

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

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

September 27–28, 2016

A one-and-a-half day, open public meeting of the Board of Scientific Counselors (BSC), Office of Infectious Diseases (OID), was held on September 27–28, 2016, 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 (Appendix).

The meeting included updates from the directors of the National Center for Immunization and Respiratory Diseases (NCIRD), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), and Center for Global Health (CGH); focused discussions on the global Zika virus outbreak and on cases of hepatitis C virus (HCV) in the United States; a report from the BSC Food Safety Modernization Act (FSMA) Surveillance Working Group (SWG); and a conversation with CDC Director Thomas Frieden and presentation by CDC Deputy Director for Infectious Diseases Rima Khabbaz and discussion on planning for the future.

Opening Remarks

BSC Chair Dr. Ruth Berkelman, Rollins Professor, Emory University, called the meeting to order and was joined in welcoming participants and facilitating introductions by Dr. Rima Khabbaz, CDC Deputy Director for Infectious Diseases, and Robin Moseley, the BSC/OID Designated Federal Official.

NCIRD Update

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

Leadership Changes

- Allen Craig is the new Deputy Director of NCIRD.
- Brandi Limbago is the new Associate Director for Laboratory Science, replacing Tim Barrett, who retired.
- Rana Hajjeh, former Director, Division of Bacterial Diseases, has left CDC to be director of communicable diseases at EMRO, World Health Organization (WHO); recruitment for a new division director is underway.
- Jane Seward, Deputy Director, Division of Viral Diseases, has retired. Recruitment for this position is also underway.

Vaccine Coverage: Maintaining and Strengthening Immunization Programs

- Vaccine coverage for children
 - Dr. Messonnier reviewed progress made in reducing vaccine-preventable childhood diseases in the United States by comparing the annual morbidity from each disease during the 20th century with the number of reported cases due to each disease in 2015. She noted 99–100% decreases in smallpox, diphtheria, measles, mumps, polio, rubella and congenital rubella syndrome, and *Haemophilus influenzae* infections, as well as 96% decreases in tetanus, and 91% decreases in pertussis.
 - Less than 1% of U.S. toddlers have received no vaccines.
 - Current focus areas include improving access to vaccines for children whose families are living below the poverty level and for children in some rural areas.
- Vaccine coverage for adolescents: human papillomavirus (HPV) vaccine
 - Current data suggest that 2 doses (rather than 3) are sufficient to build immunity to HPV.
 - Lessons learned about improving HPV vaccine coverage include
 - Provider-level interventions are effective, but difficult to bring to scale.
 - Ongoing engagement and coalition-building at the national, state, and local levels continues to be important.
- 2014 performance rates for adolescent immunization coverage, based on Medicaid/Children’s Health Insurance Program (CHIP) Children’s Health Care Quality Measures, indicate that HPV vaccination of teens lags behind rates for Tdap (tetanus, diphtheria, and pertussis) vaccine and meningococcal vaccine. An updated 2017 HEDIS (Healthcare Effectiveness Data and Information Set) measure on adolescent immunization will help advance CDC’s efforts to increase HPV coverage, which include
 - Encouraging state-level immunization-program planning efforts to include major payers and health systems, including Medicaid managed care organizations
 - Addressing HPV vaccine coverage in conversations with national payers, health systems, and Medicaid
 - Partnering with groups that focus on cancer prevention to provide educational materials to parents and clinicians
- Vaccine coverage for adults
 - According to the National Health Interview Survey (NHIS), the proportion of adults reporting vaccination with selected vaccines—including vaccines against influenza, zoster, and pneumococcal pneumonia—has held steady but has not increased significantly between 2010 and 2014. Seasonal influenza vaccine, for example, has increased 43.7% to 59.3% among children, while remaining at 40–42% among adults.
 - On September 29, the National Foundation for Infectious Diseases (NFID) and CDC held a joint press conference to kick off the 2016–17 flu vaccination campaign. National estimates were provided for influenza vaccination coverage among the general population, pregnant women, and healthcare personnel.
 - The expansion of private insurance, along with Medicaid expansion (in 32 states), is likely to increase U.S. vaccination coverage rates.

Modernizing Immunization Practice and Information Technology (IT)

- NCIRD is making IT investments to modernize immunization practice by
 - Including barcodes on vaccines so that their use can be recorded in e-health records in doctors' offices
 - Enhancing the Vaccine Tracking System (VTrckS) and the Immunization Information System (IIS)
 - Providing technical support to healthcare providers for clinical decision-making
 - Ensuring interoperability of federal, state, and local components of the IIS
- Data collected between 2006 and 2014 indicate that most children have immunization records recorded in IIS (about 89%). That is not the case for adolescents (61%) and adults (33%).
- Progress has been made at the state and local levels to improve data quality and enable only sharing of vaccine coverage data reported to CDC among states, including
 - Increasing the quality and availability of state-level data
 - 41 states are collecting data to determine kindergarten vaccination coverage.
 - 45 states are collecting data to evaluate the number of exemptions.
 - Local-level data are now available online, via [VaxView](#), with 24 states reporting local-level coverage and/or exemption data this year. VaxView includes interactive coverage data available online, for children, teens, and adults.

Challenges

- A measles outbreak occurred in an immigration and customs enforcement detention facility in Arizona last April, with 22 cases among detainees and staff.
- The epidemiology of mumps may be changing, with multiple outbreaks occurring at colleges (in 2006 and in 2014–16) and among school-aged children (2009–10).
- Reports of whooping cough have been rising since the mid-2000s.
- The live attenuated influenza vaccine (LAIV), the “nasal spray” flu vaccine, did not work effectively last year, and the Advisory Committee on Immunization Practices (ACIP) voted in June that it should not be used during the 2016–2017 flu season. CDC is working with the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), manufacturers, and international partners to understand why LAIV did not work as expected.

New Programs and Priorities

- New developments under consideration include
 - A reduced-dose HPV vaccination schedule (from 3 doses to 2)
 - More widespread use of the shingles vaccine among adults. [Studies](#) indicate that the vaccine is highly effective.
 - Introduction of a vaccine against respiratory syncytial virus (RSV)
- CDC is using innovative technologies to improve prevention and detection of vaccine-preventable diseases. Examples include
 - The Sequence First Initiative, which expands the use of whole genome sequencing- (WGS-) based diagnostics

- Increased use of “cloud sequencing” to support disease surveillance, via the [APHL \(Association of Public Health Laboratories\) Informatics Messaging Services](#) (AIMS) platform
- CDC and partners are also promoting better [water management](#) programs to reduce the risk for growth and spread of *Legionella* within water systems and devices.
- Looking forward, NCIRD major efforts include
 - Continuing to focus on disease prevention, with many successes but much more to do
 - Harnessing innovation and technology
 - Going beyond U.S. borders to build global capacity for public health
 - Sustaining and strengthening partnerships

Discussion

- Vaccine coverage in rural areas
 - BSC members discussed obstacles to improved access to vaccines for rural areas, as well as the impact of the Medicaid expansion on vaccine coverage.
 - Small medical practices in sparsely populated areas may not be able to maintain an inventory of HPV vaccines. Local solutions to these issues (e.g., options for fronting these costs) should be shared among the states.
 - Dr. Khabbaz noted that an *MMWR* report on rural health issues is expected in January.
- Increasing vaccine coverage for teens and adults
 - Vaccination of teens and adults may in the future be routinely conducted at (and promoted by) non-traditional partners, such as retail clinics and pharmacies. These partners could enter vaccination information into IIS for public health purposes.
 - Dr. Messonnier noted that there is not likely to be a single way to increase teen and adult vaccination, and that additional suggestions are welcome.
 - It was suggested that IIS might be used to track vaccine coverage among pregnant women.
 - Regarding HPV vaccine
 - BSC members commended the re-energized focus on HPV and the emphasis on the role of HPV vaccine in cancer prevention.
 - CDC might partner with school-based clinics and pharmacies to help ensure that teens return for the second dose of HPV.
 - The change to a 2-dose schedule, with the second dose provided after 6–12 months, may enable more teens to be immunized against HPV at annual check-ups.
- Legionnaires’ disease
 - BSC members discussed the need at all levels of government for more technical expertise, including expertise in environmental engineering, to advance prevention of Legionnaires’ disease.
 - Other suggestions included the need for improvements in clinical and environmental diagnostics and for evaluation of the CDC water management toolkit.
 - Dr. Berkelman noted that in its earliest days, CDC employed many entomologists and engineers in its efforts to address waterborne diseases and eliminate malaria.

- Other comments
 - Mumps vaccine issues will be on the 2017 ACIP agenda, in view of uncertainties about vaccine use during outbreaks and the increasing number of mumps outbreaks at colleges.
 - Dr. Messonnier noted that most global vaccine policy issues are addressed by CGH. NCIRD maintains laboratories that address diagnostic issues related to control of polio and measles.

Zika Virus Outbreak

Overview: CDC’s Zika Response Strategy for the Continental United States— Beth Bell, Director, NCEZID

The Zika outbreak represents the first time in history that a mosquito-borne disease has been linked to a human birth defect. Moreover, it has been more than 50 years since another infectious pathogen (rubella virus) was identified as a major cause of congenital defects.

Background

- Zika virus—discovered in the Zika Forest of Uganda in 1947—is a single-stranded RNA flavivirus. It is closely related to the viruses that cause dengue, yellow fever, Japanese encephalitis, and West Nile disease.
- Zika virus disease is transmitted primarily by *Aedes* species mosquitoes but can also be spread through congenital, sexual, and blood transmission.
- Typical symptoms include fever, rash, conjunctivitis, and myalgia; however, about 80% of infections are asymptomatic. Zika virus is detectable in serum, urine, saliva, and semen.
- According to data from ArboNET (a national arboviral surveillance system managed by CDC and state health departments) collected between January 1, 2015, and September 21, 2016, there have been
 - 3,314 travel-associated cases and 43 locally acquired mosquito-borne cases in the continental United States. Twenty-eight cases were sexually transmitted, and 8 cases involved Guillain-Barre Syndrome (GBS). Travel-associated cases have been reported from all states but Alaska.
 - 71 travel-associated cases and 19,706 locally acquired cases in U.S. territories. Thirty-seven cases involved GBS.
- According to the U.S. Zika Pregnancy Registry and the Zika Active Pregnancy Surveillance System in Puerto Rico (see below), as of September 15, 2016, 1,348 pregnant women in U.S. territories and 749 pregnant women in the 50 states and Washington, DC, have laboratory evidence of Zika infection. Twenty-one live-born infants with birth defects have been reported.

The Strategy

- The priority of the Zika response strategy for the United States is to protect pregnant women and their pregnancies. It includes three phases that depend on a jurisdiction’s level of risk: 1) preparedness, 2) confirmed local transmission, and 3) confirmed multiperson local transmission.
- Implementation requires state and local readiness and leadership, as well as a multidisciplinary approach that combines action in such areas as emergency response, disease surveillance, vector surveillance and control, birth defects surveillance and follow-up, risk communications, laboratory diagnostics, and blood safety.

- CDC has provided travel and testing recommendations for pregnant women, women of reproductive age, and their partners in areas of active Zika virus transmission in Miami, as well as advice for people living in or [traveling to South Florida](#).
- In addition to guidance for healthcare providers (see below), CDC has posted [guidance](#) on Zika testing, mosquito surveillance and insecticide testing, specimen collection, vector control, blood safety, and prevention of sexual transmission.
- As of late September 2016, CDC has also posted travel notices for 57 countries in Asia, the Caribbean, Central America, the Pacific Islands, and South America, as well as guidelines for travelers in areas with ongoing Zika virus transmission.

