Evaluating new platforms for the study of vaccines against viral and bacterial diseases
    - Maximizing the impact of current and future vaccines for pertussis control
  - Nourish a culture that makes NCIRD the Healthiest Organization by
    - Implementing a comprehensive strategy that develops and strengthens the NCIRD workforce
    - Ensuring capacity for continuous evaluation and improvement of operations
    - Improving internal communications throughout NCIRD
    - Cultivating an open, inclusive, and diverse work environment

What's Coming Up

- Upcoming events include a Public Health Grand Rounds on Legionnaires' disease (May 21), an ACIP meeting (June 26–27), and the releases of *Vital Signs* issues on acute flaccid myelitis (July 9) and maternal vaccination (October 12).
- Data on vaccination coverage during the 2018–2019 flu season will be issued on September 26, with additional vaccine data provided by the National Immunization Survey-Teen on August 22 and by NIS-Child and NIS-School on October 17.

In conclusion, Dr. Messonnier mentioned that Influenza Division Director Dan Jernigan is a finalist for the 2019 Samuel J. Heyman Service to America Medal. She also noted that NCIRD will have eight new incoming Epidemic Intelligence Service (EIS) officers in 2019.

Discussion

Measles Outbreak

- The public health task during a measles outbreak is two-fold: to track individual cases of measles (which is labor intensive, even for a single case) and to blanket affected communities with information on disease prevention. Each measles outbreak represents a program failure, because all measles outbreaks are preventable by vaccination.
- The societal cost of responding to outbreaks of measles is difficult to quantify. Ideally, cost estimates should include not only public health and medical costs but also the costs of social disruption and opportunity costs.
- Every measles case in the United States can be traced to an importation, usually associated with a U.S. traveler. Current outbreaks (e.g., in New York City and Rockland County, New York) are due to multiple importations occurring at the same time in communities with high numbers of babies and small children and low rates of vaccination.
- Some U.S. travelers have been infected with measles in countries like France where travelers do not expect to contract infectious diseases.

- Most adults born in the 1950s and 1960s are protected against measles due to natural exposures, and most adults vaccinated after 1967, when measles vaccine became available, are also protected. However, adults in high-risk settings (e.g., in communities where outbreaks are occurring) should consult with their healthcare providers about re-vaccination.
- CDC continues to focus on high-risk situations involving communities with significant numbers of unvaccinated people and to recommend vaccination for people in those communities, as well as for people who travel overseas. CDC does not recommend vaccination for people who are not in a high-risk group (i.e., the "worried well").
- Most state laboratories use PCR testing to identify active infections with measles virus because serology tests cannot distinguish between an infected person and a person who has been vaccinated. The development of a rapid point-of-care diagnostic test for active measles infections would be very useful.

Vaccine Hesitancy

- Dr. Messonnier stated that countering vaccine hesitancy requires a "hyper-local" public health focus—a "national campaign implemented locally."
- Outbreak stories can have significant impact and help counteract misinformation, especially when told by community leaders, faith leaders, or mothers of ill children.
- Local public health officials must learn how to empower community leaders to take the lead in disseminating information about vaccines. Each affected community is different and may require different forms of engagement.

Topics for Future Discussion

BSC/OID members suggested these topics for discussion at future BSC meetings:

- Maintaining the EIS program, whose class size has decreased
- Development of improved vaccines against pertussis
- Comparison of the efficacy of cell-based vaccines versus recombinant

Updates on Acute Flaccid Myelitis and on the AFM Task Force

AFM Update

Janell Routh, Medical Officer, Division of Viral Diseases, NCIRD, provided an update on current AFM epidemiology and reviewed CDC's ongoing AFM activities.

AFM Epidemiology

Of 385 AFM cases reported to CDC between January 2018 and April 2019, 237 were classified as confirmed (230 cases in 2018 and 7 in 2019) and 28 were classified as probable (26 cases in 2018 and 2 in 2019). The 230 confirmed cases reported in 2018 were detected in 41 states in all regions of the continental United States; 8 states reported 10 or more confirmed cases (California, Colorado, Minnesota, New Jersey, Ohio, Pennsylvania, Texas, and Washington). Case numbers increased in summer and fall, with most cases occurring in August, September, and October.

To determine whether a particular virus is associated with AFM, the CDC AFM laboratory has tested patient specimens to look for viruses in cerebrospinal fluid (CSF), respiratory samples, and stool. Using specimens collected in 2018 and 2019, they found that

- Only two CSF samples (3%) tested positive:
  - One tested positive for enterovirus-D68 (EV-D68).
  - One tested positive for enterovirus-A71 (EV-A71).
- Fifty-five respiratory samples (45%) tested positive, consistent with other peak years for AFM:
  - 25% of specimens were positive for EV-D68.
  - 20% of specimens were positive for other EV/RV.
- Thirteen stool samples (13%) tested positive for a mix of enteroviruses and rhinoviruses (RV) and parechoviruses. All samples tested negative for polio.
- 2019 testing has thus far yielded only one positive respiratory sample (EV/RV untyped).

Epidemiologic Studies

CDC's efforts to advance understanding of the clinical presentation and outcomes of patients with AFM are informed by the AFM Task Force's research agenda (see below). They include

- Using clinical information abstracted from 2018 AFM patient medical records to
  - Describe clinical phenotypes of confirmed cases
  - Compare clinical characteristics between cases and non-cases
  - Compare clinical data between peak and non-peak years
- Implementing long-term follow-up of AFM cases by conducting a functional assessment of confirmed and probable AFM cases at 2, 6, and 12 months post–illness onset, using a validated questionnaire
- Further exploring the temporal and geographic association between AFM cases and enteroviruses by
  - Modeling AFM case data, geographic data, and EV testing data in partnership with a commercial laboratory and AFM Task Force members
  - Conducting enhanced AFM surveillance alongside active, prospective surveillance for gastroenteritis and respiratory illness in seven pediatric academic centers (in Washington State, Texas, Missouri, Ohio, Tennessee, Pennsylvania, and New York). These studies will help define the baseline incidence of AFM and facilitate an evaluation of a possible relationship between the monthly and seasonal incidence of AFM and viral circulation patterns.
- Describing the natural history of AFM and determining risk factors for illness by
  - Participating in an ongoing NIH natural history study to improve understanding of the etiology of AFM and the clinical presentations and outcomes of patients with AFM
  - Conducting a case-series investigation to identify potential exposures common to AFM patients
  - Interviewing confirmed 2018 AFM case-patients and collecting data on multiple variables, including medical and illness exposure history, care-seeking behaviors for preceding illness and for limb weakness, trauma, intramuscular injections, vector exposure, and genetic and environmental factors

Laboratory Activities

The CDC AFM laboratory is

- Developing assays that may provide indirect evidence of viral infection. This entails
  - Working with academic partners to investigate the presence of EV-specific antibodies in CSF, which would provide additional support for a role for EV in causing AFM
  - Developing monoclonal antibodies for use in IgM and IgA assays that can detect serum and intrathecal antibodies against EV-D68
  - Investigating the immunophenotype of peripheral blood cells in AFM patients to understand what might stimulate these immune cells to respond
  - Characterizing cytokine and chemokine patterns in the CSF and serum of confirmed AFM patients, as potential biomarkers
- Exploring the association between EV-D68 and AFM. This entails
  - Gaining insight into the evolution of EV-D68, by producing complete genomic sequences for viruses detected in AFM patient specimens and generating infectious clones that can be used in neuronal and respiratory cell models to study EV-D68 infection and cytopathology
  - Further investigating the high seroprevalence of EV-D68 found in all age groups prior to a 2014 EV-D68 outbreak in Kansas City by conducting a similar study that uses nationally representative patient samples
  - Developing an assay to investigate EV-D68 antibody-dependent disease enhancement

Communication Activities

Outreach efforts include

- Preparing a *Vital Signs* issue for release in July that will
  - Review information about AFM cases reported in 2018, with information about the timing of care and about reporting lags
  - Include a factsheet for healthcare workers with key messages about diagnosis and reporting
  - Emphasize the distinction between data used for patient diagnosis and for public health surveillance. AFM diagnosis should be
    - As rapid as possible, to facilitate medical management
    - Independent of the CDC case classification (as confirmed, probable, or non-case), which is used for surveillance purposes, to evaluate disease burden and illness trends over time
- Outreach to first-line pediatric responders and AFM parent groups. Aims include
  - Connecting with primary care clinicians and urgent care and emergency provider organizations to provide AFM education and to advance AFM research on healthcare providers' knowledge, attitudes, and behaviors
  - Communicating with AFM parent groups through regular question-and-answer sessions and in-depth focus group discussions

Dr. Routh **concluded that**

- AFM cases continue to occur in seasonal, every-other-year outbreaks.

- Growing evidence suggests that enteroviruses, including EV-D68, are leading etiologic candidates; however, other causes and mechanisms for disease should be explored.
- Robust disease surveillance and laboratory investigations will improve our understanding of the epidemiology and etiology of AFM outbreaks.
- Provider outreach (e.g., via *Vital Signs*) can improve case recognition and reporting and encourage early specimen collection, facilitating improved pathogen detection.

AFM Task Force Update

Ruth Lynfield, BSC/OID chair and AFM Task Force co-chair, reviewed the charge and membership of the AFM Task Force, which includes 4 BSC members and 13 AFM clinical and research experts. The Task Force is charged with presenting findings, observations, and outcomes to the BSC and the CDC Deputy Director for Infectious Diseases, for discussion, deliberation, and decision in these areas:

- **AFM etiologies and pathogenesis.** Task Force discussions focus on
  - Evaluating current understanding of AFM and its pathogenic mechanisms
  - Reviewing data and developing hypotheses about possible or likely AFM etiologies and pathogenesis
  - Proposing new studies, study designs, laboratory techniques, assays, and other activities to address specific hypotheses about AFM etiologies and pathogenesis
  - Developing and prioritizing findings and observations to facilitate development of BSC recommendations for areas of further study or investigation
- **Clinical treatment of AFM.** Task Force discussions focus on
  - Building on existing information about clinical practices by seeking information on clinical experience with the treatment of AFM
  - Identifying research gaps in the diagnosis and treatment of AFM
  - Developing potential findings and observations on patient management

Task Force Activities

Since the December 2018 BSC/OID meeting, Task Force activities have included

- Monthly conference calls held between January and March to discuss
  - Collaborations to strengthen infrastructure for case identification and facilitate research evaluations
  - Immunology research to determine whether AFM pathology is due to the direct effect of a virus or to damage caused by an immune response to the virus
  - Host genetics and AFM
- An in-person meeting in April to
  - Review ongoing research projects and other activities
  - Prioritize virology and immunology research questions
  - Define key knowledge gaps in genetics and treatment, including rehabilitation
  - Update the Task Force about the NIH AFM natural history study

Sequence Analysis of EV-D68 Strains

EV-D68 viral protein 1 (VP1) nucleotide and protein phylogenetic trees, which include all available EV-D68 sequences, indicate that strains associated with AFM are found in clade B (consisting of three subclades, B1, B2, and B3).

