

ADVANCED MOLECULAR DETECTION

AN IN-DEPTH LOOK



**U.S. Department of
Health and Human Services**
Centers for Disease
Control and Prevention

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For the html version of this material, go to www.cdc.gov/amd/what-we-do/

Advanced Molecular Detection

Transforming disease detection and response

Leveraging New Technologies to Fight Emerging and Persistent Disease Threats

CDC's Advanced Molecular Detection (AMD) program is transforming public health by using new technologies to unlock the secrets of microbes.

By integrating traditional epidemiology with next-generation genomic sequencing (NGS) and bioinformatics, we can look at pathogens in ways unimaginable just 10 years ago. AMD provides much-needed insights into disease-causing microbes and how we can stop them. These technologies also allow us to detect antimicrobial resistance and improve vaccines. Since 2013, innovations developed through the AMD program have helped us

- Identify known and emerging infectious pathogens;
- Find disease outbreaks faster;
- Understand, monitor, and control antimicrobial resistance; and
- Develop and target measures to protect people's health.

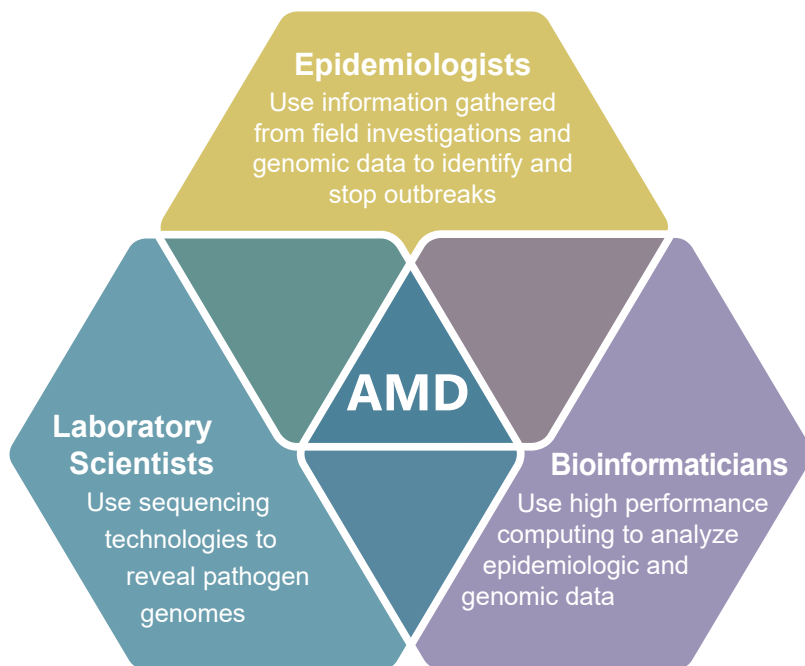
The AMD Program

The AMD program is modernizing the public health system's disease-investigation capabilities by employing the latest technologies and improving capacity in laboratory science, bioinformatics, and epidemiology throughout the nation.

CDC's Office of Advanced Molecular Detection (OAMD) works with experts across CDC to ensure the United States has the infrastructure, including technology, needed to protect Americans from infectious disease threats. OAMD collaborates with other CDC programs to facilitate development and piloting of next-generation diagnostics and protocols. These tools are then leveraged by programs across CDC to be brought to scale in state and local public health laboratories nationwide.

And the technologies that fuel AMD continue to advance at an exponential rate. Ongoing investments in AMD will ensure that public health can

- Keep pace with ever-advancing technologies;
- Continue to extend AMD methods to state and local laboratories;
- Detect and discover ways to stop antimicrobial resistance; and
- Develop systems to better integrate genomic and epidemiologic data.



Linking Scientific Disciplines

Laboratory scientists use NGS to generate genomic data on pathogens. Experts in bioinformatics and high performance computing devise ways to analyze these data. Epidemiologists then link the processed NGS data to information gathered through field investigations to identify outbreaks faster, stop the spread of disease sooner, and save more lives.