Diagnostic Testing

- Diagnostic testing for Zika includes rRT-PCR testing for viral RNA in serum and urine and serologic testing for IgM and neutralizing antibodies in serum. Due to a short period of viremia in most patients, PCR testing is used only in samples collected less than 14 days post-onset. There are difficulties distinguishing by serologic testing Zika infection from previous infection with (or vaccination against) a related flavivirus (e.g., dengue).
- FDA has issued Emergency Use Authorizations (EUAs) for two CDC assays:
 - Zika MAC-ELISA for presumptive detection of Zika IgM antibodies in serum or cerebrospinal fluid (CSF). Positive specimens are analyzed further, using plaque reduction neutralization tests (PRNT)
 - Trioplex rRT-PCR for detection of Zika, dengue, and chikungunya viral RNA in serum, whole blood, and CSF for all three diseases and also in urine and amniotic fluid for Zika
- CDC's Zika diagnostic assays have been distributed in the United States through the Laboratory Response Network (LRN) and have also been distributed internationally. As of June 2, 343 kits have been requested by 94 countries, and 338 kits have been shipped.
- Seven commercial diagnostic manufacturers have received EUAs for PCR tests for Zika virus RNA, and one has received an EUA for an IgM ELISA. Three commercial laboratories (Quest, LabCorp, and Mayo) have licensed the CDC Zika MAC-ELISA. This is the first time a CDC test has been licensed to a commercial laboratory.
- CDC is helping states at high risk of local transmission meet potential demand for Zika testing.

Public Health Communications

Health communication messages during the Zika response have been disseminated via 13 news media telebriefings, 16 press releases and statements, 5,264 posts on social media, and multiple web postings (cumulatively viewed approximately 66 million times) that include infographics, fact sheets, videos, and weekly "Zika Key Messages." A total of 22,358 phone inquiries (via CDC-INFO) have been answered, and CDC has held 12 Crisis and Emergency Risk Communication webinars. CDC is also available 24/7 to answer clinical inquiries via the Zika Pregnancy Hotline (770-488-7100).

Future Directions

To better protect pregnant women and their pregnancies, CDC and partners will

- Continue to define the clinical spectrum of Zika virus disease
- Strengthen surveillance and reporting of cases

- Follow up cases through pregnancy registries
- Improve laboratory diagnostics and expand speed and access to testing
- Implement robust vector surveillance and control programs
- Identify and promote personal protection measures
- Issue new and revised clinical and public health guidance
- Encourage innovative approaches to the prevention of Zika

Clinical Features of Congenital Zika Syndrome—Coleen Boyle, Director, National Center on Birth Defects and Developmental Disabilities (NCBDDD)

Background

- Over the past year, medical and public health professionals have reviewed mounting evidence of a link between Zika virus infection during pregnancy and microcephaly. On April 13, 2016, CDC concluded that [Zika virus is a cause of microcephaly and other brain anomalies](#).
- *Congenital Zika syndrome* (CZS) is a pattern of congenital anomalies associated with Zika virus infection during pregnancy that include microcephaly, intracranial calcifications and other brain anomalies, eye anomalies, and others (such as clubfoot and contractures).
- Research studies indicate that
 - Pregnant women are no more susceptible to Zika virus or more likely to experience severe disease than non-pregnant women.
 - Zika virus infection can occur during any trimester of pregnancy.
 - Zika virus infection in a woman who is not pregnant does not pose a risk for birth defects in future pregnancies after the virus has cleared from her blood.

Interim Guidance for Pregnant Women and Healthcare Providers

The provision of guidance to protect pregnant women and their pregnancies is a major component of CDC's response strategy. Guidance has been provided for

- Pregnant women
 - CDC recommends that pregnant women not travel to areas with Zika.
 - If a pregnant woman must travel, she should talk with her healthcare provider first.
 - If she has a partner who lives in or travels to an area with Zika, she should ensure her partner uses a condom every time she has sex or refrain from having sex during the pregnancy.
- [Healthcare providers caring for pregnant women with possible Zika exposure](#)
 - *Symptomatic pregnant women*, who
 - Are evaluated less than 2 weeks after symptom onset, should receive Zika virus rRT-PCR testing of serum and urine
 - Are evaluated 2–12 weeks after symptom onset, should be tested for anti-Zika virus IgM antibodies. If the IgM result is positive or equivocal, rRT-PCR should be performed on serum and urine samples. If the rRT-PCR result is negative, PRNT should be performed.

- *Asymptomatic pregnant women, who*
 - Live in areas *without* active Zika virus transmission, but had an exposure and *are being evaluated less than 2 weeks after their last possible exposure*, should receive rRT-PCR testing of both serum and urine. If the rRT-PCR test is negative, a Zika IgM test should be performed 2–12 weeks after the exposure.
 - Live in areas *without* active Zika virus transmission but had an exposure and *are being evaluated 2–12 weeks after their last possible exposure*, should receive IgM antibody testing. If this test is positive or equivocal, serum and urine rRT-PCR should be performed.
 - Live in areas *with* active Zika virus transmission, should receive Zika virus IgM antibody testing as part of routine obstetric care during the first and second trimesters, with immediate rRT-PCR testing of women who are IgM-positive or equivocal
- [Healthcare providers caring for infants and children with possible Zika infection](#)
 - Infants with confirmed or possible congenital exposure to Zika infection should be evaluated as soon as possible and prior to discharge from the hospital.

The CDC Foundation is supporting the Zika Contraception Access Network (Z-CAN), a network of clinics across Puerto Rico that assist women who want to delay or avoid pregnancy during the Zika outbreak. CDC is also enhancing pregnant women’s personal protection by distributing Zika Prevention Kits in affected US territories and providing targeted messages on personal protection.

Research and Surveillance to Monitor Pregnancy and Infant Outcomes—Peggy Honein, Co-Lead, Pregnancy and Birth Defects Task Force, CDC Zika Virus Response

Research on Zika Virus Infection during Pregnancy

- Research questions under investigation include
 - What is the level of risk from a Zika virus infection during pregnancy?
 - When during pregnancy does Zika virus infection pose the highest risk to the fetus?
 - What is the full range of potential health problems that Zika virus infection may cause?
 - Are there other factors (e.g., co-infections) that affect the risk for birth defects?

Data for Action: Surveillance to Monitor Pregnancy and Infant Outcomes

- CDC-supported surveillance programs to determine the timing, absolute risk, and spectrum of outcomes associated with Zika virus infection during pregnancy include
 - **U.S. Zika Pregnancy Registry:** A collaboration with state, tribal, local, and territorial health departments to collect information about U.S. women with laboratory evidence of possible Zika virus infection during pregnancy and about their infants
 - **Zika Active Pregnancy Surveillance System (ZAPSS):** A collaboration with public health and medical partners in Puerto Rico to evaluate the association between Zika virus infection during pregnancy and adverse outcomes during pregnancy, birth, and early childhood up to age 3 years
 - **U.S. Zika-related birth defects surveillance:** Zika-related birth defects surveillance established in 45 jurisdictions to monitor brain abnormalities, including microcephaly, and central nervous system defects. This activity will identify infants with birth defects and congenital Zika virus

exposure who are not included in the Zika registries because their mothers' Zika infections were not detected prenatally.

- **Proyecto Vigilancia de Embarazadas con Zika (VEZ):** A collaboration with the Instituto Nacional de Salud in Colombia. Proyecto VEZ is monitoring the health of over 1,000 pregnant women in three cities to identify the spectrum of adverse fetal and infant outcomes associated with CZS and estimate the risk of each adverse outcome by trimester of maternal Zika infection
- In addition, the Colombian Instituto Nacional de Salud, in collaboration with CDC, is conducting a prospective cohort study of pregnant women, their male partners, and their newborns called the **Zika en Embarazadas y Niños (ZEN)** project. Its aims are to characterize risk factors for Zika infection in pregnancy, identify gestational ages during which Zika infection causes fetal harm, determine the duration of viral persistence in body fluids, and identify risk factors for maternal-to-child Zika virus transmission. The plan is to extend infant follow-up from age 6 months to 5 years.

Vector Control Challenges and Successes—Lyle Petersen, Incident Commander, CDC Zika Virus Response

Background

- Zika virus is carried principally by *Aedes aegypti* and *Aedes albopictus* mosquitoes. *Ae. aegypti* is the more efficient vector, because it preferentially feeds on humans.
- *Aedes* mosquitoes are difficult to control, because they can bite indoors, feed both during the day and at night, and lay eggs near small amounts of water. Their resistance to insecticides varies in different locations and is poorly documented in most areas. Essentially, all past efforts to control *Aedes* mosquitos during outbreaks have failed.
- *Ae. aegypti* and *Ae. albopictus* are widely distributed throughout tropical areas in the Americas, Africa, Asia, and Oceania. They are also present in some temperate areas, including [large parts of the United States](#).

Vector Control in Areas of Active Zika Transmission in Miami, Florida

- Two of the first four U.S. cases of locally transmitted mosquito-borne Zika infection were linked to a small area in the neighborhood of Wynwood in Miami, in late July 2016. Further epidemiologic and laboratory investigations identified a total of 29 people in the area with recent Zika virus infection and likely exposure during late June through early August. CDC issued travel and testing guidance on August 1.
- Mosquito trapping studies showed high numbers of *Ae. aegypti* females and a large number of potential breeding sites for mosquitoes. Initial ground-based control efforts involving backpack- and truck-spraying with pyrethroid insecticides had limited effect, apparently due to insecticide resistance. Beginning in early August, these efforts were augmented with aerial spraying consisting of
 - An ultra-low volume of naled, an organophosphate insecticide that kills adult mosquitoes, within a 10-square-mile area
 - The larvicide *Bacillus thuringiensis israelensis* (Bti), within a central 2-square-mile area
- After the second aerial spraying with naled, female *Ae. aegypti* counts decreased to 1 per trap per day. Although mosquito counts gradually returned to high levels (>20/trap) in the adulticide-only spray area, they remained at about 5–10 per trap per day for more than 1 month in the area treated

with both adulticide and larvicide. No additional cases of Zika infection were identified that were likely due to post-spraying mosquito bites, and no increases in emergency department patient visits were associated with aerial spraying.

- Preliminary data show similar reductions in mosquito counts following aerial spraying in Miami Beach. Nevertheless, aerial spraying of insecticides in Miami remains highly controversial.

Vector Control Capacity and Capacity-Building

- Key areas of need include
 - Efficacy data on existing methods for controlling *Ae. aegypti* and preventing human illness in local settings. Obtaining this data will require a renewed emphasis on operational research.
 - Local information on insecticide sensitivity and resistance
 - A wider range of vector control options, including new pesticides that can be used safely for public health purposes
 - Capacity-building at the state, local, and federal levels, at mosquito control programs and at academic institutions
 - Effective risk communication to address public concerns about mosquito-borne diseases and pesticides
 - A central coordinating institution for vector control efforts
- A survey to assess core competencies among 164 vector control programs in states at highest risk for Zika virus transmission found significant gaps in local capacities to conduct mosquito surveillance, make treatment decisions based on mosquito surveillance data, use insecticides, and test for pesticide resistance. CDC's plan for moving forward includes
 - Addressing vector control capacity needs by
 - Hiring state-level vector-borne disease prevention and control specialists, working through the [Epidemiology and Laboratory Capacity for Infectious Diseases](#) (ELC) program, and establishing a Vector Control Unit in Puerto Rico
 - Supporting training and capacity-building efforts in partnership with the American Mosquito Control Association and Vector-Borne Disease Regional Centers of Excellence ([VBD CoEs](#))
 - Providing data support for operational decisions by
 - Collecting local information on insecticide sensitivity and resistance, working through the ELC program
 - Conducting field evaluations and operational research, working with the VBD CoEs
 - Improving methods for control of *Ae. aegypti* by
 - Working with research partners to expand the knowledge base and implement pilot projects to test new methods of vector control, including field trials of autocidal gravid ovitraps, such as the In2Care mosquito traps
 - Working with the Biomedical Advanced Research and Development Authority (BARDA) under an Interagency Agreement to support U.S. Environmental Protection Agency (EPA) registration of the natural product insecticide nootkatone
 - Coordinating national and international research efforts

Panel Discussion

Drs. Bell, Boyle, Honein, and Petersen addressed questions posed by BSC members.

Resources and Partnerships

- BSC members emphasized the need to build local surveillance capacity for Zika virus infection, to rebuild capacity for vector surveillance and control in many states, and to educate the community on ways to reduce mosquito breeding sites. The BSC expressed the need for sustained funding and expertise in vector control programs in the United States.
- Continued coordination among federal agencies, including CDC, NIH, BARDA, FDA, and EPA, is imperative.

Vaccine Development

- Irene Glowinski, National Institute of Allergy and Infectious Diseases (NIAID), NIH, reported that NIAID has two candidate Zika vaccines in development and is also supporting research on therapeutics and diagnostics. Dr. Petersen noted that antibody-dependent enhancement¹ has not turned out to be a problem with the one marketed dengue vaccine despite incomplete protection for all four dengue serotypes and may not be an issue in vaccine development for Zika.