AFM Research Agenda

The Task Force findings and observations led to seven categories for action and research that were provided to the BSC/OID. High priorities within each category include

- **Communication and Education**
  - Provide information about AFM to healthcare providers, parents, and the general public
- **Surveillance**
  - Conduct robust, integrated case and viral surveillance
  - Investigate the molecular epidemiology of EV-D68 strains
  - Investigate temporal and geographic correlations of AFM cases with circulating viruses
- **Diagnostic Tool Development**
  - Detect pathogens and host immune responses
  - Develop immunologic assays (e.g., EV-D68 IgM) in CSF and serum
  - Detect exposure to infectious agents by evaluating the intrathecal antibody profile of AFM patients
- **Pathogenesis**
  - Determine viral molecular determinants of neurotropism, cell death, and paralytic potential
  - Use animal models to better understand viral pathogenesis
  - Determine if there is evidence of autoimmunity
  - Develop EV-D68 infectious clones
- **Risk Factor Studies**
  - Conduct epidemiologic risk factor studies
  - Identify genetic determinants of risk involved in immune regulation that may contribute to disease susceptibility or severity
- **Therapeutics and Vaccines**
  - Consider pre-clinical vaccine candidate development work
- **Treatment and Rehabilitation**
  - Standardize AFM outcome measures (strength, quality of life, community participation)
  - Conduct long-term follow-up of AFM patients

Key Findings

- In regard to AFM etiologies and pathogenesis, the AFM Task Force concluded that
  - Non-polio enteroviruses, and EV-D68 in particular, are leading candidates for AFM etiology; investigation of other etiologies will continue. It would be helpful to develop additional diagnostic assays.

  - Disease kinetics suggest that direct infection of the spinal cord is a more likely cause of illness than antibody-mediated pathology. More can be learned through further investigation of pathogenesis.
- In regard to clinical treatment, the AFM Task Force concluded that
  - Standardized outcome measures are needed (including for rehabilitation).
  - Treatment and rehabilitation may need to be individualized for each patient. In the interim, the Task Force suggests that CDC establish a network of centers of expertise around the country to serve as a resource for clinicians.
- In addition, the AFM Task Force suggests the establishment of a federal interagency AFM group to facilitate communication and enhance complementary approaches.

Discussion

Role of Infection in Causing AFM

Dr. Lynfield reported that neurology experts on the AFM Talk Force believe that the rapid development of weakness post-infection is more consistent with a direct viral effect than with an immune response to a viral infection. Guillain-Barré Syndrome, for example, typically develops 2 weeks after infection, while AFM typically develops within 5 days. However, investigations of the possible role of an immune response in causing AFM symptoms will continue.

Detection of Viruses in CSF

Viruses are rarely detected in CSF samples from AFM patients, even using sensitive molecular diagnostic methods. Jill Taylor, co-chair of the AFM Task Force, suggested that by the time weakness appears, the causative virus may be gone. This would be the case if viremia increases suddenly, infecting the spinal cord, and then decreases rapidly after a few days. Dr. Routh reported that a study is underway in Colorado to learn about the time course of shedding and viremia during EV-D68 infections.
Dr. Messonnier emphasized the importance of educating front-line physicians to recognize early signs of AFM and provide patient samples as early as possible. Dr. Taylor noted that the medical community should be prepared for early detection of AFM cases in 2020, when the number of cases may increase as part of the 2-year cycle.

Control Studies

To investigate the apparent relationship between respiratory viruses and AFM requires comparisons of AFM patients and control patients. Dr. Routh noted that conducting a case-control study is logistically difficult because AFM cases occur all over the country, typically with one or two cases per site. At the present time, seven pediatric academic sites are conducting intensive surveillance for children with acute respiratory illness and also for healthy community controls. The seven sites are collecting swabs from children without AFM who present at emergency rooms and community clinics. This will help determine what viral pathogens are circulating when AFM cases are detected. Dr. Taylor cautioned that what is known thus far about AFM is based on low numbers.

Public Comments

Phone lines were opened for public comments at 5:30 PM on May 7. Robin Roberts, an AFM parent advocate, thanked the BSC for their efforts.

NCEZID Update

Rima Khabbaz, Director, NCEZID, provided the following updates:

- **NCEZID leadership updates**
  - Tom Hennessy, Director, Arctic Investigations Program, and Acting Director, Division of Preparedness and Emerging Infections (DPEI), retired on April 1.
  - Michael Bruce is the new Acting Director, Arctic Investigations Program.
  - Henry Walke is the new Director, DPEI.
- **Ebola outbreak in the Democratic Republic of the Congo**
  - An outbreak of Ebola in the DRC has been ongoing since August 2018. The outbreak affects 18 health zones and is the largest in DRC history.
  - Since last summer, CDC has assisted the DRC Ministry of Health and WHO with data analytics and technical assistance on surveillance, contact-tracing, infection prevention and control, vaccines, and community engagement.
  - The outbreak is occurring in a security-compromised zone, in an area of heavy cross-border movement, and in a country experiencing cholera, malaria, measles, and other highly infectious diseases.
- **Recent outbreaks in the United States**
  - A **multistate outbreak of *Escherichia coli* O103 infections linked to ground beef**. As of April 26, 2019, 177 people have been infected with *E. coli* O103 in 10 states, with 21 hospitalizations. Although no common supplier, distributor, or brand of ground beef has been associated with all cases, two companies have recalled ground beef products distributed to restaurants and institutions.
  - ***Candida auris* in Orange County, California.** In February 2019, the California Department of Public Health (CDPH) identified a case of *C. auris* in a long-term acute care hospital, and point prevalence surveys identified five additional patients colonized with *C. auris* at the same hospital. Screening at three healthcare facilities that had cared for patients from the index facility led to the identification of 20 more patients likely colonized with *C. auris*. CDPH has requested CDC assistance to further assess the spread of *C. auris* and determine whether new infection control practices are needed in long-term care facilities.
- **Prevention and response to cholera outbreaks in Eastern Africa**
  - In October 2017, the Global Task Force on Cholera Control launched *Ending Cholera: The Global Roadmap to 2030*, a unified approach to cholera prevention and control that aims to reduce cholera deaths by 90% by 2030.
  - As part of this effort, CDC has provided technical assistance to Kenya, Tanzania, and Uganda in developing cholera elimination plans and assessing laboratory needs. CDC also participated in technical workshops and helped organize a consultation on the response to cholera outbreaks that took place after a tropical cyclone hit Mozambique in March 2019.

- **Food safety updates**
  - **PulseNet**
    - The PulseNet laboratory network is transitioning from pulsed-field gel electrophoresis (PFGE) to WGS as the standard methodology for detecting clusters and outbreaks of foodborne diseases, building on the success of the WGS *Listeria* project.
    - CDC is providing state and local health departments with supplies and equipment, DNA analysis software, information technology (IT) support, and training. CDC is also uploading 6 months of historical WGS data for each state. The transition may be complete by the end of May 2019. The transition to WGS will enable states and localities to detect and investigate a larger number of disease clusters and outbreaks. Analysis of pathogens' gene sequences will facilitate the determination of bacterial serotypes and the identification of genes associated with resistance and virulence.
  - **Foodborne Diseases Active Surveillance Network (FoodNet)**
    - FoodNet—a collaboration among 10 state health departments, the U.S. Department of Agriculture (USDA) Food Safety Inspection Service, FDA, and CDC—conducts active, population-based surveillance for eight foodborne pathogens: *Campylobacter, Cyclospora, Listeria, Salmonella*, Shiga toxin-producing *E.coli* (STEC), *Shigella, Vibrio*, and *Yersinia*. FoodNet also conducts surveillance for pediatric hemolytic uremic syndrome (HUS), which is typically caused by infection with *E. coli* O157:H7.
    - On April 25, 2019, FoodNet issued new data on the incidence and trends of foodborne pathogens in the United States between 2015 and 2018:
      - *Campylobacter* accounted for 38% of all cases of foodborne disease, and *Salmonella* serotype Enteritidis accounted for 19% of all cases of serotyped *Salmonella*.
      - The proportion of foodborne infections associated with contaminated produce rose significantly, likely due to the occurrence of produce-associated multistate outbreaks of *Cyclospora* and *E. coli* O157, as well as to increased use of culture-independent diagnostic tests (CIDTs).
      - The use of reflex cultures has increased by 14%, and the use of reflex cultures that led to isolation of a pathogen increased by 15%. This likely reflects the use of reflex cultures to confirm positive results using CIDTs.
- **Advanced Molecular Detection (AMD): Workforce development**
  - With AMD capacity coming online in state and local health departments, workforce development and training is a major priority.
  - A 4-day AMD training—called the AMD Academy—was held in Atlanta in January 2019. Training for microbiologists focused on microbial genetics, and training for epidemiologists focused on use of AMD data during outbreak investigations.
  - In February, CDC's Office of Advanced Molecular Detection, NCEZID, hosted a meeting for bioinformatics regional resource (BRR) leads from the seven PulseNet regions and for representatives from the Antibiotic Resistance Laboratory Network (ARLN). BRR staff interface with CDC programs and provide state and local health departments with assistance in improving AMD analysis and training, addressing IT challenges, and recruiting bioinformaticians.

- **Antimicrobial resistance (AR)**
  - **The Antimicrobial Resistance Challenge (AMR)**
    - The AMR Challenge is a yearlong effort to accelerate the fight against antimicrobial resistance across the globe.
    - To date, CDC has received AMR Challenge commitments from over 200 companies and organizations from around the world. Examples include two health insurance companies:
      - Aetna Inc. is taking action to reduce inappropriate antibiotic prescribing.
      - Premier Health Plan has surpassed its goal of reducing healthcare-associated *C. difficile* infections per 10,000 patients by 34%.
    - The AMR Challenge will end in September 2019 with a side event at the United Nations General Assembly to recognize partners who stepped up to take action.
  - **Antibiotic resistance investments**
    - Information about CDC's antibiotic resistance investments is posted on the CDC website and includes
      - Antibiotic resistance factsheets from U.S. states, localities, and territories
      - An Antibiotic Resistance Investment Map that showcases investments in laboratory and epidemiologic expertise and public health innovation
      - Success stories reported by states and localities
  - ***Vital Signs: Staph Infections Can Kill***
    - In March, 2019, CDC published a *Vital Signs* issue that highlights the need for intensified action to address infections caused by *S. aureus*, including MRSA. Any staph infection has the potential to cause a bloodstream infection that can lead to sepsis or death. Moreover, people who inject drugs such as opioids are at higher risk of developing these infections.
  - **2019 AR threats report: Coming soon**
    - In 2013, CDC published *Antimicrobial Threats in the United States, 2013*, which ranked 18 threats as "urgent," "serious," or "concerning." An updated report (scheduled for release in fall 2019) includes more comprehensive data and provides a new ranking of pathogens, with a larger number of pathogens in the "urgent" category.
- **Vector-borne diseases**
  - The ***National Strategy for Vector-Borne Disease Prevention and Control in the United States,*** which will be released this summer, outlines strategic priorities for reversing the upward trend of vector-borne disease incidence.
  - The ***HHS Tick-Borne Disease Working Group—***established under the 21st Century Cures Act—released its first bi-annual report to Congress on November 14, 2018. The report made 28 recommendations on six topics: Epidemiology and Ecology, Disease Prevention, Diagnosis, Treatment, Access to Care and Patient Outcomes, and Issues Looking Forward. CDC leads the implementation of recommendations for public health action, including
    - Improve national surveillance for Lyme disease
    - Develop more effective tools for prevention of tickborne diseases

- **FY 2020 budget update**
  - The President's Budget request for FY 2020 proposes across-the-board reductions to the CDC budget, including a reduction of $102.9 million (about 17%) for NCEZID. However, on May 6, the House Committee on Appropriations released proposed budget figures for HHS that include a $24 million increase to NCEZID. The proposed increase includes additional funds for food safety ($6 million), combating antimicrobial resistance ($5 millions), addressing vector-borne diseases ($5 million), and maintaining and enhancing AMD ($2.5 million).
- **Upcoming events**
  - Notable events that will take place during 2019 include
    - The 50th anniversary of the CDC high-containment laboratory
    - The 20th anniversary of the Laboratory Response Network
    - Release of a *Vital Signs* issue that discusses recent trends in the global fight against rabies
    - The award of approximately $200 million to state and large local health departments in August 2019, marking the start of a new cycle of the 5-year Epidemiology and Laboratory Capacity (ELC) cooperative agreement program. The current iteration of ELC merges activities supported under the prior ELC cooperative agreement into four public health programs:
      - Cross-Cutting Epidemiology and Laboratory Capacity Program
      - Foodborne, Waterborne, Enteric, and Environmentally Transmitted Diseases Program
      - Healthcare-Associated Infections and Antibiotic Resistance Program
      - Vector-Borne Diseases Program

Dr. Khabbaz **concluded by** referring the BSC/OID members to the document *NCEZID Accomplishments 2018*, which provides stories about the work of NCEZID and its many partners.