Why We're Here

Under the AMD program, CDC has been working to build on the nation's existing public health infrastructure. In its first four years, the program increased the availability of AMD technologies to rapidly change laboratory science practice within CDC and in state and local public health laboratories.

AMD technologies deliver a greater level of detailed information on infectious pathogens while reducing reliance on older, slower, less cost-effective methods. And this work continues as CDC assists state and local public health laboratories in developing AMD capabilities and provides online systems through which local, state, and federal laboratories can share data.

Opening Data, Sharing Science

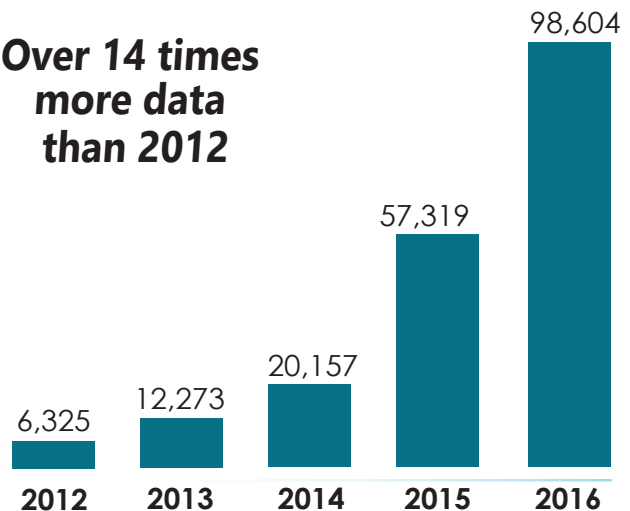
In the AMD era, CDC and state and local public health laboratories have committed to making genomic data rapidly available and on an unprecedented scale. From 2013 through 2016, CDC increased the number of submissions to GenBank* from 6,325 to over 98,600—a 1,459% increase.

Why this is important: Sharing sequence data as soon as they are available can speed up development of diagnostic tests, support basic research and collaboration, and enable real-time assessment of critical genomic changes (mutations) in pathogens that could threaten the public's health.

* GenBank is a publicly accessible collection of all available DNA sequences and is part of the National Center for Biotechnology Information (NCBI) at the National Institutes of Health (NIH).

CDC Genome Data Shared in Public Databases

**Over 14 times
more data
than 2012**

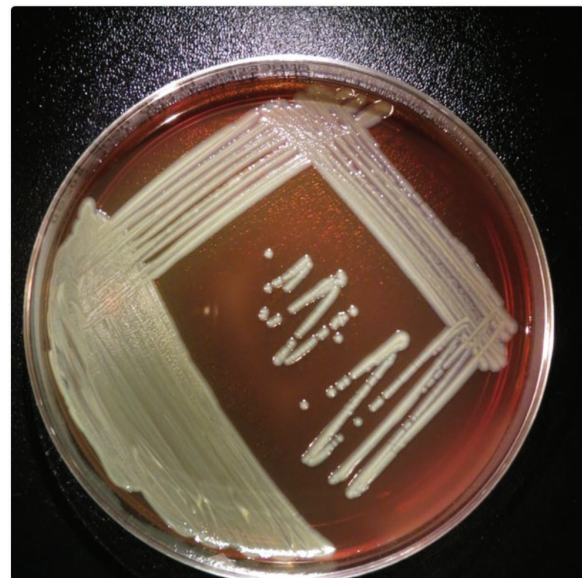


Open Data Sharing + Social Media Lead to International Collaboration

In 2016, the near-real-time public release of genomic sequences from an *Elizabethkingia anopheles* outbreak in Wisconsin resulted in a remarkable international collaboration and engagement from the global research community. Tweeted from the AMD Twitter account, @CDC_AMD, a link to the genome data led to global attention. Within 10 days of uploading the DNA sequences to NCBI's public database, CDC began collaborating with the Pasteur Institute in France and the University of Melbourne in Australia to study this rare pathogen and share insights gleaned through their collective high-performance computing systems.