Diagnostic Testing

- Guillermo Ruiz-Palacios, Mexico National Institutes of Health and Tertiary Referral Hospitals, described the preliminary results of cohort studies in Champas, in southern Mexico, in which individuals with symptomatic and asymptomatic Zika infections have been closely monitored. The period of viremia was found to last only up to a week. Within 5 to 7 days of symptom onset, blood samples no longer tested positive by PCR although urine tests remained positive. In areas endemic for dengue, more than 80% of the cohort did not have an IgM response to Zika virus, even when patients had acute infections. Dr. Petersen reported similar preliminary results in studies in Puerto Rico.
- BSC members commented that it would be useful to have IgG tests or other serologic assays that could 1) detect Zika infection beyond the 7-day window, 2) distinguish between Zika and dengue infections, and 3) facilitate screening of patients (including pregnant women) with a history of travel to areas with Zika transmission.
- Dr. Petersen reported that preliminary information suggests that nucleic acid might be detected in whole blood for a longer period of time if certain nucleic acid extraction techniques are used. This finding will be investigated further and disseminated in updated testing guidelines if confirmed.

Research Questions

- Priority research questions identified by BSC members included 1) whether Zika-related neurological symptoms occur in young children, teens, and adults; 2) whether Zika virus can be transmitted via breast milk; 3) whether co-infections or sexual transmission of Zika increases the risk of CZS; 4) whether aerial spraying of naled at low volumes poses health or environmental risks; and 5) whether current prevention messages are effective.

¹ A phenomenon noted with dengue virus infections in which a person previously infected with one serotype of a virus experiences more severe disease when later infected with a different serotype

Zika Transmission in Miami

- The following information was provided by Dr. Petersen in response to questions:
 - It is not known whether the outbreaks in Wynwood and Miami Beach were connected. Both are tourist areas with a higher likelihood of viral introduction from travelers from areas where Zika transmission is ongoing, and it is difficult to pinpoint the location of individual exposures.
 - Because the mosquito population in Florida decreases in the winter, Zika transmission may not be sustained over the winter months. However, in Key West in 2013, transmission of dengue continued for more than 18 months.
 - Mobilization of communities to get rid of mosquito breeding sites is an important, but not sufficient, component of vector control.
 - Vector control currently has “no home” in the federal government. Ideally, a national coordinating vector program would support applied research at academic institutions, provide training fellowships in vector biology and mosquito control, coordinate public and private sector partnerships, and support state and local mosquito control districts.

NCEZID Update

Dr. Bell provided the following updates.

Antibiotic/Antimicrobial Resistance (AR)

CDC Antibiotic Resistance Solutions Initiative

The CDC [Antibiotic Resistance Solutions Initiative](#) focuses on patient safety, building and expanding on success in preventing healthcare-associated infections (HAIs). Components include

- Detect and respond
 - Establish an Antibiotic Resistance Lab Network (ARLN) for nationwide detection of antibiotic-resistant pathogens
 - Support robust surveillance systems to track antibiotic-resistant infections and patterns, as well as antibiotic use
 - Build laboratory capacity in all 50 states to stop carbapenem-resistant Enterobacteriaceae (CRE)
- Prevent infections
 - Establish state-level prevention networks
 - Work with health systems
 - Learn from new patient protection discoveries
 - Leverage microbiome research
- Improve antibiotic use
 - Scale up antibiotic stewardship and sepsis education, nationwide
 - Improve AR diagnosis and treatment
 - Continue the AR isolate bank to advance development of new drugs and diagnostics

The fourth component is *innovation*: continually improving and developing new approaches to the prevention of AR that maximize public health impact.

Building on Success to Prevent HAI, AR, and *Clostridium difficile*

The CDC Antibiotic Resistance Solutions Initiative builds on past success in

- Using a regional approach to prevent HAI spread between healthcare facilities (see CDC [Vital Signs](#))
- Supporting state-level projects to prevent HAIs, AR, and *C. difficile*. Examples include
 - Using data for action (Tennessee)
 - Data were used to identify hospitals in Tennessee with the most central line-associated bloodstream infections (CLABSIs), in order to focus prevention efforts.
 - Reduction goals and priorities were established, and HAI/AR prevention activities were integrated into networks and state hospital associations funded by the Centers for Medicare & Medicaid Services (CMS).
 - CLABSIs were reduced 50% between 2008 and 2014.
 - Preventing *C. difficile* infections (CDI) (New York)
 - State prevention partnerships were established to produce and promote prevention tools and stewardship programs.
 - CDI reductions were tracked, with more hospitals and nursing homes reporting National Healthcare Safety Network (NHSN) data and with data collected by Emerging Infections Programs.
 - Hospital-onset CDI decreased 10% from 2013–2015.

As part of the Initiative, HAI/AR prevention networks—where public health and health care work together—will be established across the country.

- **Detection & Response:** In all 50 states, 6 cities, and Puerto Rico, CDC is supporting local AR expertise and laboratory capacity to improve identification and response to all emerging threats, leading to synchronized action across health care and communities to quickly protect patients and control spread.
- **Prevention & Stewardship:** In 25 states and 3 cities, CDC is aggressively expanding CRE, *C. difficile*, and other multidrug-resistant organism (MDRO) prevention and antibiotic stewardship programs, implementing proven strategies in healthcare facilities to prevent infections and transmission across healthcare settings.

Improving Antibiotic Use, Protecting Patients, and Building AR Laboratory Capacity

Action steps under the Antibiotic Resistance Solutions Initiative include

- Expanding efforts to improve antibiotic use. This aim will be achieved through
 - *Better data to drive action*, obtained by
 - Expanding NHSN antibiotic use reporting to guide local prevention
 - Using state outpatient prescribing-rate data as the basis for action
 - Supporting diagnostic innovations to improve prescribing
 - Better defining sepsis epidemiology and piloting a new sepsis surveillance definition

- *Enhanced prevention to save lives.* CDC and partners will
 - Implement CDC [Core Elements](#) for antibiotic stewardship in acute care hospitals, nursing homes, and outpatient settings and aligning sepsis prevention and stewardship programs in hospitals
 - Tailor state programs to improve prescribing in hospitals and communities
 - Assess the impact of strategies to improve prescribing and to treat and prevent sepsis
- *Heightened public awareness to improve antibiotic use and prevent sepsis.* Activities include
 - Expanding the [Get Smart: Know When Antibiotics Work](#) program
 - Promoting sepsis recognition and awareness among healthcare professionals, patients and families, and partners
- Protecting patients by developing health policies that promote antibiotic stewardship
 - CDC works with many partners to integrate proven infection control and AR prevention strategies into national policies. For example,
 - The Joint Commission used technical input from CDC to develop a new standard that calls for antibiotic stewardship programs in diverse healthcare settings, including critical access hospitals, ambulatory care organizations, nursing care centers, and office-based surgery practices.
 - Other potential federal policies may require healthcare facilities to implement infection control programs that include antibiotic stewardship and antibiotic use monitoring. These policies may require reporting of data on antibiotic use.
- Protecting patients by setting national targets for outpatient antibiotic prescribing
 - 47 million unnecessary antibiotic prescriptions are written every year. A [recent study](#) found that prescribing practices vary among states, patient populations, and provider specialties.
 - The National Strategy for Combating Antibiotic-Resistant Bacteria (CARB) includes the following stewardship targets for 2020:
 - Establishment of antibiotic stewardship programs in all acute care hospitals and improved antibiotic stewardship across all healthcare settings
 - Reduction of inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient settings
- Creating a CDC ARLN (see also page 20). ARLN will
 - Conduct nationwide testing to fill data gaps, in order to inform AR prevention and response efforts
 - Track changes in resistance for hard-to-treat pathogens
 - Conduct sentinel surveillance for new and unusual resistant threats
 - Pilot strategies to collect critical public health data in an era of culture-independent diagnostics

A map showing the locations of the seven ARLN laboratories (with information on their testing functions) is available on the [Antibiotic Resistance Lab Network](#) page of the CDC website.

- Using WGS for next-generation tracking of AR
 - WGS enables rapid detection of genes that make bacteria resistant to antibiotics, allowing public health officials to pinpoint the sources of outbreaks caused by antibiotic-resistant pathogens. WGS also provides detailed data to identify new resistance patterns and trends.
 - In partnership the NIH National Center for Biotechnology Information, FDA, and the U.S. Department of Agriculture (USDA), CDC is building on the advanced molecular detection (AMD) *Listeria* Project to provide AR sequencing data and perform outbreak analyses.

Foodborne Antibiotic-Resistant Infections, Drug-Resistant Gonorrhea, and Multidrug-Resistant TB (MDR-TB)

- Combating foodborne antibiotic-resistant infections by building laboratory capacity to
 - *Detect and describe resistant bacterial rapidly.* CDC and partners will build state laboratory capacity to use WGS to rapidly identify foodborne drug-resistant bacteria, including *Campylobacter* and *Salmonella*.
 - *Find outbreaks faster by increasing laboratory testing.* Every *Salmonella* isolate will be tested for drug resistance.
 - *Improve health outcomes.* With greater laboratory capacity, states will be able to track, investigate, and control outbreaks of life-threatening *Salmonella* infections.
 - *Promote responsible antibiotic use in food-producing animals.* Responsible use of antibiotics to prevent drug resistance will be advanced by providing tools, information, and training to practicing veterinarians.
- Combating other community antibiotic resistant threats, including
 - *Resistant gonorrhea.* The aims are to rapidly detect resistant gonorrhea, rapidly respond to reduce the spread of resistant gonorrhea, and improve patient treatment.
 - *MDR-TB.* The aims are to identify new interventions against MDR-TB domestically and internationally, create a National TB Stockpile to prevent TB medicine shortages, and expand overseas TB screening for new visa categories.

Innovation and Research

- Innovative implementation of proven AR prevention strategies
 - CDC is working with many partners to implement proven prevention strategies to change clinical practice and maximize public health impact.
 - Efforts conducted in partnership with health systems include
 - Working with CMS quality improvement partners on infection control and stewardship
 - Testing regional interventions (e.g., in Orange County, California, and in Chicago) to reduce the incidence of MDRO infections
 - Improving antibiotic use through implementation and evaluation of Core Elements of Antibiotic Stewardship at hospitals, nursing homes, and outpatient settings
 - Improving antibiotic use and stewardship in veterinary practice

- Efforts conducted in partnership with academic investigators (e.g., at Prevention Epicenters) include
 - Testing innovative strategies for improving the use of personal protective equipment, hand hygiene, and environmental cleaning
 - Conducting multicenter randomized controlled trials, for example,
 - Of early discontinuation of empiric antibiotics started for possible respiratory infections among patients on mechanical ventilation
 - To detect hospital-based outbreaks compared with routine methods for detecting and containing outbreaks
 - Conducting multicenter studies to, for example,
 - Define factors, exposures, and fecal microbiota characteristics that predict acquisition of enteric MDROs in a multicenter cohort of ICU patients
 - Evaluate pre-operative antimicrobial therapy as a risk factor for surgical site infection
- Microbiome applied research. Aims include
 - Predicting the impact of new and old antibiotics on the microbiome (e.g., by evaluating the disruptive potential of each antibiotic)
 - Determining how to tailor antibiotic stewardship to a patient’s microbiome and/or to a specific population of patients (e.g., in a hospital unit or doctor’s office)
 - Developing and testing microbiome diagnostics and protocols (e.g., diagnostics that measure and monitor a patient’s risk for colonization or transmission)
 - Supporting development of therapeutics that restore and protect the microbiome when antibiotics must be used
- The AR Isolate Bank
 - CDC and FDA have established an AR isolate bank that will help researchers develop new diagnostic tests and antibiotic drugs.
 - As of late September 2016, the bank includes 398 unique isolates on 11 panels, including new threats like *Candida auris* and *Escherichia coli* that carry the *mcr-1* gene. Since July 2015, CDC has processed 211 orders.

Advanced Molecular Detection

Future directions for the AMD Initiative include

- Expanding sequencing technology capacity to additional states and applying it to additional pathogens (e.g., influenza, TB, and foodborne pathogens monitored by the National Antimicrobial Resistance Monitoring System (NARMS) and PulseNet, the national laboratory network that connects foodborne illness cases to detect outbreaks)
- Addressing disease surveillance gaps caused by the decreased availability of microbial isolates, due to greater use of culture-independent diagnostic tests (CIDTs). As recommended by the BSC Infectious Disease Laboratory Working Group, CDC and partners will identify and implement both stop-gap measures and long-term solutions to meet this challenge.