Discussion

Antimicrobial Resistance as a Global Issue

- The AMR Challenge and the WHO *Global Action Plan on Antimicrobial Resistance* assume that countries will identify their own approaches to achieving AMR goals, based on their needs and resources. CDC is committed to helping selected countries implement these approaches.
- The emergence of *C. auris* illustrates how rapidly drug-resistant diseases can spread around the world. Infectious disease modelers in the United Kingdom are modeling the potential global health impact if impoverished countries do not receive help in addressing the spread of antimicrobial resistance.
- CDC and partners are conducting a study that uses WGS to compare the microbiomes of overseas travelers before they leave the United States and after they return, to identify travel-related changes, including the acquisition of drug-resistant bacteria. The study may also examine whether changes to a traveler's microbiome affect the microbiomes of the traveler's household contacts.
- Addressing antibiotic resistance in countries where antibiotics can be purchased without a prescription requires a multisectoral, interagency effort, beyond what CDC can do alone. Moreover, the balance between drug access and stewardship must be determined locally. In countries where

the availability of antibiotics is already limited, bacterial diseases like TB might go untreated if antibiotics were available only by prescription.

One Health Approach to Antimicrobial Resistance

- Antimicrobial-resistant bacteria are common contaminants in fecal wastes and water. The role played by contaminated water and waste in the emergence of antimicrobial resistance is a One Health issue that lies at the intersection of human health, animal health, and the environment.
- In 2018, CDC co-sponsored a conference in Vancouver to consider the environment (e.g., soil and water) as a potential source of drug-resistant pathogens that can affect human health. Its conclusions are described in *Initiatives for Addressing Antimicrobial Resistance in the Environment: Executive Summary*.
- Michael Craig, Senior Advisor for Antibiotic Resistance, noted that the role of water and waste in the emergence of antimicrobial resistance is likely to be a significant component of "CARB 2.0"—an updated version of the *U.S. National Strategy for Combating Antibiotic-Resistant Bacteria* (CARB).
- The Minnesota One Health Antibiotic Stewardship Collaborative is an example of a multidisciplinary effort to address factors in human medicine, animal medicine, and the environment that favor the emergence of antimicrobial resistance.

Antibiotic Drug Development

- The updated AR threat report might serve as a guidepost for providing incentives for antibiotic development to address particular threats. Dr. Khabbaz noted that the AR threat report will include a watch list for new threats that will be updated as needed.
- Drug development to combat both bacterial and fungal diseases (like *C. auris*) is a major goal for CARB-X. NIH and the Biomedical Advanced Research and Development Authority (BARDA) are working with drug manufacturers, including small biotech companies, to improve the drug development pipeline.
- CDC continues to support many approaches, in addition to drug development, to prevent the emergence and spread of antimicrobial resistance. For example, CDC and healthcare partners are piloting interventions to detect, trace, and control drug-resistant infections in hospitals.

Sepsis Guidelines

- The CDC guidelines for management of severe sepsis highlight opportunities for early prevention (i.e., in persons with underlying conditions). The guidelines are intended for use with adult patients but might in the future be expanded to include best practices for treating pediatric patients.
- At a future meeting, CDC will update the BSC on ongoing efforts conducted in partnership with CMS, BARDA, and the Office of the HHS Assistant Secretary for Preparedness and Response to improve early detection and cure of sepsis.

Suggestions from the BSC/OID

- **Improved antibiotic stewardship standards for hospitals**
  - The BSC voted to send a letter supporting new stewardship standards to improve infection prevention and reduce antibiotic overuse in U.S. hospitals. Proposed in 2016, these standards were posted for comment but have not yet been finalized. If these rules are not finalized by June, the proposal will expire.

- Kathy Talkington, The Pew Charitable Trusts, will work with Ruth Lynfield to draft a BSC letter that will be circulated for review and comment.

- **Selection and amplified transmission of drug-resistant pathogens**
  - Misuse of antibiotics in human medicine (e.g., in treating pediatric earaches) is thought to be a major driver of the emergence and spread of resistance. However, other factors—such as the development of resistance in food animals and hospital transmission of drug-resistant bacteria—might actually be more important.
  - To better understand the emergence of drug-resistant pathogens of public health concern, CDC might use molecular epidemiologic studies to investigate the respective roles of
    - Factors that favor natural selection of resistant microbes (e.g., misuse of antibiotics in human and veterinary medicine)
    - Factors that amplify the spread of drug-resistant microbes *after* they have been selected (e.g., contamination of food products and disease transmission within a hospital)
  - Molecular studies may also determine whether all strains of *E. coli,* for example, can develop resistance, given high drug use and misuse, or whether a subset of bacterial strains gives rise to most emerging threats.
- **Reflex testing following positive CIDT results**
  - It was suggested that FoodNet determine whether the increase in reflex testing following positive CIDT results
    - Reflects testing at both state laboratories and hospital laboratories
    - Is paid for by insurance companies when conducted at hospital laboratories

Communications

- Recent articles in the *New York Times* raised concerns about *C. auris* infections and the need for greater transparency about transmission of *C. auris* is in healthcare facilities. CDC has issued updated public health information about *C. auris*, including information about how hospitals monitor and control *C. auris*.
- Tracking data suggest that *CDC Vital Signs* is generally successful at reaching targeted audiences (e.g., clinicians, public health workers, patients, and parents), and its issues are often cited in newspaper articles and television reports. Efforts are underway to further improve the uptake of *Vital Signs* and to apply the *Vital Signs* outreach approach to other efforts.

Vector-Borne Diseases Workgroup Report

The Vector-borne Diseases Workgroup (VBD WG) was established jointly by the BSC/OID and the BSC/NCEH/ATSDR to advance public health efforts to detect, prevent, and respond to VBDs. The VBD WG is co-chaired by Jim Le Duc, BSC/OID, and Melissa Perry, BSC/NCEH/ATSDR, and its membership includes scientists with expertise in public health, entomology, pesticides, and ecology.

Workgroup Tasks

Dr. Le Duc reviewed the five tasks of the VBD WG:

1. **Developing and evaluating VBD prevention and control tools,** beginning with a public health assessment of the safety, efficacy, and feasibility of available and innovative vector control methods. Other components will include
   - Evaluating novel control methods
   - Modeling the most effective tactics for prevention and response
   - Determining the relative effectiveness of non-pesticidal tools such as traps and genetically modified vector populations
   - Developing strategies for the collection and use of data on vectors and pathogens
2. **Clarifying CDC/ATSDR's role in monitoring human exposures to pesticides and adverse health effects following pesticide use,** through surveillance, biomonitoring, and epidemiologic investigations
3. **Establishing a strong public health workforce in vector control,** by
   - Developing a cadre of public health entomologists
   - Providing targeted training for state and local health departments
   - Developing, maintaining, and improving day-to-day mosquito control programs
   - Ensuring that appropriate infrastructure is in place during outbreaks
   - Improving responses and decreasing the need for emergency measures
4. **Improving overall risk communications for VBD,** through
   - Use of transparent and clear language
   - An emphasis on balancing risks between vector control methodologies and disease transmission
   - Encouragement of proactive community engagement
5. **Enhancing collaborations between public health organizations, academia, and industry** to
   - Strengthen existing VBD prevention and control strategies and develop new ones
   - Assess the risks of particular vector control strategies

Activities and Progress

- The VBD WG has held four teleconferences:
  - On July 6, 2018, the VBD WG confirmed its membership, discussed its timeline, and reviewed tasks and key issues identified by the Division of Vector-Borne Diseases (DVBD)/NCEZID and by NCEH.
  - On October 1, 2018, the VBD WG reviewed strategic plans on VBD developed by DVBD and NCEH.
  - On November 7, 2018, the VBD WG reviewed progress to date and discussed workgroup tasks, areas of VBD expertise within DVBD and NCEH, and the pending release of a report from the HHS Tick-Borne Disease Working Group. Ben Beard, DVBD Deputy Director, is the CDC representative to the HHS working group.

- On March 29, 2019, the VBD WG reviewed the draft *National Strategy for Vector-Borne Disease Prevention and Control in the United States*.

- Progress as of April 2019 includes
  - Identification of opportunities for collaboration between DVBD and NCEH. Common themes and interests include
    - Training and workforce development, which may involve the DVBD vector-borne disease regional centers of excellence and the NCEH training modules on vector control for environmental health professionals
    - Communication issues, including the need for clear, coordinated messaging, especially during emergencies
    - Collaboration with state and local health departments as principal partners and "customers"
    - Common interests in rodents as reservoirs/vectors of disease
  - Identification of unique VBD expertise in NCEH and DVBD, including expertise in
    - Toxicology of pesticides and integrated pest control (NCEH)
    - Rodent control (NCEH)
    - Tickborne diseases (DVBD)
    - Vector-borne disease monitoring and vector surveillance (DVBD)
    - Multidisciplinary vector-borne disease prevention and control (DVBD, NCEH)
- The VBD WG has begun an in-depth discussion of risk communications (Task 4) that takes into consideration
  - The importance to the public of CDC's endorsement of control strategies
  - Consideration of how to better coordinate messaging during emergencies

National Strategy and Agency Action Plans

- A concerted, sustained national effort to reverse the upward trend of vector-borne disease incidence is laid out in the draft *National Strategy for Vector-Borne Disease Prevention and Control in the United States*, which was submitted for clearance in April 2019. Components include
  - **Vision:** A nation where vector-borne diseases no longer threaten human health and well-being
  - **Mission:** Protect people from illness, suffering, and death due to vector-borne diseases
  - **Five goals:**
    - *Improve understanding:* Understand when, where, why, how often, and how people are exposed to and get sick or die from vector-borne diseases
    - *Detect & Diagnose:* Develop, evaluate, and improve tools and guidance for the diagnosis and detection of vector-borne diseases
    - *Prevent & Control:* Develop, evaluate, and improve tools and guidance for the prevention and control of vector-borne diseases
    - *Treat & Mitigate:* Develop and assess drugs and treatment strategies for vector-borne diseases

    - *Disseminate tools, Facilitate processes, and Build capacity:* Disseminate and support the use of effective public health and vector control products, tools, and programs to detect, diagnose, and respond to vector-borne disease threats
- CDC led the development of the *National Strategy*, in partnership with NIH, FDA, BARDA, USDA, DoD, the Environmental Protection Agency, the National Park Service, and the U.S. Geological Survey.
- Each agency is drafting an agency-specific action plan for implementing the goals of the *National Strategy*. The *CDC Action Plan* will identify high-priority actions for public health and establish a timeline and benchmarks for measuring progress.

Next Steps

The VBD WG plans to

- Hold a focused discussion on workforce development for vector control (Task 3)
- Consider how VBD programs at CDC can advance implementation of the *National Strategy*
- Discuss the *CDC Action Plan for Vector-Borne Disease Prevention and Control in the United States*

Request to the BSC/OID

The VBD WG seeks BSC suggestions on which priority activities to include in the *CDC Action Plan* and how to implement them (e.g., how to engage industry in the development of VBD prevention and control tools and methods).