CDC releases real-time whole genome sequence for WI #Elizabethkingia outbreak.
1.usa.gov/1Ub9eaN



RETWEETS
20

LIKES
9



Antimicrobial Resistance (AR)

Each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics and more than 23,000 people die from these infections. AR costs the U.S. healthcare system over \$20 billion per year.

Pneumococcus by the Numbers

- #1** cause of bacterial meningitis in children younger than 5 years old in the U.S.
- ~400,000** people are hospitalized because of pneumococcal pneumonia in the U.S.
- ~5,000** hospitalizations from pneumococcus-related bloodstream infections



Identifying Antimicrobial Resistance Markers

Streptococcus pneumoniae bacteria, or pneumococci, are a common cause of bloodstream infections, pneumonia, meningitis, and middle ear infections in young children. And these bacteria are becoming increasingly resistant to existing antibiotics.

Using whole genome sequencing, scientists can look at three different genes in *S. pneumoniae* bacteria that each encode a distinct penicillin-binding protein (PBP). From these three proteins, scientists can identify the PBP type. Knowing the PBP type, scientists can determine how resistant *S. pneumoniae* is to beta-lactam antibiotics, a class of antibiotics that includes penicillin.

This knowledge can change how scientists investigate *S. pneumoniae* infections and help them develop tests that can tell which antibiotics are best for treating a specific patient's bacterial infection.

Gonorrhea by the Numbers

- 2nd** most common nationally reported disease
- >300,000** cases reported by public health depts
- >820,000*** estimated new cases
- 30%** of new infections are resistant to at least one antimicrobial used for treatment

* Many cases of gonorrhea go unrecognized or unreported



Combatting Antimicrobial-resistant Gonorrhea

CDC is looking at DNA markers of antimicrobial resistance in *Neisseria gonorrhoeae* genes that can indicate the bacterium's susceptibility to antimicrobials. Using AMD technologies, researchers developed a system that can accurately predict how well antibiotics work 87%–99% of the time. In 2016, CDC began a pilot project with the state laboratories in Hawaii and Texas to use AMD methods with the antimicrobial surveillance system. In the first year, Hawaii's lab identified a cluster of *N. gonorrhoeae* that was resistant to a frontline antibiotic, azithromycin, and was less susceptible to two others, cefixime and ceftriaxone. This type of information is critical to helping the United States stay one step ahead of antimicrobial resistance.

AMD technology has the potential to greatly advance our understanding of gonorrhea and to improve surveillance for resistance, inform vaccine development, and potentially change the diagnosis and treatment paradigm into customized treatment for individual patients.

Healthcare-associated Infections (HAIs)

At any time in the United States, at least one in 25 hospitalized patients has a healthcare-associated infection (HAI). Additionally, an increasing number of antimicrobial-resistant organisms cause HAIs.

Discovering Dangerous Fungus in U.S. Hospitals

In 2016, CDC researchers used AMD technology to identify *Candida auris* for the first time in the United States. *C. auris* is a fungus that can cause serious and frequently fatal infections. CDC scientists detected *C. auris* infections in 13 U.S. patients. AMD technology revealed strains closely related to each other, which helped investigators understand how *C. auris* was spreading in healthcare settings. CDC has since helped identify another 85 U.S. cases and continues to work with state and local public health departments and healthcare facilities to control its spread. Based in part on AMD findings, CDC issued infection control guidelines to help curb further infections and is using AMD technology to monitor transmission of this emerging pathogen.