- Advancing workforce development, by
 - Funding states to form regional training networks and collaborate with academic partners
 - Providing on-line training for epidemiologists through the Integrated Food Safety Centers of Excellence (CoEs)

An external review of the AMD Initiative will be held December 1–2, 2016. The aim is to gather expert insight and ideas on the AMD program’s progress and opportunities for the future. The external review will take place 5 years after the Bioinformatics Blue Ribbon Panel, which helped spur the development of the AMD program.

Sepsis

Sepsis Investigation

- CDC and partners conducted a retrospective chart review in four New York hospitals last January to describe clinical characteristics, comorbidities, and potential opportunities for infection prevention among patients with sepsis.
- The review, which was conducted as part of an Epi-Aid investigation, suggested that improving the use of available infection prevention strategies could have a substantial impact on reducing sepsis. Those interventions include vaccination, reducing transmission of pathogens in healthcare environments, and appropriate management of chronic diseases.

Vital Signs Report on Sepsis

- The August issue of *Vital Signs* provided educational information to healthcare providers on recognition and treatment of sepsis ([CDC Vital Signs report on sepsis, Making Health Care Safer](#)). Based on information from the review,
 - Sepsis begins outside of the hospital for nearly 80% of patients.
 - 7 in 10 patients with sepsis had recently used healthcare services.
- A CDC video about the impact of sepsis on a family was viewed approximately 18,000 times in 24 hours.
- A #ThinkSepsis promotion and Twitter chat with ABC News’ Dr. Richard Besser reached more than 75 million on social media collectively.

Future CDC Activities Planned to Prevent Sepsis

- Release a multi-year sepsis awareness campaign in 2017 that will include print materials, short videos, and public service announcements. The campaign will build upon the data in the *Vital Signs* report.
- Develop a reliable and consistent national sepsis surveillance definition
- Establish national sepsis burden estimates and trends based on objective clinical measures
- Expand work in multiple states to better describe risk factors, clinical characteristics, intervention opportunities, and antibiotic use among patients with sepsis
- Engage with critical care experts, clinicians, and the public to increase awareness to support sepsis prevention and early intervention measures

Outbreak Investigations

Emerging Threats

Recent CDC investigations have involved three emerging threats:

- *Elizabethkingia anopheles*: A common bacterial organism in the environment (water and soil) that, in rare instances, can cause serious infections
 - CDC was notified by Wisconsin of outbreak of *Elizabethkingia anopheles* infections in January.
 - Sixty-five cases were detected in Wisconsin, Illinois, and Michigan, with a 32.3% case-fatality ratio (21 deaths).
 - The outbreak peaked in mid-February to mid-March, with the last case identified on May 30.
 - CDC and the Wisconsin Department of Health Services interviewed patients and family members, and CDC tested samples from patients, environmental sources, healthcare products, and water.
 - The detection of clusters of cases within the outbreak suggest the possibility of several recurrences from the same or multiple sources. However, the source remains unidentified.
- Bacteria that carry *mcr-1*: A gene that makes bacteria resistant to colistin, the last-resort drug for some multidrug-resistant infections
 - As of late September 2016, the [mcr-1 gene](#) has been detected in the United States in 4 human and 2 food-animal isolates.
- *C. auris*: A multidrug-resistant yeast that can infect the bloodstream and cause severe illness
 - *C. auris* is difficult to identify with standard laboratory methods and has caused outbreaks in healthcare settings.
 - Investigative activities include
 - Using WGS to identify strains and determine if the yeast has been transmitted between patients
 - Collaborating with international partners to understand emergence and relatedness of isolates
 - Working with EPA and FDA to identify the best disinfectants for *C. auris*

A New Outbreak Vehicle

CDC has also investigated the first multistate outbreak of *E. coli* infections linked to flour.

- The outbreak involved two strains of *E. coli* (O121 and O26) that caused 46 cases of illness in 21 states.
- Ill people reported eating raw dough or raw batter made with General Mills flour, before getting sick; the same strains of *E. coli* were detected in patient samples and in sacks of flour.
- More than 45 million pounds of flour was recalled, as well as additional products made from flour (bread, brownie, cake, and muffin mixes).

Improved Detection and Response

CDC also investigated a multistate outbreak of *Listeria* associated with a brand of frozen foods.

- WGS indicated that *Listeria* isolates from ill people were closely related to *Listeria* isolates from CRF Foods frozen products and isolates found in a supplier's environment.
- The outbreak caused 9 cases in 4 states, with 3 deaths; cases occurred between 2013 and 2016.
- The recall included 2 years' worth of frozen vegetable and fruit products, including more than 350 products, with more than 40 brand names.
- The outbreak highlighted the ability of *Listeria* to find harborage sites in food production facilities.

PulseNet Update

- 2016 marks the 20th anniversary of PulseNet.
- [*An Economic Evaluation of PulseNet*](#) published in March in the *American Journal of Preventive Medicine* concluded that PulseNet saves approximately \$500 million per year in medical costs and lost productivity by averting thousands of cases of foodborne illness (see page 33).

Ebola Research

- Key studies include
 - The Liberia Men's Health Screening Study, to assess the persistence of Ebola virus in semen and help prevent sexual transmission
 - Detection of biomarkers for severe or moderate disease in patients with Ebola virus disease:
 - Severe disease is associated with higher viremia and elevations in pro-inflammatory cytokines and chemokines.
 - Moderate disease is associated with elevations in biomarkers of immune activation and control.

These findings suggest that immune modulation might be investigated as a treatment modality for Ebola virus disease.

Discussion

BSC members

- Agreed that prevention of AR can best be addressed as a patient safety issue
- Encouraged intensified collaboration with healthcare partners to improve antibiotic stewardship and with USDA, FDA, and industry partners to decrease the use of antibiotics in agriculture
- Endorsed CDC's plans for applied research on how antibiotics affect microbiomes and suggested that viromes might be considered as an area for future study

CDC might also consider

- Developing a new laboratory definition of CRE for use by clinical laboratories
- Ensuring that campaigns on patient safety and antibiotic use
 - Describe why patients should not take antibiotics when they are not needed (e.g., because of side effects, *C. difficile* infections, and disruption of the microbiome)

- Encourage widespread use of a point-of-care test to distinguish between bacterial and viral infections, as soon as one becomes available, recognizing that many infections may be caused by both viral and bacterial pathogens
- Intensifying efforts to address AR issues related to pediatric medicine, through
 - Partnerships with pediatricians and pediatric professional societies
 - Validation of NHSN definitions used in pediatric hospitals and pediatric acute tertiary and quaternary care facilities
- Taking an expanded role in studies and trials to identify ways to change clinical and patient behaviors to improve antibiotic use
- Helping veterinary partners apply lessons learned from antibiotic stewardship efforts in human medicine to animal medicine

In response to questions and comments on laboratory issues, Dr. Bell noted that

- CDC has developed an assay for *mcr-1* that will be distributed as widely as possible.
- ARLN will help state laboratories by identifying infectious threats like *C. auris* that are difficult to distinguish from related pathogens. ARLN activities will also allow CDC laboratories to focus on emerging issues.
- ARLN will help determine the best way forward to implement reflex culture testing.
- CDC will continue to assist state laboratories in transitioning PulseNet activities from pulsed-field gel electrophoresis (PFGE) to WGS.

NCHHSTP Update

Jonathan Mermin, Director, NCHHSTP, reviewed the budget outlook for fiscal year (FY) 2017, noted recent staffing changes, and highlighted selected recent accomplishments of the five NCHHSTP divisions.

FY 2017 Budget Outlook

The proposed NCHHSTP budget for FY 2017 includes level funding for TB, HIV, STD, and school health, and a \$5 million increase for viral hepatitis. However, both the Senate and House bills reject the additional funds for viral hepatitis, and the Senate bill includes a \$5 million decrease for TB and STD prevention.

Leadership Changes

- Sara Zeigler is the new NCHHSTP Associate Director for Planning and Policy.
- Patricia Dietz is the new Associate Director for NCHHSTP's Program and Performance Improvement Office.
- Brian Edlin is the new NCHHSTP Chief Medical Officer.
- Stephanie Zaza, Director of the Division of Adolescent and School Health, retired July 2016 after 25 years of service to CDC.
- Susan Robinson, NCHHSTP Associate Director for Health Communication Science, has accepted an appointment at Georgia Institute of Technology Institute for People and Technology for a year as a visiting researcher.

- Wayne Duffus, NCHHSTP Associate Director for Health Equity, has accepted a position in South Africa with the Center for Global Health.

Division Highlights

Division of HIV/AIDS Prevention

- *Held an external peer review panel on March 3–4.* The Division of HIV/AIDS Prevention is developing an action plan to implement the panel’s recommendations, which include 1) evaluate state and local HIV/AIDS surveillance and epidemiologic capacity, 2) integrate surveillance and program activities into a new funding opportunity announcement, 3) develop and implement an effective data-to-care system, and 4) build national HIV/AIDS molecular surveillance capacity while instituting pilot projects.
- *Released [Updated Guidelines for Antiretroviral Postexposure Prophylaxis after Sexual, Injection-Drug Use, or Other Non-occupational Exposure to HIV, United States, 2016](#).* The *Updated Guidelines* expand the recommendations for medical practitioners issued in 2005.

Division of Viral Hepatitis (*also see pages 38–42*)

- *Deployed [Global Hepatitis Outbreak and Surveillance Technology \(GHOST\)](#) in May 2016.* GHOST is a web-based system, based on an AMD project, which enables public health officials to use genetic information to identify outbreaks of viral hepatitis.
- *Released the [2014 Viral Hepatitis Surveillance Report](#).* The report found that rates of acute hepatitis B virus (HBV) infection are relatively stable, with the exception of increases reported in Appalachia; that new cases of acute HCV infection have more than doubled between 2010 and 2014; and that acute cases of HCV infection are occurring most often among young persons who inject drugs living in rural and suburban areas.
- *Reported a [22% increase](#) between 2001 and 2014 in the rate of women of childbearing age who test positive for HCV.* The rate increased from 139 to 169 per 100,000 women, and the proportion of infants born to women living with HCV increased by 68%. The increase was greatest in Kentucky, where the HCV infection rate among women of childbearing age tripled between 2011 and 2014.
- *Published CDC [Program Guidance for Implementing Certain Components of Syringe Services Programs, 2016](#),* which describes CDC’s role in new [U.S. Department of Health and Human Services \(HHS\) guidance on syringe services programs](#) (SSPs)—part of the response to the growing opioid epidemic that has led to outbreaks of HIV and viral hepatitis among persons who inject drugs (PWID). In December 2015, Congress gave states and local communities the option of using federal funds to support certain SSP components. Although federal funds cannot be used to purchase sterile needles or syringes to inject illegal drugs, they can be used for staff salaries, supplies, HIV or HCV testing kits, naloxone, educational materials, and condoms.

Comprehensive SSPs can help prevent HIV and viral hepatitis infection among PWID by providing free access to sterile syringes; disposal of used syringes; medication-assisted drug treatment; screening and treatment for HCV, HBV, and HIV; and counseling and support services. Although 13 states and 3 counties in West Virginia have performed “determination of need” assessments for SSPs, a “vulnerability map” indicates that few persons who need these services live in counties that operate SSPs.

Division of Tuberculosis Elimination

- Issued updated versions of [Self-Study Modules on Tuberculosis](#). The revised modules, which reflect updated CDC guidelines, are designed for use by outreach workers, nurses, physicians, health educators, and other healthcare workers.
- Another important development involves a [draft recommendation by the U.S. Preventive Services Task Force on screening for latent tuberculosis infection \(LTBI\) in populations at increased risk](#), which represents a significant step toward tuberculosis elimination in the United States. The recommendation has a grade of B, indicating that “there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.”

Division of Adolescent and School Health

- Published [Sexual Identity, Sex of Sexual Contacts, and Health-Related Behaviors Among Students in Grades 9–12—United States and Selected Sites, 2015](#)
 - The report found that lesbian, gay, and bisexual (LGB) students report higher levels of physical and sexual violence and bullying than their peers, as well as higher rates of injection drug use and heroin use. Twenty-nine percent reported having attempted suicide in the past 12 months, which is four times higher than the rate among all teens.
 - The report also found a significant decrease in the percentage of high school students who report HIV-related behaviors.