Discussion

BSC Feedback

- **The *CDC Action Plan* should include international VBD issues that can have a domestic impact, because what happens abroad affects the United States.** For example, U.S. travelers may return home infected with yellow fever that spreads locally via mosquito bites.
    - Dr. Beard noted that the *National Strategy* focuses primarily on domestic issues, but includes some international priorities, including yellow fever. Lyle Petersen, DVBD Director, added that CDC currently works with selected countries and the Pan American Health Organization (PAHO) on yellow fever issues, including mass vaccination strategies and plans for fractional dosing. CDC and NIH are planning joint exercises on how to respond if yellow fever arrives in the United States. CDC is also creating a prioritized list of arboviruses that might become domestic threats.
- **Federal agencies should work together to address priority issues outlined in their agency-specific action plans.** Cross-cutting issues include workforce development, vaccine development and use, and molecular diagnostics.
    - Dr. Khabbaz noted that a public health workforce assessment is underway at CDC. Dr. Beard reported that an informal state-level assessment conducted during the Zika response by the Association of State and Territorial Health Officials (ASTHO) found that few health departments employ entomologists. Discussions are underway on how best to train public health entomologists and ensure that health departments will be able to hire them. One idea is to use the ELC program to train an entomologist for each of the 64 ELC jurisdictions.

- **Industry partners may help implement *National Strategy* Goal #2: Detect & Diagnose.** Private sector engagement may be obtained by
  - Helping diagnostics companies understand the growing need for rapid diagnostics for tickborne diseases and why it would be mutually beneficial to support R&D in this area
  - Providing economic data on the impact of the rising incidence of tickborne diseases in the United States. In addition to medical costs, these data should include estimated costs due to changes in climate that expand the habitats of insect disease vectors.
    - Dr. Beard noted that under-reporting of Lyme disease is well documented. A study conducted in 2014 found that 3 to 4 million diagnostic tests for Lyme disease are used each year, at a cost of $492 million.
    - While mosquito control is typically the responsibility of local governments, tick control is left to individual homeowners and is very expensive.
- **It is important to consider the potential effects of pesticides used to control insect disease vectors on other, non-harmful insects, such as bees.**
  - Insecticide safety continues to be a major concern, as it was during the Zika response. CDC is considering better control tools, including anti-Lyme vaccines for rodents. If pesticides are used, local public health workers must monitor their impact in terms of disease control, pesticide resistance, and harm to non-targeted insects.
- **It is critical that states receive resources to advance vector-borne disease prevention and control.** Funds might be provided via the ELC program.

Other Issues

- **Emerging arboviruses.** Improving tools for the diagnosis of emerging arboviruses—and transferring those tools to state and local partners—is a current focus of CDC scientists at DVBD in Fort Collins, Colorado. This effort will help fulfill two *National Strategy* goals: *Improve understanding* and *Detect & Diagnose*.
- **Alpha-gal allergy.** Current data suggest a possible link between tick bites and the development of alpha-gal allergy. CDC and partners are working to define the spectrum of clinical disease and the distribution of cases.

Food Safety Modernization Act Surveillance Working Group Report

The goal of the FSMA SWG is to provide advice and recommendations regarding the improvement of foodborne illness surveillance to the HHS Secretary (through the BSC/OID) in the areas of

- Governmental coordination and integration
- Evaluating and improving surveillance systems
- External stakeholder collaboration and communication

FSMA SWG May 6–7 Meeting Topics

Tim Jones, State Epidemiologist, Tennessee Department of Health, and FSMA SWG chair, reported on the FSMA SWG meeting held on May 6–7. Topics included

Challenges and Opportunities of WGS for Illness Detection and Response

- **WGS laboratory updates**
  - The PulseNet transition from PFGE to WGS is nearly complete.
    - Fifty states and 64 laboratories have converted to BioNumerics 7.6.[6]
    - Forty-eight states and 55 laboratories have been certified in WGS analysis of *Listeria, Salmonella, Escherichia,* and *Campylobacter*.
  - PulseNet laboratories in 50 states have met WGS requirements for sequencers; standardized sequencing procedures, software tools, and sequence quality parameters; use of internationally agreed-on pipelines; storage of raw sequence data in the public domain; pipeline validation by end users; and contribution of sequences to a high-capacity server at CDC. Work is underway to include PFGE and WGS data in the same database, implement CLIA (Clinical Laboratory Improvement Amendments) validation of reference tools, certify end users, and train laboratorians and epidemiologists.
  - WGS is likely to identify a larger number of disease clusters than PFGE, making it necessary to determine which WGS-detected disease clusters to investigate ("cluster triage"). Other issues include the costs of WGS and the need to establish standards for international data-sharing and data quality. Cost issues include insufficient resources in some states to generate WGS data on all submitted *Salmonella* isolates and the eventual need to replace BioNumerics with an alternative platform that is better suited to address future data requirements.
- **WGS trainings for epidemiologists**
  - Educational opportunities for epidemiologists have included PulseNet webinars, OutbreakNet teleconferences, and SEDRIC (System for Enteric Disease Response, Investigation, and Coordination) trainings. PulseNet and OutbreakNet have held regional meetings for epidemiologists; CSTE and CDC's Office of Advanced Molecular Detection, NCEZID, have held molecular epidemiology trainings; and the Integrated Food Safety Centers of Excellence have offered webinar trainings on BioNumerics and WGS interpretation.
- **WGS and antimicrobial resistance**
  - The National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) has begun using WGS data (resistance determinants) to predict antimicrobial resistance. The addition of WGS to predict antimicrobial resistance means that
    - Isolates that are not physically sent to NARMS, but that have WGS performed in the state laboratories, can have their gene sequences analyzed for predicted resistance.
    - In outbreaks, predicted resistance results from WGS are available in a few weeks compared with traditional antimicrobial susceptibility testing (AST), which can take substantially longer to yield results.

[6] BioNumerics is a platform for the management, storage, and statistical analysis of all types of biological data. BioNumerics is used by networks around the globe to share and identify strain information.

    - Resistance can be accurately predicted for a wide range of enteric bacterial pathogens such as *Salmonella* (Typhi and non-typhoidal), *Campylobacter*, *Shigella* and *E. coli* (STEC).
  - New mechanisms of resistance can be identified using WGS, and although AST methods remain the gold standard for reliable resistance testing, resistance can be predicted with high accuracy using WGS. In the future, NARMS will increasingly use WGS data submitted by public health laboratories to identify isolates with new or concerning resistance patterns. This will allow rapid identification and investigation of patients with infections due to emerging or very concerning ("scary") resistance patterns.
  - In summary, WGS will allow for predicting antimicrobial resistance in all sequenced isolates and will help CDC identify new or concerning resistance patterns. It will facilitate real-time responses and allow for genetic comparison of isolates and their resistance determinants that are identified globally. WGS enables more timely detection of antibiotic-resistant foodborne bacterial outbreaks and a more comprehensive surveillance system for antibiotic-resistant foodborne bacterial pathogens.

- **Clades of concern**
  - Analysis of WGS data allows the identification of "clades of concern"—groups of closely related bacterial strains that persist for years, causing repeated outbreaks from similar sources and increasing the numbers of sporadic cases. These strains are often multidrug-resistant and may not be easy to identify as the causative agents of outbreaks. In the future, clades of concern are likely to be the focus of intensive investigations, tracebacks, and environmental assessments. They may also advance the development of new prevention measures by industry and regulatory partners.
  - Two clades of concern were identified during the investigation of an outbreak of multidrug-resistant strains of *E. coli* O157:H7 associated with romaine lettuce grown in Yuma, Arizona, in spring 2018.
    - The outbreak involved 210 cases in 36 states, with 96 hospitalizations, 27 cases of HUS, and 5 deaths. The lettuce was traced back to 23 growing fields, across a span of 50 miles.
    - WGS analysis found that *E. coli* O157:H7 isolates associated with 22 PFGE patterns fell into two clades, both associated with water from an irrigation canal. One of the clades was linked to two previous outbreaks (both in 2017)—one involving 9 cases mainly in California and Colorado, and one involving 17 cases spread throughout the United States, with no suspected vehicle.
  - Another clade of concern was identified during a second outbreak of *E. coli* O157:H7 associated with romaine lettuce that began later in 2018.
    - The outbreak involved 62 cases in 16 states, with 25 hospitalizations, and 2 nonfatal cases of HUS, and the lettuce was traced back to several fields in Santa Maria, California.
    - WGS analysis found that *E. coli* O157:H7 isolates associated with 10 PFGE patterns belonged to a single clade associated with a sediment sample collected from an irrigation pond. This clade was different from the two Yuma clades but was associated with three separate events over 3 years: a cluster of 20 cases in 2016, an outbreak associated with leafy greens in 2017, and an outbreak involving 62 cases associated with romaine lettuce in 2018.
  - Other examples of clades of concern include those responsible for multidrug-resistant *Salmonella* Infantis in chickens and multidrug-resistant *Salmonella* Reading in turkeys.

FSMA SWG Feedback on the Use of WGS for Illness Detection and Response

- **What do you see as CDC's role in helping to prevent, or limit, the emergence of multidrug-resistant strains in food animals and subsequent transmission to humans?** CDC's role might include
  - Analyzing new, ongoing, and recurring clades of concern
  - Strengthening public health capacity to analyze large, complex data sources like WGS
  - Investigating
    - Drug resistance associated with produce
    - Drug resistance associated with sporadic illnesses, as well as with outbreaks
    - Environmental sources of resistance, which might lead to the identification of resistance genes before human illness is detected
- **How can we engage regulatory, animal, and agriculture partners in addressing public health problems where there is unclear, or a lack of, regulatory oversight?** CDC might consider
  - Working with federal agency partners to develop an interdisciplinary, interagency One Health approach to investigating outbreaks of foodborne diseases
  - Engaging the USDA Animal and Plant Health Inspection Service in joint efforts to address farm-related infectious disease issues (e.g., joint investigations and interagency data-sharing)
  - Having the new Prevention Coordination Unit of the Division of Foodborne, Waterborne, and Environmental Diseases (DFWED), NCEZID, lead CDC's efforts in this area
- **What do you see as opportunities for WGS in the next year?** WGS will increase identification of disease clusters and outbreaks and help regulators and policy-makers focus on priority areas. Challenges will include investigating a larger number of outbreaks, which will likely involve cluster triage. Another challenge will be to communicate the importance of WGS data to the public and to stakeholders.

Water as a Food Safety Program: "The Water We Eat"

- Contaminated water can impact food quality and contribute to foodborne outbreaks. Recent water-related foodborne disease outbreaks were linked to contaminated irrigation water, including outbreaks involving *E. coli* O157:H7 associated with lettuce, *Cyclospora* associated with spinach, hepatitis A virus associated with green onions, and multiple outbreaks associated with berries. However, in most cases, there are few environmental data to help establish etiologic connections.
- Focus areas and activities for addressing the food/water nexus include
  - Building capacity at the federal, state, and local levels to conduct environmental investigations, including outbreak responses and root-cause analyses
  - Conducting research on irrigation water quality, produce washwater systems, and water quality in processing facilities
  - Advancing health promotion related to safe water, sanitation, and hygiene
  - Contributing to science-based "ag water"[7] best practices and policies

[7] "Ag water"—also known as agricultural water or farm water—is water committed for use in the production of food and fiber.

- As cited above, recent examples of environmental investigations include investigations of outbreaks associated with romaine lettuce grown in
  - Yuma, Arizona, where *E. coli* O157:H7 was detected in a canal used to irrigate the fields where the lettuce was grown. The canal was adjacent to a concentrated animal feeding operation (CAFO).
  - Santa Maria, California, where *E. coli* O157:H7 was detected in the sediment of a reservoir used to irrigate the field where the lettuce was grown. Although this reservoir was fed by protected ground water sources, the surface storage design exposed the water to animal feces.
- At the present time, however, there is little national capacity to conduct environmental investigations, and there is no dedicated program for field and laboratory training in the food/water nexus. The CDC Waterborne Disease Prevention Branch conducts ad hoc training in sample collection as part of outbreak responses, and CDC is planning to expand Laboratory Response Network activities to include water-related emergency preparedness. Interagency collaboration is key to capacity-building in this area.