Division of STD Prevention

- Reported on data collected by the [Gonococcal Isolate Surveillance Project](#), which found that
 - The percentage of gonorrhea isolates with decreased susceptibility to azithromycin increased more than 300% between 2013 and 2014.
 - Seven cases of gonorrhea with azithromycin resistance and reduced susceptibility to ceftriaxone have been identified in Hawaii. However, no treatment failures have been reported, thus far, and three new drugs are in the pipeline.

Challenges and Opportunities

Dr. Mermin summed up the NCHHSTP update by emphasizing these findings:

- The incidence of acute HCV increased 2.5-fold, and HCV mortality increased 18%, between 2010 and 2014.
 - New HCV cases are occurring primarily among young, white persons with a history of injection drug use.
- STD rates are increasing and gonorrhea resistance is on the horizon.
- Some high-risk groups continue to exhibit limited HIV viral suppression rates and continued HIV transmission.
- LGB high school students experience substantial health disparities.
- After 23 years of decline in TB incidence, TB cases are level.
 - About 13 million persons in the United States have latent TB infection.

Questions

Dr. Mermin posed three questions for BSC members' discussion:

- How can we expand LTBI diagnosis and treatment?
- What if any role should NCHHSTP have in addressing LGB youth health beyond prevention of HIV, STDs, hepatitis, and TB?
- How do we ensure comprehensive SSPs are implemented where needed?

Discussion

- **LTBI.** To expand LTBI diagnosis and treatment, BSC members suggested greater outreach to healthcare providers who are unfamiliar with the new LTBI regimen, which is shorter and less toxic than earlier treatments. Dr. Mermin noted that the state of California has received funds for expanded identification and treatment of persons with LTBI, with the goal of eliminating TB in that state.
- **LGB youth health.** It was suggested that NCHHSTP continue to collect data on suicide rates and levels of physical and sexual violence and bullying, as well as on infectious diseases. Some BSC members also emphasized the need to better protect youth and to enforce laws for sexual assault of males who are minors. Dr. Mermin noted that all CDC centers (including those that focus on injury prevention, chronic diseases, and infectious diseases) can work toward the common goal of “empowering children with information and tools so that they can stay healthy throughout their life.”
- **Health services for PWID.** To help stem the spread of diseases related to the opioid epidemic, BSC members suggested enlisting public health partners such as the Council of State and Territorial Epidemiologists (CSTE) and the National Association of County and City Health Officials (NACCHO) to assist states in applying for funds to support SSPs and other PWID-related health services, which may be provided in different ways in different jurisdictions (e.g., by pharmacies or mobile clinics in small communities). Other suggestions included working with faith-based and community-based organizations to bring public health resources to isolated communities (e.g., areas in Appalachia), and having clinicians order tests for HIV, HCV, and STDs (including gonorrhea and syphilis) as one diagnostic “package.”
- **Drug-resistant gonorrhea.** Development of point-of-care gonorrhea diagnostics that incorporate detection of resistance would be a major advance. Dr. Gail Bolan, Director of the Division of STD Prevention, noted that new tests are in the pipeline and that nine jurisdictions are funded under the CARB Strategy to pilot the use of E-tests as a way to detect susceptibility and resistance until novel rapid molecular tests are in place.
- **Congenital syphilis.** BSC members expressed concern about increases in congenital syphilis and the possibility that the United States is moving toward an epidemic of syphilis among women and children. Dr. Bolan noted that CDC has begun working with states with high rates of congenital syphilis to identify and implement better prevention practices.

Conversation with the CDC Director

In his opening remarks, CDC Director Thomas Frieden discussed the response to the Zika outbreak, as well as global efforts to address antimicrobial resistance.

Zika Outbreak

- Dr. Frieden expressed concern about the ongoing outbreak in Puerto Rico, including the resistance by some to aerial spraying for vector control.
- He also noted progress made in vector control in Florida. [Data from mosquito surveillance in a Miami neighborhood](#) indicate that spraying with both an adulticide and a larvicide can interrupt local transmission. This represents the first time that arboviral transmission has been stopped in the middle of an outbreak.
- Although it is hoped that vaccines against Zika virus disease will be developed soon, better methods of mosquito control and better diagnostics are urgently needed.

Global Efforts to Address Antimicrobial Resistance

- Global leaders committed to working to reduce AR in their countries at a [United Nations General Assembly meeting in New York on September 21, 2016](#), and agreed on four focus areas: 1) finding resistance faster and more completely; 2) stopping resistance more quickly; 3) preventing resistance with better stewardship and infection control, vaccination, and treatment; and 4) using innovation to prevent resistance (e.g., via microbiome research, development of point-of-care diagnostics, better infection control practices in hospitals).

Discussion

Vector Control

- BSC members stressed the continued need to strengthen U.S. vector control programs for mosquito- and tick-borne diseases, many of which are increasing annually in the United States.
- Dr. Frieden said that expertise and investment in vector control is limited at the federal, state, and local levels. Infrastructure improvements are needed to increase public health capacity to monitor mosquito populations, implement vector control activities, and share data with jurisdictions that operate vector control programs.

Response Issues

- Many public health issues—including AR and the Zika outbreak—require an intense, multidisciplinary (and often global) response to reduce illness and death. BSC members discussed the benefits of establishing a national public health emergency fund to support rapid response efforts whenever they are needed. Dr. Frieden said that past experiences with Zika, MERS-CoV, SARS, Ebola, and the H1N1 pandemic underscore the potential benefits of such a fund.
- The complexity of the Zika response has required coordinated action across all CDC centers, drawing on expertise in STDs, vector-borne diseases, vector control, birth defects, blood safety, occupational health, and environmental health. One complicating factor is that the virus can be spread through both mosquito bites and sexual contact; it is possible that sexual contact will account for a larger proportion of disease transmission as the outbreak continues. Dr. Frieden noted that CDC may need

to update guidance as more is learned about sexual transmission and the persistence of Zika virus in body fluids.

Research

- Some BSC members suggested that CDC conduct more economic impact studies and more behavioral studies.
 - Studies that demonstrate the health benefits and cost-effectiveness of infectious disease programs can help build public health infrastructure; they may also help policy makers and the public better understand the benefits of a strong public health system. An example is the [recent study evaluating the costs and benefits of PulseNet](#).
 - Behavioral studies are essential for effective implementation of interventions.
- In regard to research on Zika virus disease,
 - Studies are underway in Mexico, Puerto Rico, and Colombia to learn more about the outcomes of Zika infection during pregnancy and how to care for affected infants.
 - Scientists at the Vector-Borne Disease Regional Centers of Excellence will focus on development of new methods of vector control and better diagnostics for Zika virus infection.
- The AMD Initiative represents a new model for research collaboration with state health departments and academic institutions that might be useful in other areas.

Latent TB Infections

- In response to a question about international standards of care, Dr. Frieden noted that strategies to address TB and LTBI depend on the situation in a given country. Innovations such as shorter treatment regimens for LTBI may provide even greater benefits when it is possible to identify which individuals are likely to progress from LTBI to active TB.

Antimicrobial Resistance

- It was suggested that future public health campaigns to advance antibiotic stewardship in the United States stress the use of point-of-care tests that distinguish bacterial from viral pathogens, once these tests become available. Public knowledge about these tests will be very important.
- In regard to global action on AR, Dr. Frieden noted that some interventions that prove effective in the United States may be of use to other countries. CDC will continue to work with international partners to build AR laboratory networks, develop diagnostic technologies, improve hospital infection control, and implement antibiotic stewardship programs.

CGH Update

Rebecca Martin, Director, CGH, reviewed challenges and opportunities related to public health work conducted under the [Global Health Security Agency](#) (GHSA), whose goal is to help create a world safe and secure from infectious disease threats and elevate global health security as a national and global priority.

GHSA: Background

- GHSA is a partnership of over 50 nations, international organizations, and non-governmental stakeholders. Its aims are to 1) PREVENT and reduce the likelihood of outbreaks, 2) DETECT threats

early to save lives, and 3) RESPOND rapidly and effectively. There are over eight U.S. agency partners including CDC, the United States Agency for International Development (USAID), the U.S. Department of Defense (DoD), USDA, and the U.S. Department of State.

- CDC is working with 31 partner countries to implement “GHSA Action Packages” in such areas as AR, zoonotic diseases, biosafety/biosecurity, immunization, disease surveillance, national laboratory systems, workforce, and rapid readiness.
- As part of these efforts, CDC has led development of tools and implementation in Joint External Evaluations (JEEs) to measure capacities to prevent, detect, and respond to infectious disease threats in GHSA partner countries. Thus far, JEEs have been completed in 16 countries and scheduled in 26 countries, with 21 more expressing interest. JEEs identify needs and gaps in critical public health infrastructure and serve as a roadmap to effectively target resources.
- Other CDC activities include
 - Participating in 81 response missions between September 2015 and July 2016, through CDC Global Rapid Response Teams
- Support for global health security will continue through FY 2019.

GHSA: Milestones

GHSA milestones, through June 30, 2016, include

- Assessments, monitoring, and evaluation
 - 5 countries (Côte d’Ivoire, Ghana, Guinea-Bissau, India, Sierra Leone) have documented gaps in disease surveillance, as part of an assessment of data collection and analysis.
- Curriculum and training
 - 7 countries (Bangladesh, Cameroon, Côte d’Ivoire, Indonesia, Nigeria, Togo, Vietnam) have trained community leaders, networks, health volunteers, and others on detection and reporting of unusual events.
 - 6 countries (Cameroon, Ethiopia, Nigeria, Sierra Leone, Togo, Vietnam) have disseminated national training curriculums, standard operating procedures, tool kits, best practices, and procedures to disease surveillance programs to meet International Health Regulation (IHR) standards.
- Systems implementation and cross-sectional planning
 - 10 countries (Bangladesh, Benin, Cameroon, Ethiopia, Guinea, Guinea-Bissau, India, Mauritania, Sierra Leone, Vietnam) have reliable systems in place at the national and/or subnational levels for capturing public health events from a variety of sources.
 - 4 countries (Burkina Faso, Cameroon, Sierra Leone, Vietnam) have developed plans to implement a joint system with Ministries of Health, Agriculture, and Defense for disease surveillance, with defined roles, responsibilities, and procedures for monitoring priority diseases.
 - 5 countries (Benin, Democratic Republic of the Congo [DRC], India, Nigeria, Togo) have developed plans and procedures to enhance disease surveillance capacity for port health services at points of entry.

GHSA: Tailoring Projects to Countries' Needs

Country-specific examples of GHSA projects include

- **India: Improving detection, treatment, and prevention of MDR-TB**
 - Health facilities are a major source for generation and transmission of infections caused by pathogens with antimicrobial resistance.
 - The GHSA project in India builds capacity to detect and prevent AR associated with healthcare settings by
 - Enhancing laboratory detection of AR pathogens
 - Strengthening facility-based infection prevention and control programs
 - Implementing surveillance of infections caused by AR pathogens
 - Understanding antimicrobial use practices and promoting stewardship
 - Specific aims include
 - Developing a WGS laboratory to sequence 500 drug-resistant TB strains and conduct matched phenotypic drug-susceptibility testing to better understand existing resistance patterns
 - Conducting assessments and providing training for hospital infection control units
 - Supporting the MDR-TB treatment adherence and social support counseling program
- **Ethiopia: Controlling zoonotic diseases**
 - Activities focus on rabies, brucellosis, and anthrax in animals and humans. They include
 - Enhancing laboratory capacity, disease surveillance, and information sharing
 - Creating joint outbreak response capacities
 - Initiating disease prevention and control activities
 - Implementation includes creating and strengthening inter-sectoral collaborations among animal and human health agencies to detect and respond to zoonotic diseases.
 - Progress to date includes
 - Completing assessments of 2 national reference laboratories (human and animal), 2 regional public health laboratories, 3 regional veterinary laboratories, and 3 university laboratories
 - Co-hosting a rabies workshop for 26 public health and animal health stakeholders
 - Training 14 staff on basic principles of biosafety
- **Cameroon: Responding to cholera through integrated systems for public health emergency management**
 - Emergency response teams in Cameroon reduced response times from 8 weeks (a cholera outbreak) to 1 week (a Lassa outbreak) to 24 hours (cases of H5N1).
 - The leader of the H5N1 response has completed the Public Health Emergency Management Fellowship at CDC, as a GHSA Acceleration Project.

GHSA Challenges and Opportunities

- **Challenges**
 - Capacity building is a long-term effort that limits the ability to describe quick impact.

- It is necessary to address emergent crises while the number of protracted crises (Syria, El Niño, cholera in Africa, Zika) continues to increase.
- The political context in which humanitarian work takes place changes over time.
- **Opportunities**
 - Leveraging CDC’s workforce and science expertise to enhance country and partner capacity to develop, implement, and evaluate priority global initiatives
 - Leveraging with partners

Why GHSA Matters: Zika and Yellow Fever

- International Zika response strategy
 - The goals of the CDC and USAID response strategy are to
 - Minimize the number of pregnancies affected by Zika
 - Improve understanding of Zika virus to predict its long-term consequences on at-risk populations in affected countries, including the United States
 - CDC and USAID are working with GHSA partners to advance and coordinate response activities in the following areas: laboratory capacity; disease surveillance; epidemiology and public health studies; maternal and child health interventions and service delivery; innovations; emergency operations and management; and vector control.
 - Examples include working with partners in
 - Guatemala to expand laboratory training and capacity building
 - Colombia to strengthen understanding of adverse pregnancy outcomes associated with Zika infections through a cohort study
 - Brazil to identify and test innovative methods for vector control
 - Florida to use combined spraying of a larvicide and an adulticide for vector control
 - Puerto Rico to enhance risk communications and health promotion activities
- Yellow fever outbreaks in Angola and the DRC
 - Yellow fever in Angola
 - The Angolan Ministry of Health requested response assistance from CDC in January 2016.
 - CDC has deployed 46 staff members since February; at the present time, 3 CDC staff are working in Angola.
 - CDC has provided technical assistance in
 - Disease surveillance, planning for a vaccine campaign, vaccine coverage surveys, and studies of adverse events
 - Knowledge, Attitudes, and Practice (KAP) studies in jurisdictions where vaccine coverage was low
 - Laboratory training
 - The outbreak included 4,100 suspected cases of yellow fever, including 884 laboratory-confirmed cases.
 - To date, 16 million people have been vaccinated in 73 districts.

- Yellow fever in the DRC
 - The DRC Ministry of Health requested response assistance from CDC in June 2016.
 - CDC has deployed 8 staff members, to date, including a staff member assigned to the Global Outbreak Alert and Response Network (GOARN).
 - CDC response activities were coordinated by a staff member assigned to the DRC from CGH’s Division of Global Health Promotion.
 - CDC has provided technical assistance in
 - Disease surveillance
 - Vaccination campaigns, including a fractional-dosing vaccine study
 - The outbreak included 2,707 suspected cases of yellow fever, including 76 laboratory-confirmed cases.
 - 7.6 million people were vaccinated within about 2 weeks in 32 health zones of the Kinshasa Province.
 - Another 1.5 million people were vaccinated in affected provinces bordering Angola.

Global Is Local: Progress Towards Implementing the National Action Plan for Combating MDR-TB

- The *National Action Plan for Combating Multidrug-Resistant Tuberculosis* has 3 goals:
 1. Strengthen domestic capacity to combat MDR-TB
 2. Improve international capacity and collaboration to combat MDR-TB
 3. Accelerate basic and applied research and development to combat MDR-TB
- The targets of the strategy include
 - 2016: Initiate appropriate treatment in 25% of patients with MDR-TB in 10 high-burden countries
 - 2018: Initiate appropriate treatment in 35% of patients with MDR-TB in 10 high-burden countries
 - 2020:
 - Initiate appropriate treatment in 50% of patients with MDR-TB in 10 high-burden countries
 - Reduce by 15% the number of cases of MDR-TB in the United States
 - Reduce global TB incidence by 25% compared with 2015
 - Successfully treat 16 million TB patients in high-burden countries
 - Achieve and maintain treatment
- Progress in achieving the global health goals of the *National Action Plan for Combating Multidrug-Resistant Tuberculosis* includes efforts to
 - Improve international capacity and collaboration to combat MDR-TB
 - CDC developed TB BASICS (Building and Strengthening Infection Control Strategies), a standardized toolkit for assessing TB infection prevention and control practices.
 - CDC participated in a national assessment of the TB laboratory diagnostic network in Nigeria.

- China completed an inventory pilot study in 9 provinces—making use of technical and financial support from CDC—to inform disease surveillance standards of practice for China’s National Center for TB Control and Prevention.
- Accelerate basic and applied research and development to combat MDR-TB
 - CDC leads the Enhanced TB Infection Control in Healthcare Facilities (EnTIC) Trial, a 2-year assessment of the effectiveness of an enhanced infection control intervention package in Southeast Asia.
 - CDC assessed the diagnostic and clinical cascade for MDR-TB in Mumbai, India, through direct observation and consultations with TB program staff and healthcare providers.

Questions for the BSC

1. The GHSA supplemental funding to CDC is for 5 years; what would you propose to CDC in its efforts to secure funding in the future?
2. Within the GHSA, are there other partners you would recommend that CDC collaborate with, either technically or for policy or sharing information, towards building public health infrastructure in the 17 U.S. government partner countries?
3. How should CDC share best practices and information on its global and domestic linked technical work and guidance?
4. Which strategies should CDC adopt, or how should CDC engage globally, in strengthening research and development capacity at the global, regional, and country levels?

Discussion

Resources and Partnerships

- BSC members suggested that CDC might extend its GHSA activities through collaboration with universities (including schools of public health), CSTE members, non-governmental organizations, and public health experts from Canada and other donor countries. Laboratorians from schools of public health and epidemiologists from CSTE, for example, might participate in assessments and peer-to-peer exchanges.
- One way to help ensure sustained funding for global health work initiated under GHSA might be to demonstrate the global security benefits of this work, as well as economic benefits to partner countries.
- Funds to reduce MDR-TB in high-burden countries might include grants from the World Bank, the CDC Foundation, or other donors.

Strengthening Research and Development Capacity

- CDC should consider
 - Partnering with the [Consortium of Universities for Global Health](#) to expand global health research in areas such as vaccine development and translation of research findings into practice
 - Noting lessons learned by the NIH Fogarty International Center about research capacity-building

Other Areas of Concern

- BSC members also discussed
 - The impact of refugees and displaced persons on public health systems
 - The impact of changes in our climate and other environmental conditions on infectious diseases and the need for more attention to our potable water supply
 - The development of guidelines and standards of care for infectious diseases of importance to global health (WHO)

OID Planning for the Future

Dr. Khabbaz reviewed progress made over the past few years toward fulfilling the three elements of the [CDC infectious disease framework](#), which include strengthening public health fundamentals; implementing high-impact public health interventions; and advancing policies to prevent, detect, and control infectious diseases. She also discussed future steps in three areas that require sustained attention to ensure continued progress:

- The [Advanced Molecular Detection Initiative](#), which expands the use of next-generation genomic sequencing and high-performance computing to detect and control infectious pathogens
 - Future activities include
 - Expanding the use of sequencing technology to additional states and additional pathogens (e.g., influenza, TB, and foodborne pathogens monitored by NARMS and PulseNet)
 - Addressing disease surveillance gaps caused by the decreased availability of microbial isolates resulting from greater use of CIDs. As recommended earlier by the BSC, CDC and partners will identify and implement both stop-gap measures and long-term solutions to meet this challenge.
 - Advancing workforce development, by
 - Funding states to form regional training networks and collaborate with academic partners
 - Providing on-line training for epidemiologists through the Integrated Food Safety Centers of Excellence
 - An external group of experts has been convened to advise OID on new sequencing technologies and on prioritizing AMD projects involving different pathogens. The results of this assessment will be provided to the BSC in January.
- The CDC Antibiotic Resistance Solutions Initiative, which provides critical support to combat antibiotic-resistant bacteria
 - The CDC report [Antibiotic Resistance Threats in the United States, 2013](#) contributed to efforts to develop the initial National Strategy for Combating Antibiotic-Resistant Bacteria in 2014, and then to funding for CDC's Antibiotic Resistance Solutions Initiative in 2016.
 - Future steps include activities conducted under the CDC Antibiotic Resistance Solutions Initiative to advance the four antibiotic resistance goals:
 1. *Finding resistance faster and more completely.* A major aim of the new ARLN is to ensure rapid identification of new resistance patterns.

2. *Stopping resistance more quickly.* The AR Isolate Bank established by CDC and FDA will help advance the development of new antibiotic drugs and treatments.
 3. *Preventing resistance with better stewardship and infection control, vaccination, and treatment.* Intensified efforts to prevent AR include activities to strengthen Antibiotic Stewardship Programs in hospitals throughout the country.
 4. *Using innovation to prevent resistance.* Examples include using point-of-care diagnostics to distinguish between bacterial and viral infections and developing new AR prevention approaches based on microbiome research.
- CDC will also continue to work with global partners to advance the [WHO Global Action Plan on Antimicrobial Resistance](#), as discussed at the [United Nations General Assembly meeting on September 21](#).
 - The [Global Health Security Agenda](#), an international partnership to create a world safe and secure from infectious disease threats
 - CDC will continue to provide GHSA partner countries with technical assistance to implement GHSA “Action Packages” that include activities to help countries improve national laboratory systems and immunization programs, combat antimicrobial resistance, and establish emergency operation centers.

Other thinking-ahead efforts included discussion of staffing plans to sustain the ongoing Zika response; contingency plans for use during government shut-downs; and broader plans for maintaining and improving the public health workforce and infrastructure into the next decade. Dr. Khabbaz also mentioned a new project to help OIG identify ways to advance infectious disease modeling at CDC. She concluded by recommending a series of “[We Were There](#)” lectures developed by the CDC Office of the Associate Director for Science that describe past events of public health concern, including the outbreak of Legionnaires’ disease in 1976 and the early days of the AIDS epidemic in the United States.

Discussion

- The BSC members stressed that CDC should be “nimble and flexible” in incorporating cutting-edge research results and new technologies into public health activities. They also stressed the importance of forward thinking for the next global health emergency, in terms of vaccine development, therapeutic options, and the use of modeling to guide decision making.
- Areas suggested for strategic planning included expansion of collaborative partnerships with universities and other federal agencies (e.g., to advance workforce development and conduct applied infectious disease research); increased efforts to work with the healthcare community to align public health and clinical care goals; consideration of an expanded role for CDC in efforts to link human and animal antibiotic resistance issues (e.g., antibiotic use in animals and the presence of antibiotics in soil and potable water); and increased social science research to identify factors that influence the behavior of clinicians and patients.
- Some BSC members noted that infectious disease modeling has great potential and could be used to conduct cost-benefit analyses, better understand disease transmission, guide resource allocation, and improve outbreak responses.

Report from the Food Safety Modernization Act Surveillance Working Group

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

Harry Chen, Chair of the FSMA SWG, reported on the group's May 2–3 meeting.

FSMA SWG May 2–3 Meeting

In addition to finalizing the FY 2016 Annual Report, the FSMA SWG focused on four areas during the May 2–3 meeting:

1. PulseNet

- A recent [economic evaluation](#) concluded that the health and economic benefits of PulseNet and the foodborne disease surveillance system are substantial.
 - Benefits include reduction of reported illnesses, due to the availability of increased information; enhanced industry accountability; and more rapid recalls. Each year, an estimated 270,000 foodborne illnesses are prevented, saving approximately \$507 million in medical costs and lost productivity.
- Activities to celebrate the [20th anniversary of PulseNet](#) include press releases, a digital press kit, infographics (including logos and maps), an updated newsletter for state partners, and an APHL blog describing PulseNet success stories.

FSMA SWG feedback on transitioning PulseNet to CIDTs and WGS:

The transition from PFGE to CIDTs and WGS will bring many changes affecting methods used in foodborne disease outbreak detection and epidemiologic investigation, types and capacity of laboratory equipment, and the availability of samples for reflex cultures. At its next meeting, the FSMA SWG intends to discuss the need for a comprehensive plan to implement this transition.