FSMA SWG Feedback on Water-Related Food Safety Investigations

To meet the challenge of preventing disease due to emerging threats, the FSMA SWG recommends

- Developing a better understanding of potential water impacts on food safety
- Erring on the side of health protection while the evidence base is still developing
- Conducting research and root-cause analysis to characterize risk and inform effective prevention
- Ensuring rapid, coordinated, and multisectoral responses that will improve our ability to
  - Identify the contamination source
  - Trigger the risk management process
  - Return to operation as quickly as possible
  - Interpret and translate environmental data quickly

Additional feedback was provided in response to these questions:

- **What should CDC be doing to support increasing state capacity for water-related food safety investigations?** Actions may include
  - Providing data about the burden of waterborne disease to justify public health expenditures
  - Seeking support for hiring environmental scientists, including microbiologists
  - Providing state-level training in water sampling and testing and in environmental studies
  - Expanding the roles of regional laboratories and Centers of Excellence with relevant expertise
- **Should CDC obtain and synthesize more information on water contributions to foodborne disease outbreaks?** CDC might systematically analyze the role of water in foodborne outbreaks, prospectively and retrospectively.
- **Should CDC be involved in collecting and analyzing data to understand environmental root causes and conduct risk characterizations for how water is used in food production?** CDC should consider
  - Providing technical support for regulatory investigations
  - Conducting and collaborating on non-regulatory research studies

CDC Updates Presented at the May 6–7 FSMA SWG Meeting

- **Globalization of the food supply: Implications for the United States**
  - Data from the USDA Economic Research Service indicate significant increases in the proportions of fruit and nuts, vegetables, and fish and shellfish that are imported into the United States. The number of outbreaks linked to imported foods has also increased, and many of these outbreaks have been linked to new vehicles, including broccoli powder on a food snack, hot peppers, black pepper, tahini sesame paste, fresh papaya, frozen fruit pulp, pine nuts, scraped tuna, sugar cane juice, and sprouted chia seed powder.
  - Challenges in addressing foodborne outbreaks associated with imported foods include
    - An increasing and constant consumer demand for imported foods
    - An increasing global food supply (growing by about 7.6% per year) that currently accounts for more than 20% of the U.S. food supply
    - Importation of food products from more than 150 countries, through more than 300 ports. More than 200,000 foreign firms are registered by FDA to import food.
- **Culture-independent diagnostic tests and incidence rates for foodborne diseases**
  - An analysis of FoodNet data indicates that the incidence of most foodborne infections rose during 2018 as compared with 2015–2017. Significant increases in incidence were reported for *Campylobacter*, *Salmonella*, *Yersinia,* and *Listeria*. These findings may be partially attributable to an increased use of CIDTs.

FSMA SWG Feedback on the Interpretation of Incidence Rates

It is important to count cases identified by CIDTs, which account for an increasingly large portion of reported cases. However, interpretation of incidence measures is complicated because

- Increases in case detection may be due to
  - Increased use and sensitivity of CIDTs
  - Increased use of syndromic panels that identify more than one pathogen and/or identify pathogens that in past years were not included in most test panels
  - Changing laboratory and provider testing practices
- The number of culture-confirmed cases is decreasing as laboratories switch to CIDT. However, this decrease may be offset in part by an increase in reflex-culture testing of CIDT-positive cases.
- In summary, disease incidence may appear to be increasing due to increased testing and detection, false positives, and poly-microbial detections.

Future Topics

Future discussion topics for the FSMA SWG may include

- Periodic reviews of enteric surveillance systems
- Updates on interagency collaborations (e.g., the Interagency Food Safety Analytics Collaboration [IFSAC], the Interagency Foodborne Outbreak Response Collaboration [IFORC], and the Interagency Collaboration on Genomics and Food Safety [Gen-FS])
- Challenges related to imported foods
- Root-cause identification and analyses

- Building state capacity and workforce development to address foodborne diseases
- Orphan illnesses such as cryptosporidiosis, toxoplasmosis, and hepatitis A
- Industry updates related to data-sharing, legal issues, and traceback investigations
- Identification of "stealth sources"—such as spices—that can serve as vehicles for foodborne pathogens
- Population surveys of foodborne diseases
- Prevention of foodborne diseases

Dr. Jones **concluded by** thanking Dale Morse, Associate Director for Food Safety, DFWED, for his service to the FSMA SWG and wishing him well on his retirement.

Discussion

U.S. Burden of Foodborne Disease

- Rob Tauxe, Director, DFWED, reported that IFSAC is using multiple data sources to identify the proportion of infectious disease attributable to 17 types of food and to prepare an estimate of the full U.S. burden of foodborne disease. IFSAC plans to work with academic partners to use disability-adjusted life years and modeling to capture the long-term impact of the U.S. burden of foodborne disease.

Sources of Water Contamination

- Animal reservoirs, such as CAFOs, could be the source of the *E. coli* strains that contaminated irrigation water used to grow romaine lettuce in Arizona and California. Contaminated irrigation water used in crop-dusting mixtures could potentially spread a pathogen across many farms.
- A multisectoral discussion is underway about how to treat irrigation water and what it would cost. Treating water sprayed over crops, for example, would be less expensive than moving a CAFO away from an irrigation canal.

PulseNet Transition

- CDC is working with NIH and other partners to meet the challenge of managing and storing WGS data.
- Dr. Tauxe noted that this is not the first time that the public health community has experienced a major technological transformation in how we track and control foodborne diseases. PFGE was a new idea in the 1990s, but over time PFGE became the new laboratory standard.
- Dr. Khabbaz expressed CDC's continued commitment to helping state and local levels build capacity to use WGS and investigate the increased numbers of foodborne disease clusters and outbreaks that will likely be detected by CIDTs.

Other Comments

- Automated electronic laboratory reporting of foodborne diseases is the gold standard for reporting in most hospital emergency departments. Gathering ancillary epidemiologic data—which comes from many sources—is now a greater challenge.
- Research is needed to evaluate the long-term health consequences of foodborne disease infections and improve food safety and health policy.

CGH Update

Serena Vinter, Acting Deputy Director for Strategy, Policy, and Communication, provided three in-depth examples of CGH activities, from the Divisions of Parasitic Diseases and Malaria (DPDM), Global HIV and TB (DGHT), and Global Health Protection (DGHP).

Treatment of Severe Malaria in the United States

- DPDM protects the health of Americans and members of the global community by
  - Preventing, tracking, and treating malaria and parasitic diseases in the United States
  - Implementing the President's Malaria Initiative and working with the U.S. Agency for International Development (USAID), WHO, and other partners to prevent, control, and eliminate neglected tropical diseases (NTDs) and malaria
  - Conducting innovative research to accelerate control and elimination of malaria and NTDs worldwide
- **Background.** Although the United States was officially declared malaria-free in 1951, the potential for malaria transmission remains because the mosquito that transmits malaria—the *Anopheles* mosquito—is present in almost all states.
  - Sixty-three local outbreaks of malaria have been reported since the U.S. National Malaria Surveillance System began in 1957. The last one occurred in Florida, in 2003, affecting eight people. It started with an imported case of malaria.
  - The geographic distribution of malaria cases in the United States is wide, with every state reporting at least one case in 2015. However, most cases (about two-thirds) are concentrated in 11 states. Nearly all these cases are imported, and the numbers have increased as international travel has increased. Between 1973 and 1977, approximately 380 malaria cases per year were reported; between 2010 and 2015, the annual average rose to 1,700 cases, of which about 300 are severe.
- **A new first-line treatment for severe malaria that is not FDA-approved**
  - Production of intravenous quinidine—the only FDA-approved drug to treat severe malaria—was discontinued in December 2017, with product distribution continuing through March 2019. As of April 1, intravenous artesunate—the WHO-recommended global standard for treatment of severe malaria—replaced intravenous quinidine as the first-line treatment for U.S. cases of severe malaria. However, intravenous artesunate is neither FDA-approved nor commercially available in the United States.
  - Working with the Walter Reed Army Institute of Research and the U.S. Army Medical Materiel Development Activity, CDC arranged to make intravenous artesunate available through an FDA expanded-use investigational new drug (IND) protocol:
    - Prior to April 1, 2019, when a clinician requested artesunate to treat a case of severe malaria, CDC would authorize release of the drug (which the Army provides to CDC quarantine stations) only if the first-line drug—quinidine—was not an option. As of April 1, 2019, intravenous artesunate is reserved for treatment of severe malaria and may also be provided under the IND protocol if a patient is unable to tolerate oral medications.
    - The drug, as well as transport to the closest major airport, is provided free. Ten quarantine stations currently stockpile intravenous artesunate, and CDC is constantly evaluating the pre-positioning of this drug.

- FDA approval of intravenous artesunate is unlikely in the near future because a drug company must submit a new drug application to FDA to start the review process and no such application is currently in the pipeline.

Dolutegravir: HIV Treatment and Risks

- DGHT works with ministries of health and WHO to advance HIV epidemic control as part of PEPFAR (President's Emergency Plan for AIDS Relief). As of September 30, 2017, DGHT has supported
  - Antiretroviral therapy (ART) for over 7.3 million people living with HIV, which represents one-third of all people on treatment, worldwide
  - ART for more than 388,000 children under the age of 15
  - Voluntary medical male circumcision procedures for 7.5 million men, to help prevent the spread of HIV
- **Background**
  - PEPFAR recommends dolutegravir (DTG), an integrase inhibitor, as the first-line ART regimen for people living with HIV. As compared with other ART options, DTG is better tolerated, is more effective at viral suppression, is as affordable (or moreso), and presents a higher barrier to the development of drug resistance. Studies indicate that the benefits of DTG for HIV treatment of pregnant woman substantially outweigh the risks and that administration of DTG results in more than three times fewer deaths among women, as compared with other ART regimens.
- **Identification and investigation of a potential safety issue**
  - However, in May 2018, interim analysis of data from an ongoing surveillance study in Botswana identified a possible association between DTG and neural tube defects in newborns. An updated analysis in July 2018 identified 4 cases of neural tube defects in 600 newborns (0.67%). This rate is approximately seven times higher than in babies of women taking other antiretroviral drugs at the time of conception and women who were HIV-negative.
  - To investigate this issue, DGHT and the Division of Congenital and Developmental Disorders, National Center on Birth Defects and Developmental Disabilities, are working in partnership with
    - The Botswana Ministry of Health and Wellness, to scale up surveillance for neural tube defects to cover 94% of the births in Botswana
    - The Kenyan Ministry of Health and Kenya's National AIDS and STI Control Program, to conduct a retrospective/prospective case-control study of women living with HIV served by 24 clinics across the country
  - PEPFAR currently recommends that
    - DTG should be offered to all people living with HIV as the preferred first-line ART regimen.
    - Women of childbearing potential should be counseled about the neural tube defect issue and the benefits of DTG and be offered an informed choice.
  - The neural tube defect issue is under discussion by the WHO Advisory Committee on Safety of Medicinal Products.