2. Foodborne antimicrobial resistance

- The implementation of CDC's Antibiotic Resistance Solutions Initiative includes key activities described in the CARB Strategy. They include establishment of
 - An ARLN of seven regional laboratories to detect infectious disease threats using gold-standard laboratory capacity. The network focuses on capacity-building in regional and state laboratories; identifying pathogen-specific solutions for CRE, *Salmonella*, and gonorrhea; public health assessments for *C. difficile* and new AR threats; and improved communications and education on AR.
 - An AR Isolate Bank, which currently includes 228 isolates, to support the development of new diagnostic tests and antibiotic drugs. CDC has processed 63 isolate orders from academic and private sector researchers since July 2015.

- Planned activities to combat foodborne AR include
 - Increasing state laboratory capacity to rapidly investigate foodborne AR outbreaks using WGS. For FY 2017 the specific aim is to expand capacity to use WGS to screen foodborne bacteria in all 50 states, 6 large cities, and Puerto Rico.
 - Preventing multidrug-resistant *Salmonella* outbreaks with targeted, rapid response to newly discovered *Salmonella* resistance
 - Ensuring that veterinarians have tools, information, and training to prevent AR and promote antibiotic stewardship
- NARMS plays a key role in identifying AR foodborne bacteria in humans and animals (and providing isolates to the AR Isolate Bank) by maintaining surveillance for *Salmonella*, *Shigella*, *E. coli* O157, *Vibrio* (non-cholerae) and *Campylobacter* infections. NARMS is a collaboration among CDC, USDA, and FDA that analyzes isolates of drug-resistant enteric bacteria from humans, farm animals, and retail meat.

FSMA SWG feedback on enhancing surveillance for foodborne antimicrobial resistance

Actions suggested by FSMA SWG members for CDC and its public health partners include

- *Using WGS to identify AR threats while maintaining traditional phenotypic resistance-monitoring to identify new resistance patterns*
- *Leveraging existing data systems to expand standardized data collection and link epidemiologic information to human clinical isolates submitted to NARMS*
- *Improving timely integration and sharing of AR data from food animals, retail meat, and human clinical specimens*
- *Providing sufficient funding to USDA and FDA to support access and collection of on-farm data to assess use of antibiotics in food animals and measure the effects of changes in food animal antibiotic use regulations*

3. Traceback investigations

- The three major pillars of a traceback investigation are
 1. Epidemiologic evidence, including data from interviews of ill persons, distribution of cases in results of epidemiologic studies, and the history of the pathogen and past outbreaks
 2. Evidence of a suspected vehicle linked with ill persons that indicates a common point where contamination may have occurred. This should be followed by an assessment of the production facility at that common point.
 3. Laboratory results from testing a suspected vehicle or the production facility where contamination may have occurred

Evidence from each pillar is evaluated in concert to determine if data support the conclusion that a suspect food is the cause of the outbreak. A vehicle is considered a “likely source” when clear and convincing evidence is available from two of the three pillars.

- ***FDA Core Network perspective on regulatory investigations***
 - *Regulatory traceback and traceforward investigations* are performed when a food item has been linked to an outbreak investigation. These investigations are conducted by regulatory agencies and rely on the collection of records to support possible legal actions. Those

- records must be reviewed over the whole period of time that covers the production and distribution of the suspected product.
- A *traceback investigation* aims to identify the entity that supplied the contaminated product; a *traceforward investigation* aims to identify the entities that received the contaminated product.
 - Advantages. When definitive conclusions can be made (e.g., by taking a detailed look at shipment histories), the regulatory agency can take action when the investigation is complete.
 - Disadvantages. These investigations can be slow, labor-intensive, and resource-intensive. Records may be difficult to read or interpret, and investigators require special training.
 - Challenges include
 - The need to act fast when an outbreak is ongoing
 - Poor consumer recollection of consumption history and lack of specific product information
 - The identification of multiple product varieties, multiple products w/multiple ingredients, or multiple sources of a product
 - Lack of a rapid and rigorous mechanism to link shipments (or items in a shipment) from farm to fork
 - Poor record-keeping at firms within the distribution chain
 - ***USDA Food Safety and Inspection Service (FSIS) perspective on regulatory investigations***
 - USDA/FSIS investigation objectives include
 - Determine whether reported human illnesses are associated with an FSIS-regulated product (i.e., meat, poultry, or processed egg product) and (if so) identify where the product was produced and how it was distributed
 - Collect information 1) to guide the response and prevent further exposure and 2) for use as evidence to support any necessary enforcement action
 - Identify contributing factors and recommend actions or policies to prevent future occurrences
 - Essential elements for a successful and timely investigation include
 - Strong relationships with federal, state, and local public health partners
 - Early detection and identification of actionable traceback information
 - Information-sharing with industry to identify contaminated products and prevent further illness
 - Environmental assessments are a common component of traceback investigations. They are conducted in coordination with federal, state, local, and territorial health departments as well as environmental and agriculture agencies/departments.
 - Specific product information, such as FSIS-regulated establishment number and lot code, is critical for evaluating production practices and assessing other evidence required for regulatory action.

- **Informational/epidemiologic tracebacks**

- CDC conducts informational/epidemiologic product-tracing to determine whether food items consumed by multiple case-patients have a source of production or a distribution point in common. It can be difficult to identify a contaminated ingredient as the cause of the outbreak if that ingredient is consumed as part of many different foods.
- During an epidemiologic investigation, obtaining information about the specificity of food exposures among case-patients is as important as increasing the specificity of the case definition. Tracing a suspect product's distribution pathway back to its source may be the only way to confirm that the product is the carrier of the foodborne pathogen causing the outbreak.
- Product-tracing may be useful if
 - A cluster of cases caused by the same microbial strain (as identified by PFGE or WGS) likely represents a common source outbreak
 - Cases occur in multiple locations or jurisdictions (e.g., in multiple states)
 - Interviews of case-patients reveal no obvious common exposure in a particular jurisdiction, suggesting that the outbreak vehicle is a commercially distributed food item
 - A vehicle cannot be clearly implicated with traditional epidemiologic, laboratory, and environmental investigation methods alone
- There is no fundamental distinction between product-tracing conducted as part of an epidemiologic investigation (to obtain exposure information) and product-tracing used in support of regulatory action. However, these activities may differ in timing and in extent of record collection and documentation.
- The usefulness of pathogen-specific surveillance in preventing ongoing disease transmission is directly related to the speed of the investigation process. When product-tracing is required to help identify or confirm an outbreak vehicle, it must be done quickly.

FSMA SWG feedback on improving informational/epidemiologic tracebacks

Actions suggested by FSMA SWG members for CDC and its public health partners include

- *Improving coordination and communication among all partners*
- *Identifying statutory strategies that allow for an emergency declaration that suspends normal procedures and permits enhanced information-sharing during emergencies*
- *Using lessons learned from previous outbreak investigations to implement the FSMA [product-tracing rule](#), which requires enhanced record-keeping*
- *Recognizing consumer preferences for labeling and transparency in food-sourcing*
- *Utilizing all opportunities to educate industry partners on traceback needs (e.g., good record-keeping practices)*
- *Addressing challenges to traceback investigations of imported foods*
- *Exploring potential roles for 1) the Council to Improve Foodborne Outbreak Response (CIFOR) Industry Workgroup in developing non-regulatory model practices for traceback investigations and 2) the Integrated Food Safety Centers of Excellence in developing traceback trainings and exercises*

4. Integrated Food Safety Centers of Excellence

- [CoEs](#) are located in Colorado, Florida, Minnesota, New York, Oregon, and Tennessee. Their aims include strengthening surveillance and outbreak investigations; analyzing the timeliness and effectiveness of outbreak responses; training public health staff in investigation techniques; educating and building the food safety workforce; improving the capacity of information systems; and evaluating and communicating best practices.
- CoEs serve as navigators between the states in the CoE's geographic region and the resources and services the CoEs provide. CoEs may continue working with institutions outside of their region with whom they have existing professional relationships. A given CoE may also provide assistance to states outside of its region if the CoE is the most appropriate match for the requested service.
- CoE services include one-on-one consultations on disease surveillance, outbreak investigations, long-term projects (e.g., database improvements), CIFOR toolkit evaluations, training tools (e.g., for collaborative team trainings, mentorship programs, and on-line trainings), questionnaire templates, needs assessments, case series, and other foodborne disease surveillance tools and products.
- Examples of ongoing activities include
 - A foodborne illness introductory video series, a web-based foodborne illness complaint system, and the CoE [products website](#) (Florida)
 - [ECHO](#) (Extension for Community Health Outcomes) Learning Communities for Foodborne Illness Outbreak Responders and other projects to train the next generation of public health leaders (Colorado)
 - A regional learning collaborative that includes representatives from all states and some cities in the Northeast; a symposium on diagnostics; and tools for WGS training tools (New York)
 - Aggregated information from 10 states and cities on exposures to mercury via consumption of contaminated fish and the [International Outbreak Museum](#) (Oregon)
 - [Web-based courses](#) and other training tools, including the Student Outbreak Rapid Response Team Curriculum, [Epi-Ready](#), and FDA's Food Related Emergency Exercise Bundle ([FREE-B](#)) (Tennessee)

FSMA SWG feedback on which CoE activities should be emphasized

Actions suggested for the CoEs by FSMA SWG members include

- *Expanding their research activities, including collaboration with other academic institutions*
- *Measuring their impact and reach*
- *Improving ease of access and search features for CoE websites*
- *Packaging CoE tools and products to meet the needs of various groups, including schools of public health, environmental health specialists, and public health epidemiologists*
- *Coordinating with other governmental entities, including CDC rapid response teams, CDC's National Center for Environmental Health, the U.S. Department of Homeland Security, and Food Safety Centers of Excellence established by FDA/Center for Food Safety and Applied Nutrition (CFSAN) and USDA/FSIS*

Potential Future Topics

Proposed topics for 2017 FSMA SWG meetings include updates on the transition to use of CIDTs and WGS and an ongoing review of activities of the Interagency Food Safety Analytics Collaboration (IFSAC). Other potential future topics include the Foodborne Diseases Active Surveillance Network (FoodNet) Population Survey and its uses; integrated data systems; periodic updates on CoEs, the Interagency Foodborne Outbreak Response Collaboration (IFORC), and norovirus surveillance; foodborne disease and imported foods; orphan foodborne illnesses (e.g., toxoplasmosis, cryptosporidiosis, and hepatitis A); assessing the impact of FSMA; food allergies and anaphylaxis; and chemical contamination of food.

FY 2016 FSMA SWG Annual Report to the HHS Secretary

A BSC call will be scheduled later to vote on approval of the draft annual report.

Discussion

- **Reporting issues.** Regional differences in the numbers of reported foodborne outbreaks could be due to better prevention efforts; differences in the ways that states classify outbreaks; or varying capacities for sample collection, laboratory testing, and/or outbreak investigation in some states and localities.
- **Impact of CIDTs**
 - Positive impacts of CIDTs are likely to include faster diagnosis and improved detection of norovirus outbreaks; less welcome impacts may include fewer isolates for PFGE analysis by PulseNet and possible difficulties with test interpretation when PCR panels detect more than one pathogen.
 - Maintenance of culture-based phenotypic surveillance for foodborne pathogens is necessary to identify emerging patterns of drug resistance.
 - The increased flow of data on norovirus infections resulting from improved detection via CIDTs might be overwhelming to local health departments, or it could lead to more outbreaks being detected and controlled.
- **Investigations of foodborne disease outbreaks**
 - Enhanced detection of norovirus outbreaks, which can spread via food or water or from person to person, will also require training in the use of WGS to guide investigations. Such training might be provided through the ELC Cooperative Agreement and by the CoEs.
 - CoEs can also provide tools and training for informational/epidemiologic investigations to identify contaminated foods and for environmental health assessments conducted as part of FDA-led traceback investigations.

Hepatitis C Virus Control

John Ward, Director, Division of Viral Hepatitis, NCHHSTP, reviewed progress towards controlling the “twin epidemics” of HCV infection in the United States—defined as the ongoing epidemic of morbidity/mortality among baby boomers (persons born during 1945–1965) who contracted HCV infections decades earlier and who may be unaware of their infection until symptoms develop along with the new epidemic of HCV infections among young adults linked to the current epidemic of opioid use.

Key Messages

Dr. Ward summarized the current status of HCV prevention and control efforts with five key messages:

1. 3.5 million persons in the United States are living with HCV; high mortality rates are likely to occur among those whose infection is untreated.