Measuring the Progress of Global Health Security Activities

- DGHP advances global health security in part through support of the Global Health Security (GHS) Agenda, a worldwide effort to strengthen every country's capacity to prevent, detect, and respond to health threats. DGHP also manages and coordinates the
  - Global Disease Detection Program
  - Global Disease Detection Operations Center
  - Field Epidemiology Training Program
  - Global Rapid Response Teams
- DGHP is working with ministries of health in 17 priority countries to measure progress in advancing GHS, using
  - The **Joint External Evaluation (JEE) tool.** JEEs are voluntary, external assessments of a country's capacity to prevent, detect, and respond to infectious diseases and other public health threats.
    - For each country, DGHP calculates JEE scores for 15 indicators in four core technical areas: Surveillance Systems, Laboratory Systems, Workforce Development, and Emergency Management. The scores range from 1 for "no capacity" to 5 for "sustainable capacity."
    - A comparison of JEE scores based on mid-year FY 2017 reporting and end-of-year FY 2018 reporting indicates significant progress. By the end of 2018, the average overall capacity score for the four core technical areas across the 17 countries was 3.0 out of 5.0.
  - The **Infectious Disease Vulnerability Index.** Developed by the RAND Corporation in 2016, the Vulnerability Index aims to assess countries' vulnerabilities to infectious disease threats and help inform decision-making about capacity-building needs.
    - DGHP calculated the vulnerability scores of the 17 priority countries to identify geographic areas with low capacity scores and high vulnerability scores.

In conclusion, Ms. Vinter emphasized three core strategies for accelerating progress in advancing the GHS Agenda:

- Fostering strategic collaborations and building relationships with external partners
- Building the scientific evidence base for global health security
- Strengthening program alignment, unity, and efficiency in CGH

Discussion

Malaria Prophylaxis and Travelers' Health

- Americans about to travel overseas may not consult their primary care providers or may call when it is too late to arrange malaria prophylaxis. Some travelers may consult the CDC Yellow Book.
- Kathrine Tan, Malaria Branch, DPDM, reported that the travelers at highest risk for malaria tend to be immigrants who are visiting relatives in their countries of origin and do not think about consulting doctors about travel risks. Many U.S. physicians who travel also do not regard themselves as at risk.

- Suggestions for CGH and the NCEZID Division of Global Migration and Quarantine, which issues the CDC Yellow Book, include
  - Partnering with airlines to provide people bound for malaria-endemic countries with health information and/or to remind them (perhaps using electronic messages) to consult their physicians
  - Preparing a *Vital Signs* issue about malaria prophylaxis for travelers. Ms. Vinter noted that CGH has proposed this idea for 2020.
  - Partnering with pharmacies to post travel health notices in their stores
  - Arranging for travelers to self-administer prophylactic treatment for malaria. Dr. Tan noted that travelers often do not use medicine for malaria prophylaxis correctly, even when it is prescribed by a physician.
  - Providing local health departments with training in how to encourage travelers to protect themselves from infectious diseases
  - Considering additional ways to
    - Screen travelers for malaria and other diseases
    - Provide health messages to travelers during infectious disease emergencies

Trends in U.S. Malaria Incidence

- Trends in U.S. malaria incidence over time may be calculated by dividing the number of cases by the number of people traveling abroad per year (i.e., the number of cases per episode of travel).
- Dr. Tan noted that such calculations may be difficult to interpret, because the denominator usually includes persons who received malaria prophylaxis. In any case, the numbers generally indicate an increase in U.S. malaria cases that is commensurate with the increases in international travel.

Laboratory Biosafety and Biosecurity

- BSC members suggested that CDC consider working with ministries of health and WHO to
  - Advance biosecurity by strengthening national laboratory capacities to detect bioterrorism pathogens
  - Review biosafety and biosecurity practices at the more than 50 Biosafety Level 4 (BSL-4) laboratories around the world
- Dr. Le Duc, Director of the Galveston National Laboratory, noted that some BSL-4 laboratories are located in countries without reliable sources of power. This issue should be raised with GHS partners, including the Defense Threat Reduction Agency.
- Ms. Vinter mentioned that Africa CDC, ministries of health in sub-Saharan and southern African countries, and CDC have organized a meeting on laboratory biosecurity to take place in June 2019.

GHS Priority Countries

- Phase I and Phase II GHS countries were selected through a national security interagency process. As part of this effort, CDC provided epidemiologic evidence about disease risk. The 2014–2016 Ebola outbreak in West Africa also informed Phase I and Phase II country selection.
- Phase I countries receive direct investments, while Phase II countries (including the DRC) receive technical assistance only.

- The National Security Council (NSC) is leading an ongoing interagency conversation about where GHS will focus in the future.

Areas for Future Discussion

- CDC might consider sharing ideas and information about next steps for working with WHO and ministries of health to
  - Expand opportunities for TB treatment
  - Improve surveillance for antimicrobial resistance in low-resource settings

CDC One Health Office

The CDC One Health Office (OHO), NCEZID, was established in 2009, with CDC as the first U.S. federal agency to have such an office. The CDC One Health Office works to strengthen One Health approaches in the United States and around the world by uniting national and international partners to effectively collaborate across sectors and leverage resources to address health threats, including zoonotic diseases, at the human-animal-environment interface. Casey Barton Behravesh, OHO Director, provided the following updates:

Prioritization of Zoonotic Diseases by International Partners

- International OHO activities include helping countries achieve One Health–related capacity-building goals established under the Global Health Security Agenda, which includes a Zoonotic Disease Action Package.
- As part of this effort, OHO coordinates One Health Zoonotic Disease Prioritization (OHZDP) workshops that bring together stakeholders from many different sectors to identify the zoonotic diseases and pathogens of greatest local public health concern.
- OHZDP workshops have been conducted in multiple countries and, for the first time in 2018, in regions, to prioritize the zoonotic diseases that pose the biggest health threat. Participants can then more efficiently build their laboratory capacity, conduct disease surveillance, plan outbreak response and preparedness activities, and create disease prevention strategies to reduce illness and death in people and animals.
  - The first regional workshops were held for the Economic Community of West African States, which includes 15 member countries, and for U.S. southern land border states. These regional workshops reflect increased interest among partners to work together at the regional level to prepare for shared threats to people, animals, and the environment. CDC's One Health experts also facilitated national workshops in Mozambique, Ghana, and Uzbekistan. In Uzbekistan, they pilot-tested a new toolkit to help the country develop a One Health strategy to prevent the diseases identified as being high priorities.
  - In late March, staff from CDC's One Health Office traveled to Fairbanks, Alaska, where they met with staff from the Arctic Investigations Program, DPEI, NCEZID, and with participants from state, local, federal, and tribal partners to facilitate an OHZDP workshop in Alaska. While the One Health Office has helped to conduct over 20 workshops to help countries and regions prioritize zoonotic diseases of greatest concern, this was the first time it had been done at the state level.
  - More information and country reports are available on the One Health Zoonotic Disease Prioritization webpage.

- WHO, the World Organisation for Animal Health (OIE), and the Food and Agriculture Organization of the United Nations (FAO) have formed a "Tripartite Collaboration" to address One Health threats that pose risks to public health, animal health, and global health security. The Tripartite Collaboration promotes cross-sectoral collaboration and provides assistance with strategic planning, tools, and resources.
- The Tripartite organizations have developed *Taking a Multisectoral, One Health Approach: A Tripartite Guide to Addressing Zoonotic Diseases in Countries*, with technical consultation and donor support from CDC. This guide, referred to as the Tripartite Zoonotic Guide (TZG), can also be used to address other health threats at the human-animal-environment interface, such as food safety and antimicrobial resistance.
  - The TZG provides principles, best practices, and options to assist countries in achieving sustainable and functional collaboration at the human-animal-environment interface. Examples and lessons learned from countries' experiences are also included. The guide is currently available in English and will be translated into the five other official languages of the United Nations.
  - Countries can use the TZG and its associated operational tools (which are currently being developed) to build or strengthen national capacities in the following areas: multisectoral One Health coordination; investigation and response; surveillance and information-sharing; mapping country context; joint risk assessment; planning and preparedness; risk communications; and workforce development. Options for monitoring and evaluating the impact of these activities are included, allowing countries to improve their zoonotic disease frameworks, strategies, and policies. Moreover, taking the One Health approach presented in the TZG helps countries to make the best use of limited resources and reduces indirect societal losses, such as impacts on livelihoods of small producers, poor nutrition, and restriction of trade and tourism.
  - The next steps are to develop Operational Tools for the key technical areas in the guide to assist countries in better operationalizing One Health. CDC experts are involved in the development and piloting of these new Operational Tools for three technical areas: (1) multisectoral, One Health coordination; (2) surveillance and information-sharing; and (3) joint risk assessment.

Prioritization of Zoonotic Diseases in the United States

- **U.S. One Health Zoonotic Disease Prioritization workshop**
  - CDC, the U.S. Department of the Interior (DOI), and USDA organized an OHZDP workshop to further joint efforts to address zoonotic disease challenges in the United States.
  - The eight prioritized zoonotic diseases for the United States are zoonotic influenza viruses, salmonellosis, West Nile virus, plague, emerging coronaviruses (e.g., severe acute respiratory virus and Middle East Respiratory Syndrome), rabies virus, brucellosis, and Lyme disease.
  - Next steps have been initiated to address One Health needs around the priority zoonoses and recommended action items, including the following:
    - The One Health Office leads coordination of the CDC-DOI-USDA efforts to develop a One Health Strategic Plan for the United States, including an interagency working group meeting February 25–27 to finalize a draft document. The draft is expected to be ready for review in spring 2019.

    - The One Health Office also re-established and currently chairs the One Health Federal Interagency Network, an information-sharing network that brings together relevant federal partners working in One Health on a bi-monthly basis.
  - A final workshop report co-authored by CDC, DOI, and USDA outlining the process, the resulting list of prioritized zoonoses, and discussions and recommendations by the participants on how to jointly address the priority zoonotic diseases and strengthen One Health in the United States is expected to be published in spring 2019.

- **Influenza and Zoonoses Education among Youth in Agriculture Project**
  - CDC's NCIRD and NCEZID partner with CSTE for this innovative program that educates youth about zoonotic diseases, delivers disease prevention messages, and strengthens One Health networks among state human and animal health departments and agricultural communities across rural America.
  - The program has a direct potential reach of 7.2 million youth through 4-H and Future Farmers of America but can also influence their family, mentors, friends, agricultural producers, and others.
  - Additional information about this program is available on the Influenza and One Health pages of the CDC website.

Healthy Pets, Healthy People

- OHO also coordinates the CDC Healthy Pets, Healthy People program, which provides information about the health benefits and risks of pet ownership and disseminates resources for clinicians, veterinarians, and pet owners. The Healthy Pets, Healthy People program is a "one stop" shop for information about zoonotic diseases that affect all types of animals, including pets, wildlife, and livestock.
- More than 60% of U.S. households have pets, including reptiles and other unusual pets. National Pet Week is May 5–11, 2019.

Connecting with One Health Partners—Communication and Continuing Education

- OHO coordinates Zoonoses & One Health Updates (ZOHU) Calls—monthly webinars that provide timely information on zoonotic and infectious diseases, antimicrobial resistance, food safety, vector-borne diseases, recent outbreaks, and related health threats at the human-animal-environment interface. Continuing education credits are available to participants from a variety of health professions in these calls.

Discussion

Priority Zoonotic Diseases

- The eight diseases on the U.S. list of priority zoonotic diseases are not ranked; all are considered important.
- Forty diseases were considered at the workshop, and prioritization scores are provided in the workshop report.
- Rabies, which remains a huge challenge around the world, is one of the eight priority zoonotic diseases. WHO, FAO, OIE, CDC, and many other partners have joined a campaign to eliminate rabies by 2030.

- Chronic wasting disease—which is caused by prions—was one of the 40 diseases discussed at the workshop.