- HCV infection is characterized by high incidence, prevalence, morbidity, and mortality. Public advocacy for HCV control is limited, and the costs of medication are high.
- Injection drug use is currently the predominant mode of HCV transmission; healthcare-associated transmissions such as through needlestick injuries also occur but are relatively infrequent compared with the number of new HCV cases related to injection drug use. Other routes of HCV transmission include perinatal (for which there is a 6–12% transmission risk for HCV-exposed newborns and which is increasing in some areas) and sexual transmission (for which HIV-infected MSM have the highest risk—13/1,000 person years).
- Based on findings from a National Health and Nutrition Examination Survey (NHANES) [study](#) conducted from 2003–2010, about 2.7 million Americans are infected with HCV. An additional 360,000 to 384,000 homeless and incarcerated persons (not surveyed by NHANES) may also be infected.

2. Increasing numbers of HCV-related deaths and increasing numbers of new HCV infections are occurring in the United States.

- The number of new acute HCV cases is rising, with the largest number of cases related to injection drug use, mostly among people in their 20s. Those who inject drugs tend to be suburban, rural, and white and equally male and female; many injection drug users have previously used prescription opioids. Older people with chronic HCV infections are predominately baby boomers (born between 1945 and 1965). The NHANES study also found that persons in the baby boomer age group account for 81% of HCV cases and 73% of deaths, due to disease progression over many years.
- The natural history of HCV infection affects diagnosis and treatment efforts. Acute HCV infection is followed by chronic infection in about 75% of patients; chronic infection often leads to mild fibrosis and then to moderate-to-severe fibrosis. Approximately 16% of infected persons develop cirrhosis of the liver after 20 years; the percentage rises to 41% among those infected for more than 30 years. Each year, 1–5% of those with cirrhosis develop hepatocellular carcinoma. The overall risk of death from cirrhosis and cancer after 45 years of infection is 19%.
- Modeling studies suggest that without expanded HCV diagnosis and treatment, among persons currently infected with HCV, an estimated 1.47 million will develop cirrhosis in their lifetime, including 350,000 with liver cancer, leading to 897,000 deaths.

3. Proven strategies and tools can stop transmission of HCV, increase the number of persons cured, and avert deaths from the virus.

- Components of HCV control include 1) one-time testing of all persons born between 1945 and 1965; 2) testing of PWID; and 3) care and treatment for those who test positive, *with a regimen of new drugs that have been shown to have a 90% success rate.*

This strategy can lead to a 73% reduction in liver cancer and 93% reduction in liver-related mortality.

4. Barriers to the delivery of life-saving approaches include safe, curative therapies.

- Challenges include limited provider knowledge about HCV, lack of clinical decision tools, limited public health data to monitor performance, and few individuals to assist patients (e.g., patient

navigators). Other barriers include the high cost of HCV therapy and insurance issues related to reimbursement for testing (e.g., for patients seen at emergency departments or for in-patients) and treatment.

5. Efforts are underway to lay the foundation for eliminating HCV.

- Key strategies to improve access to HCV testing, treatment, and cure include improving education for providers and the public, disseminating clinical decision tools and models of care, developing affordable diagnostics, and targeting health disparities.

Issues of Special Concern

Dr. Ward identified HCV control issues of special concern, including

- **Cost issues.** Treatment costs remain a formidable barrier, although access to HCV treatment is improving for Medicaid beneficiaries. In November 2015, CMS cautioned states about restrictive HCV treatment policies. Since then, a drug treatment with lower costs has been approved, and 14 of 36 Medicaid programs with restrictive policies have lowered their requirements. In addition, reductions in drug costs between 2014 and 2016 have made HCV treatments significantly more cost-effective.
- **Perinatal cases of HCV.** Increases in opioid use in several states (e.g., Kentucky, Tennessee, Virginia, and West Virginia) have been associated with higher numbers of HCV cases, including [perinatal cases of HCV](#). For example, in 2014 in Kentucky, 1 in 67 births was to an HCV-infected woman (the number was 1 in 308 for the United States as a whole).
- **Super-infections of HIV and multiple strains of HCV.** Analysis of transmission patterns within a cluster of HCV cases in a rural area of Indiana among PWID—using WGS and [Global Hepatitis Outbreak and Surveillance Technology](#) (GHOST)—identified multiple introductions of HCV and super-infections of HIV and different strains of HCV. Of 130 HCV-infected persons identified in the cluster, 50 were infected with more than one genotype of HCV.

The Way Forward

CDC activities to improve HCV prevention among PWID include [implementing guidance](#) on syringe SSPs; supporting state and local HCV surveillance, response planning, and outbreak investigation; and conducting prevention research. Most recently, a CDC-supported HCV prevention study found that adding HCV drug treatment to prevention services for PWID (i.e., opioid substitution treatment and SSPs) has a major impact.

Examples of recent U.S. planning efforts to reduce HCV transmission and disease include

- HCV Elimination Projects initiated by the Cherokee Nation and the state of Georgia (2015)
- A report on [Eliminating the Public Health Problem of Hepatitis B and C in the United States: Phase One](#), issued by the National Academy of Sciences, Institute of Medicine (IOM), which states that
 - 90% of HCV infections are curable; 80% of new HCV infections are preventable.
 - The elimination of hepatitis C and hepatitis B as public health threats is achievable.
- Substantial issues must be addressed to meet elimination goals. The IOM is developing a “Phase Two” report entitled: *A National Strategy for the Elimination of Hepatitis B*, which is expected in early 2017. The Phase One and Phase Two reports include technical input from CDC provided under an interagency agreement.

Global planning efforts are also underway. In May, 2014, the World Health Assembly encouraged the development of global elimination goals for hepatitis C, and in May, 2016, it endorsed a [WHO viral hepatitis strategy](#) and HCV elimination goals.

Discussion

Dr. Ward posed three questions for BSC member discussion:

1. Based on the HCV-related experiences in your state/community, what are the critical issues that CDC should be addressing?
2. A key priority for increasing identification of HCV infections is expanding the use of reflex testing.
 - What suggestions do you have for working with commercial and public health labs to increase adoption of innovative approaches? And, for working with payers to ensure coverage?
3. Given the importance of emergency preparedness efforts, how should we encourage and assist public health officials to plan for and respond to outbreaks of HCV as part of their emergency preparedness efforts?

Critical Issues

BSC members stressed the importance of renewed advocacy and outreach to improve HCV detection and treatment and to prevent infections in infants born to HCV-infected women. They also encouraged CDC to make the business case for the cost-effectiveness of intensified HCV control efforts.

Critical issues identified by BSC members include

- **HCV surveillance.** CDC should consider
 - Expanded use of WGS to identify genotypes
 - Use of residual HIV blood spots for HCV testing, based on needs in different jurisdictions
 - Assisting CSTE in developing a case definition for reporting perinatal HCV infections
- **Barriers to care.** CDC, professional societies, and other partners should inform family practice clinicians about new HCV treatments and provide a “roadmap to care” for patients with HCV.
- **Perinatal HCV.** CDC should consider
 - Working with CSTE, the Health Resources and Services Administration (HRSA), and professional societies to raise awareness about the rise in cases of congenital HCV
 - Using data on trends and risk figures to assess the potential benefit of routine HCV testing of mothers and babies in some communities
 - Working with partners to develop guidelines for HCV treatment during pregnancy and for management of exposed infants
- **Cost-effectiveness modeling**
 - Infectious disease models can help evaluate the cost-effectiveness of strategies to address the baby-boomer HCV epidemic and the epidemic in PWID, as well as strategies for responding to an HCV outbreak (see below). These models can also estimate the costs of treating all persons who test positive for HCV, especially if drug costs continue to decrease.
 - Current CDC models focus on use of interventions in vulnerable populations. CDC might use modeling to help develop a comprehensive disease prevention package for PWID designed to improve health and decrease lifetime medical costs.

- **Correctional health.** NCHHSTSP has established a workgroup on correctional health and may convene a cross-agency workgroup on this topic. Aims of the workgroup include identifying federal prisons, state prisons, and jails whose inmates are at high risk for HCV, HIV, and STDs, and developing a comprehensive approach to addressing those diseases, including testing and treatment on entrance and exit. BSC members supported the establishment of a cross-CDC group, given the many diverse preventable health problems in this vulnerable population and their families.
- **Global HCV prevention.** The vision of the WHO strategy issued in May is to eliminate viral hepatitis as a public health problem. CDC is working with WHO and many other partners to move towards fulfillment of this ambitious goal.

Reflex Testing

- Reflex testing could be a regulatory standard for HCV testing. At certain testing companies, it is already standard practice to conduct RNA testing of all HCV-positive samples.
- Standardized procedures for reflex testing should cover sample collection and interpretation of results. Sample collection might include obtaining two samples (one for initial testing and one for reflex testing so that the patient does not have to provide a second sample and also to avoid the risk of contamination during aliquoting).
- Addressing these issues will yield significant benefits in public health data.

Emergency Preparedness

- HCV is the single most common infection in opioid drug users, and it is likely that small, undetected outbreaks are continuing among PWID. Going forward, improved detection will require heightened awareness in the medical and public health communities and improved response will require partnerships with emergency response groups, public health departments, and professional societies across the country.
- Dr. Ward reported that initial work to model responses to outbreaks among opioid users indicates that SSPs and related interventions are highly cost-effective. Once HCV is introduced into a given community, rates among PWID typically rise rapidly, often reaching 70%. If only a few persons are treated, the affected population is rapidly re-infected; if the whole population is treated, HCV can be kept at low levels. Once tracking-and-treating activities stop, however, HCV is likely to return.

Additional Comments

- HCV testing and treatment should be a priority for the U.S. health system, as it is for the [Veterans Administration](#).
- The BSC may return to the topic of HCV prevention after publication of the IOM Phase Two report.

Next Steps

A BSC teleconference will be scheduled in January 2017. Planned agenda items include

- Discussion and vote on the FSMA SWG Annual Report to the HHS Secretary
- Report back from the December 2016 external review of CDC's AMD activities

APPENDIX: Meeting Participants

BSC Members

Ruth Berkelman	Beth Lautner	José Romero <i>(representing ACIP)</i>
Jack Bennett	Mike Loeffelholz	Guillermo Ruiz-Palacios
Kristy Bradley	Ruth Lynfield	Susan Sharp
Harry Chen	Beth Marlowe	Theresa Tam
Irene Glowinski	José Montero <i>(by phone)</i>	Jill Taylor
Jean Hu-Primmer <i>(representing FDA)</i>	Andy Pavia	Judy Wasserheit
Salmaan Keshavjee	Lee Riley	

Partners and Public Visitors

Jeff Engel <i>(Council of State and Territorial Epidemiologists)</i>	Walt Orenstein <i>(National Foundation for Infectious Diseases)</i>
Lilly Kan <i>(National Association of County and City Health Officials)</i>	Christy Phillips <i>(Pediatric Infectious Diseases Society)</i>
Jim Le Duc <i>(University of Texas Medical Branch)</i>	Kathy Talkington <i>(The Pew Charitable Trusts)</i>
Bonnie Maldonado <i>(Stanford University)</i>	Kelly Wroblewski <i>(Association of Public Health Laboratories)</i>

CDC Staff

Beth Bell	Marta Gwinn	Toby Merlin
Gail Bolan	Gillian Hale	Jonathan Mermin
Coleen Boyle	Peggy Honein	Nancy Messonnier
Chris Braden	Marsha Houston	Joe Miller
Denise Cardo	Dan Jernigan	Steve Monroe
Evelyn Cater	Vik Kapil	Robin Moseley
Sean Courtney	Rima Khabbaz	Atis Muehlenbachs
Francesco Criscuolo	Munmun Khan	Fei Fan Ng
Kim Distel	Wendi Kuhnert	Jim Nowicki
Vivien Dugan	Alexandra Levitt	Mark Pallansch
Brian Edlin	Kerri Lipton	Antonio Perkins
Leah Fischer	Barbara Mahon	Lyle Petersen
Alicia Fry	Rebecca Martin	Bob Pinner
Sidorela Gllava	Tonya Martin	Amanda Poe
Tom Gomez	Alison Mawle	Karyn Richman
Aja Griffin	Lionel McNamara	Alyson Rose-Wood