Challenges to Implementing the One Health Approach

- **Engaging clinicians.** OHO is working with medical schools and state medical associations to disseminate information about One Health activities. Recent outreach efforts by partners include a One Health meeting held by the University of Saskatchewan for students from allied health professions schools and a presentation at IDWeek 2018 on zoonotic diseases of pets.
- **Funding streams.** While funding may be found for individual One Health projects—e.g., from organizations concerned with medicine, veterinary science, or environmental studies—a dedicated source of One Health funding to support collaborations on shared priorities is lacking.
- **Workforce issues.** The absence of a public health veterinarian in many state health departments is a critical gap. This gap was highlighted in the U.S. Joint External Evaluation in May 2016.
- **Unclear language**
  - Although the One Health approach has been discussed for more than a decade, interested groups have defined the One Health approach in different ways.
  - CDC and partners, including the Tripartite Collaboration, have developed definitions that can be applied to all zoonotic disease issues. As stated on the CDC website,

    > One Health is defined as a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

Ebola Outbreak in the Democratic Republic of the Congo, 2018–2019

Inger Damon, Director, Division of High-Consequence Pathogens and Pathology, NCEZID, and co-lead, CDC Ebola Coordination Team, provided an overview of the ongoing Ebola outbreak in the DRC.

Background

- On August 1, 2018, the DRC Ministry of Health confirmed an Ebola outbreak in eastern DRC. Earlier in the year, an unrelated outbreak had occurred in the Equateur Province, ending in July.
- The outbreak in eastern DRC is occurring in a highly insecure environment with armed conflicts that have made response activities difficult.[8]
- On September 26, the USAID Office of Foreign Disaster Assistance deployed a Disaster Assistance Response Team to the DRC that included disease experts from CDC.
- Since then, CDC has provided technical assistance to the DRC Ministry of Health and WHO with disease tracking, case investigation, contact-tracing, infection prevention and control, safe burials, community engagement, risk communications, and vaccinations.

[8] Maxmen A. "The World Has Never Seen Anything Like This": WHO Chief on Battling Ebola in a War Zone. Nature. May 2, 2019.

Current Status

- The Ebola outbreak in the DRC is the 10th and largest Ebola outbreak ever reported there. It is the 28th Ebola outbreak reported in Africa, second in size only to the 2014–2016 outbreak in West Africa, which involved 28,600 cases.
- As of May 7, 2019, the outbreak has involved 1,585 confirmed cases and 1,045 deaths. The epi curve indicates that the outbreak is not slowing; 276 cases of Ebola virus disease (about one-fifth of the total) have occurred over the past 3 weeks.

Vaccination

- Vaccination data were collected between May 1, 2018, and March 25, 2019, (n=93,965) and analyzed by the Institut National pour la Recherche Biomedicale (INRB) and WHO. Preliminary results suggest high efficacy of the rVSV-ZEBOV-GP Ebola vaccine when delivered using the ring vaccine strategy.[9] The rVSV-ZEBOV-GP Ebola vaccine is the Merck vaccine developed during the outbreak in West Africa.
- The WHO Strategic Group of Experts (SAGE) issued new Ebola vaccine recommendations on May 7 that
  - Endorse operational adjustments to make the vaccination process faster and allow vaccine administrators to adjust the dosage, based on available efficacy data
  - Expand the population eligible for vaccination with rVSV-ZEBOV-GP
  - Introduce an additional experimental vaccine developed by Johnson & Johnson. This additional experimental vaccine might be used to immunize lower risk populations than those targeted for the Merck vaccine.
  - Redouble ongoing efforts to train nurses, doctors, and medical students from Ebola-affected communities to work on vaccination teams

Modeling Studies to Estimate Future Cases

- The percentage of people with Ebola who are effectively isolated has *decreased* from 33% to 30%.
- Modeling studies suggest that if the percentage of people with Ebola who are effectively isolated *does not change*,
  - Approximately 19,800 people will become sick with Ebola by late September 2019.
  - The number of new cases each week will rise at an increasing rate, and there will be approximately 2,700 new cases each week by the end of September 2019.
  - The outbreak will continue at least through February 2020.
- However, if the percentage of people with Ebola who are effectively isolated increases by approximately 10% each month for the next 4 months, the outbreak would likely end by early November 2019, with a total of approximately 5,400 cases.

[9] WHO. Preliminary Results on the Efficacy of rVSV-ZEBOV Ebola Vaccine Using the Ring Vaccination Strategy in the Control of an Ebola Outbreak.in the Democratic Republic of the Congo: An Example of Integration of Research into Epidemic Response. April 12, 2019.

Challenges

- Violence in the Ebola-affected communities has hampered all response activities, including case identification, contact-tracing, and vaccination. Since January 2019, there have been
  - 119 attacks on Ebola response workers or operations
  - 42 direct attacks on health facilities
  - 85 health personnel injured or killed
- Community mistrust has increased for a variety of reasons. The International Federation of Red Cross and Red Crescent Societies, supported by analyses from CDC, is assessing community attitudes and encouraging community cooperation, which is crucial to the response.
- Much needs to be done to control the outbreak:
  - Case identification and isolation and contact-tracing and follow-up must improve.
  - Infection control training for healthcare workers must be reinforced. Training for healthcare workers is also needed to ensure that patients with Ebola virus disease are recognized and referred to appropriate centers for treatment.
  - Better options for vaccination delivery must be explored.

Deployments

- Ray Arthur, Director of the Global Disease Detection Operations Center, CGH, reported that CDC has conducted more than 250 deployments since August 2018 to aid in the outbreak response.
- CDC staff were deployed to the DRC, as well as to
  - Neighboring countries, including Uganda, Rwanda, and South Sudan, to assist ministries of health in improving preparedness in case of disease spread
  - WHO headquarters in Geneva, to provide assistance with border health issues, data management, infection control, and health communications
- An Ebola response team in Atlanta is also supporting the response.

Dr. Damon **concluded by** honoring her WHO colleague, Dr. Richard Mouzoko, from Cameroon, who was killed during an attack on an Ebola treatment center in the DRC.

Discussion

Ring Vaccination

- Vaccine efficacy data suggest that the ring vaccination strategy is working, although the lack of a control group makes the interpretation less certain. CDC and partners are working with Merck to increase the availability of the rVSV-ZEBOV-GP vaccine, and the SAGE dosing recommendations will help extend its use.
- WHO's decision to introduce a new, two-dose vaccine poses challenges in terms of logistics and community acceptance. However, immunologic studies suggest that this vaccine may be as effective (or more effective) than the one-dose rVSV-ZEBOV-GP vaccine.
- SAGE has continued to recommend ring vaccination rather than mass vaccination. In any case, current vaccine supplies are insufficient for mass vaccination.

- Disease transmission continues to occur in locations where ring vaccination cannot be implemented because of security concerns.

Risk of Cross-Border Disease Spread

- Thus far, Ebola cases have spread only in isolated areas in the DRC. If sustained transmission were to be established in a city with an international airport, the CDC Division of Global Migration and Quarantine would work with the NSC and interagency bodies to discuss additional prevention measures to reduce the risk of spread to the United States.

Response Challenges

- Dr. Damon explained that the decrease in patient isolation to 30% is due to security issues rather than to lack of isolation facilities. Patient isolation and other response activities (e.g., contact-tracing and vaccination) stop for significant periods of time after each security incident.
- Discussion is ongoing about how to better engage local communities so that response teams can work in greater safety.
- Under-reporting of Ebola cases is also a challenge. Many deaths have been reported that are not known to be contacts of earlier cases, suggesting that some cases go unrecognized.

General Discussion

Dr. Lynfield acknowledged the service of Mark Riddle, ex officio member from DoD, and Sheldon Campbell, liaison representative from the Clinical Laboratory Improvement Advisory Committee, who have completed their BSC rotations.

Dr. Butler requested advice on areas that require additional focus. Suggestions included

- Ensuring the interoperability of IT systems, including laboratory IT systems, at federal, state, and local agencies
- Addressing workforce development as a cross-cutting issue that affects a range of public health workers, including laboratorians, epidemiologists, entomologists, and public health physicians
- Understanding the causes of sporadic cases of disease, as well as outbreak cases

It was also suggested that speakers at BSC meetings explain in more detail what feedback and input they might find most useful.

Conversation with Robert Redfield, CDC Director

CDC Director Robert Redfield reviewed national priorities outlined in the *CDC Strategic Framework: A Bold Promise to the Nation*, including End Epidemics, Eliminate Diseases, and Secure Global Health and Ensure Domestic Preparedness.

Dr. Redfield emphasized the need to invest in core capacities—including data systems and laboratory capacities—that improve the ability to address a range of public health issues, from the measles epidemic to the opioid crisis. As part of this effort, CDC must address workforce issues and expand private sector partnerships.

Dr. Redfield highlighted four infectious disease priorities:

- **Eliminate new HIV infections.** Although the number of new HIV diagnoses has declined, progress in ending HIV in the United States has stalled, with the annual number of HIV diagnoses remaining the same between 2013 and 2016.[10] Data on the burden of HIV in the United States show areas where HIV transmission occurs more frequently. More than 50% of new HIV diagnoses occurred in only 48 counties; Washington, DC; and San Juan, Puerto Rico. In addition, 7 states have a substantial rural burden, with over 75 cases and 10% or more of their diagnoses in rural areas.
  - The targets of the new initiative to end HIV in the United States include a 75% reduction in new infections in 5 years and a 90% reduction in 10 years. This will be achieved by
    - Diagnosing all people with HIV as early as possible after infection
    - Treating HIV infections rapidly and effectively to achieve sustained viral suppression
    - Protecting people at risk for HIV, using potent and proven prevention interventions, including PrEP
    - Responding rapidly to HIV clusters to prevent new infections
    - Establishing local HIV HealthForce teams in targeted areas to expand HIV prevention and treatment
  - Even without a vaccine or a cure, effective tools are available to achieve these goals. No science should be "left on the shelf."
- **Increase immunizations for vaccine-preventable diseases.** Vaccines are our most powerful tools for disease prevention and our only tool for disease eradication. Vaccine-preventable diseases include
  - **Influenza.** The U.S. burden of influenza is huge, in terms of both lives and costs. In the 10 years between the 1996–1997 and 2016–2017 influenza seasons, 303 million people were infected with influenza, leading to 4.2 million hospitalizations and 360,000 deaths. The medical costs were $370 billion.
  - **HPV and Hepatitis B.** It is important to educate the public about vaccines that prevent cervical cancer and liver cancer.
  - **Measles.** The ongoing measles epidemic has highlighted the dangers of vaccine hesitancy. Intensified efforts are needed to explain the dangers of vaccine-preventable diseases and counteract misinformation.
- **Eradicate wild type polio.** CDC continues to assist ministries of health in Pakistan and Afghanistan with the polio eradication effort and to provide technical assistance when recurrences are reported in countries where polio has been eliminated.
- **Stop global outbreaks at their source.** The outbreak of Ebola in the Democratic Republic of the Congo is not yet controlled, and response activities are hampered by security issues. CDC must prepare for the likelihood that serious outbreaks will continue to occur in areas of heightened insecurity.

Dr. Redfield **concluded by** welcoming Dr. Butler as the new Deputy Director for Infectious Diseases.

[10] CDC. HIV Surveillance Report, 2017, vol. 29.

Discussion

HIV and Homelessness

- In some jurisdictions, it will be critical to address homelessness as part of ending the HIV epidemic. Dr. Redfield stressed that each jurisdiction will need to define local needs and areas of focus, which may include homelessness, mental illness, and opioid use. Eliminating HIV requires reaching out to people who are outside the health system, to develop a system of care that goes to the people who need it. It also requires eliminating stigma, which is the enemy of public health.
- The HIV initiative aims to empower local jurisdictions by setting goals and providing guidance on how to achieve them. Much may be learned as the initiative progresses.

Congenital Syphilis

- It is important that healthcare providers understand the value of screening for infectious diseases during pregnancy. Each case of CS should trigger a "social autopsy" to figure out what went wrong.
- Dr. Redfield stressed that medical care to prevent STDs and CS (like medical care to address addiction) should be part of primary care and family medicine, where it is less likely to be stigmatized. Along with Medicaid expansion, re-integration of STD screening into primary care will lead to more women receiving quality prenatal care.

Public Health Data on Gun Safety

- Data from the CDC National Violent Death Reporting System (NVDRS) can help determine how best to go forward to improve gun safety. NVDRS is expanding to include all 50 states, the District of Columbia, and Puerto Rico.

Workforce Development

- Participation in major efforts like PEPFAR and the initiative to end HIV in the United States may inspire the younger generation of health professionals to embark on careers in public health. Graduates of fellowship programs like the Public Health Associate Program may be encouraged to join the HIV elimination effort.
- Primary care clinicians are the "eyes and ears" of public health. At the present time, however, burnout and early retirement among older clinicians—as well as a preference for 9-to-5 working hours among younger clinicians—is reducing the primary care workforce. Dr. Redfield stressed that the foundational work of front-line primary care clinicians—like the work of old-time "family doctors"—requires greater recognition.
- It is becoming more difficult to fill public health physician positions at the state and local levels, and EIS classes are getting smaller, with fewer physicians in each class.
- CDC has developed a new training program called Future Leaders in Infections and Global Health Threats (FLIGHT), a multi-year leadership development program for physician and veterinarian EIS graduates. This postdoctoral, 3-year program will prepare an elite cadre of physicians and veterinarians with the skills to be effective scientific leaders and translate public health science or research into successful infectious disease programs with global applications.

Health Impact of Climate Change

- Rising air temperatures may extend the habitats of mosquitoes and ticks that carry infectious pathogens, and rising ocean temperatures may increase algal blooms associated with the bacteria that cause cholera.
- CDC can help educate the public about adaptation to and mitigation of the health effects of extreme weather events due to changes in climate.

Implementation of a World-Class Data and Analytics Strategy for Public Health

Chesley Richards, CDC Deputy Director for Public Health Science and Surveillance, used the first-ever picture of a black hole to demonstrate the power and potential of big data analysis. The CDC Public Health Data Strategy describes how this power can be harnessed to improve the nation's health.

Current Status

Janet Hamilton, Director of Science and Policy, CSTE, testified to Congress on April 9, 2019, that "data are moving slower than the disease . . . . The nation's public health data systems are antiquated and in dire need of security upgrades . . . . Significant consequences . . . [include] delayed detection and response, lost time, lost opportunities and lost lives."

Vision

- The CDC Public Health Data Strategy aims to develop world-class data and analytics to transform today's reality—and take advantage of new opportunities for life-saving prevention and response—by creating a "new world" of public health data that are more timely, accurate, and accessible. Implementation of the Strategy will move the public health community from
  - ***Reacting*** when an epidemic occurs to ***anticipating***: Getting ahead of an epidemic to stop it
  - ***Collecting data*** without the ability to rapidly analyze it to ***understanding data***: Facilitating faster analysis to gain real-time insights
  - ***Storing data in silos*** that restrict data-sharing between systems to ***sharing data on platforms***: Generating interoperable, accessible data for action
  - ***Looking back*** by using data to see what has already happened to ***looking forward***: Using data to predict and prevent threats
  - ***Moving slowly***, using outdated, paper-based systems with multiple points of data transfer, to ***moving fast***: Creating a digital highway to transfer data in real time
  - ***Using resources inefficiently***, with new resources always required to do new data collection, to ***connecting resources***: Leveraging existing resources and making common investments for the future
- Implementation of the Strategy will also advance the goals of the CDC 24-7 plan, *Using Science and Innovation to Prevent, Detect, and Respond*, which calls for accelerating public health action through world-class data, analytics, and laboratories; an elite public health workforce; strategic communication; and rapid outbreak response.

Strategy

- The CDC Public Health Data Strategy provides a roadmap for transitioning public health from a culture of primarily historical data analytics to a culture of predictive data science, supported by modern IT platforms and enterprise services that advance CDC's public health mission.
- By 2024, CDC will operate with a "new normal" for using and managing data, working across programs to advance agency initiatives and emerging priorities. The seven imperatives of the Strategy are as follows:
  - **Cloud:** CDC data will be in a cloud.
  - **Common Portal:** Data reporting to CDC will be through a common portal.
  - **Interoperability:** CDC data will be interoperable within CDC and externally.
  - **Data Sharing:** CDC data will be shared and public, while protecting privacy and confidentiality.
  - **Enterprise Level:** At the organizational level, CDC data will be catalogued, have metadata, and be labeled with appropriate access and privacy controls.
  - **Analytical Tools:** CDC scientists will have efficient access to relevant data science tools and the capability to perform both historical and predictive analyses.
  - **State and Local Support:** State and local health departments will be supported to accomplish complementary goals.

Selected Examples and Opportunities

- Implementation of the CDC Public Health Data Strategy will
  - Enhance CDC's leadership role in deploying data science tools to state and local partners. Examples include analytic tools for advanced molecular detection and infectious disease modeling.
  - Accelerate the use of common reporting streams by public health platforms such as the National Center for Health Statistics (NCHS) Mortality Surveillance System, the National Notifiable Diseases Surveillance System, and the Digital Bridge
  - Transform and improve data systems that collect information on HIV, antimicrobial resistance, and healthcare-associated infections
  - Facilitate public health linkages to healthcare, via improved immunization information systems and analytic tools that improve disease reporting and clinical decision-making
- Progress in accelerating the use of common reporting streams—and getting rid of silos—is illustrated by the Influenza Division's decision to replace its 50-year-old influenza mortality database with mortality data from NCHS.

Next Steps

Implementation of the CDC Public Health Data Strategy requires improving governance; developing partnerships with academic and private sector partners; recruiting additional data scientists; and updating CDC data-sharing policies, templates, and data registries.

Dr. Richards thanked Ms. Hamilton and CSTE Executive Director Jeff Engel for their partnership. Ms. Hamilton said that CSTE welcomes feedback from BSC members on data science issues.

Discussion

Data Science Workforce Development

- Building the public health data science workforce is a crucial, long-term effort that requires multiple approaches.
  - In regard to recruitment, Dr. Richards said that opportunities to use advanced data tools at CDC will attract well-qualified people. Some data scientists who are good candidates for private sector jobs may be more interested in advancing CDC's mission that in obtaining high salaries. However, these individuals do not want to go backward in terms of using skills that are not up to date.
  - In regard to enabling CDC employees to upgrade their skills, Dr. Richards mentioned online trainings and in-house guidance from private sector and academic data scientists who work at CDC via Interagency Personnel Agreements.

Interoperability

- Greater use of interoperable data sets will enable state and local partners to
  - Build data science capacity in partnership with CDC
  - Link state-level databases to CDC databases to support in-depth analyses
  - Maintain an individual's health-related electronic records (including immunization records) in one place and make them available via a secure portal
- It is important to learn from other jurisdictions about when to terminate a data science approach that is not working and when to modify or scale up an approach that shows promise.

Engagement with the Private Sector

- CDC and state health departments are working with private sector partners to advance the goals of the CDC Public Health Data Strategy. However, further consideration is needed to decide which "pieces" of public health data management should be handed off to the private sector. Issues include the following:
  - The risk of advancing a private sector interest over public health interests
  - Ensuring privacy and confidentiality, which is also a priority for HHS and the federal government as a whole
- CDC aims to provide the research community with as much data as possible, while taking into account privacy and confidentiality. CDC has turned down private sector data requests due to privacy concerns and has sometimes been unable to share data with other government agencies due to confidentiality concerns.

Digital Bridge

- It was suggested that CDC engage vendors of electronic records used by acute and long-term care healthcare facilities and encourage them to take public health needs into account. Dr. Richards said that such an effort is already underway, via the Digital Bridge collaborative effort.
- The Digital Bridge is a forum that brings together decision-makers in healthcare, public health, and health IT to develop a nationally consistent and sustainable approach to using electronic health data.

- The first Digital Bridge project involves electronic case reporting (eCR) from clinicians to health departments, in automated and digital form. This project builds on the CDC electronic laboratory reporting system developed under the leadership of Bob Pinner, Associate Director for Programs, Surveillance and Informatics, NCEZID.
- Each partner in the Digital Bridge—whether representing clinicians, public health workers, or IT developers—has a vested interest in the eCR project and provided input during its initial development. For example, public health organizations—including CDC, CSTE, the Association of Public Health Laboratories (APHL), and the National Association of City and County Health Officials (NACCHO)—provided a list of data fields for inclusion in eCR.
- The eCR project was piloted in Utah and Houston for 2 years, with seed money from the Robert Wood Johnson Foundation. The current goal is to scale up eCR for use in other jurisdictions.
- Future Digital Bridge projects may concern
  - Syndromic surveillance from emergency departments
  - Collection of real-time data from emergency departments on opioid use and overdoses
  - Collection of data on immunizations

Public Comments

Phone lines were opened for public comments at 3:15 PM. No comments were made.

Closing Comments

Dr. Butler thanked the BSC members for their engagement and participation, and Dr. Lynfield said that a draft letter supporting new antibiotic stewardship standards for hospitals would be sent out shortly for review.

The next in-person BSC meeting is scheduled for December 4–5, 2019. The meeting was adjourned at 3:30 PM.

APPENDIX: Meeting Participants

BSC Members

Tammy Beckham
Sheldon Campbell
Barbara Cole *(by phone)*
Jeff Duchin *(by phone)*
Emily Erbelding *(by phone)*
Mary Hayden
Denise Hinton *(by phone; representing FDA)*
Tim Jones
Salmaan Keshavjee *(by phone)*
Beth Lautner *(by phone)*
Jim Le Duc
Mike Loeffelholz
Hugo Lopez-Gatell
Ruth Lynfield
Bonnie Maldonado
Jeanne Marrazzo
Susan Philip
Mark Riddle
Lee Riley
José Romero
Susan Sharp
Kathy Talkington
Jill Taylor
Jon Temte
Debbie Yokoe

Partners and Other Public Visitors

Meredith Allen *(Association of State and Territorial Health Officials)*
Leslie Benson *(Boston Children's Hospital)**
Joel Berger*
Ann Carter*
Brandon Goldberg
Janet Hamilton *(Council of State and Territorial Epidemiologists)*
Robert Hood-Cree *(Leidos)*
Lilly Kan *(National Association of County and City Health Officials)*
Jeffrey Kluger *(TIME magazine)**
Kevin Messacar *(University of Colorado)**
Jim Nowicki *(DRT Strategies)*
Walt Orenstein *(National Foundation for Infectious Diseases)*
Robin Roberts *(AFM parent advocate)**
Monica Schroeder *(Council of State and Territorial Epidemiologists)*

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Susy McKay
Amy McMillen
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Nancy Messonnier
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Lyle Petersen
Taran Pierce
Bob Pinner
Sam Posner
Amanda Raziano
Sarah Reagan-Steiner
Robert Redfield
Chesley Richards
Janell Routh
John Sarisky*
Isaac See
Martha Sharan
Don Sharp
Sharon Slocumb
Jeanette St. Pierre*
Duane Stone
Bill Switzer*
Danielle Tack
Rob Tauxe
Sharon Tsay
Chris Van Beneden
Kate Varela
Gabriella Veytsel
Serena Vinter
Henry Walke
Cindy Weinbaum
Sarah Wiley
Michael Williams
Sabrina Williams

*These individuals were recorded as having participated by phone. Others not listed may have called in as well.

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 7–8, 2019, are accurate and complete.

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

08/14/19
Date