Finding Emerging Mobile Resistance Genes

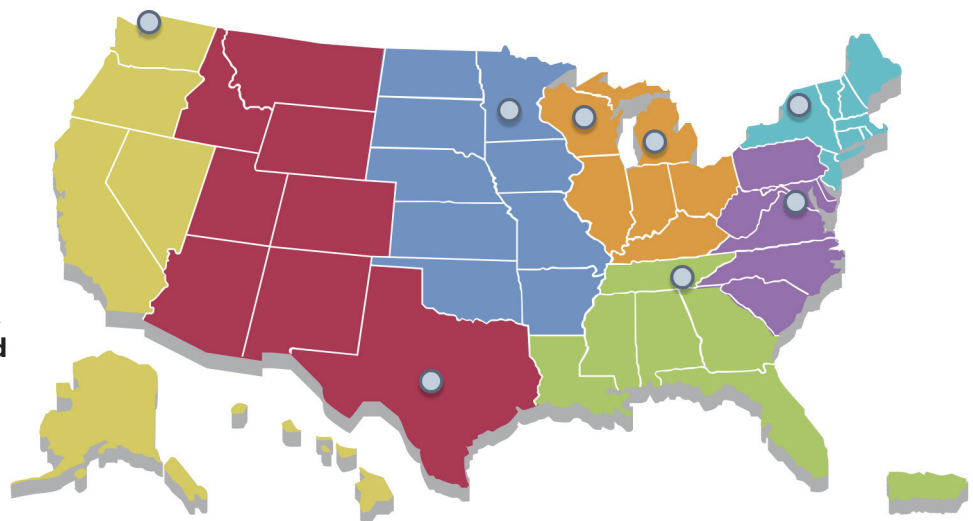
AMD technology allows us to more readily search for and identify novel and emerging ways in which antimicrobial resistance spreads. CDC and federal partners have been hunting for mobile colistin resistance and other emerging and novel antibiotic resistance genes in the United States. In 2016, as part of a coordinated public health response, the Department of Defense identified plasmid-mediated colistin resistance (*mcr-1* gene) for the first time in the United States. The bacteria carrying the *mcr-1* gene were found in a urine sample from a U.S. woman who had not recently traveled outside the country. The *mcr-1* gene makes bacteria resistant to an antibiotic (colistin) used as a last-resort drug to treat patients with multidrug-resistant infections. The *mcr-1* gene is particularly concerning because it exists on a plasmid, a small piece of DNA that can move from one bacterial species to another, carrying the resistance with it.

Since its first description, *mcr-1* has been reported on 5 different continents, including more than 20 different countries, and found among many additional Enterobacteriaceae including *Enterobacter*, *Salmonella*, *Shigella*, and *Klebsiella*. As both government and non-government labs continue to aggressively search for *mcr* genes in human isolates, CDC anticipates additional reports of *mcr* genes in humans. CDC will continue to work with state and local public health departments to investigate and respond to these findings to attempt to contain and slow spread of bacteria carrying this gene in humans.

Why this is important: One of the most striking impacts AMD technology has had on HAI outbreak investigations is the ability to detect not only plasmid-mediated outbreaks that can span many bacterial species, but also simultaneous outbreaks caused by multiple plasmids carrying the same resistance gene. Consequently, we now recognize two types of HAI outbreaks: "classic" outbreaks due to a single pathogen and newly recognized outbreaks due to a promiscuous plasmid spreading antibiotic resistance across multiple pathogens.

Regional Laboratories Using AMD Technology to Detect Antimicrobial Resistance

CDC is currently supporting public health laboratories, including seven regional, state-based laboratories, to detect and aid in the response to resistant pathogens of various types, including resistant, hospital-acquired infections.



PulseNet and Foodborne Diseases

Each year, approximately 48 million Americans—one in six—get sick from foodborne diseases.

To stop outbreaks of foodborne illness, we need to identify which pathogen is making people sick and then find the food source that is contaminated with the same pathogen strain. Since 1996, PulseNet, a national laboratory network, has used bacterial DNA “fingerprinting” methods to connect foodborne illnesses to detect outbreaks. AMD technology is improving PulseNet’s ability to link food sources to illnesses. In 2013, CDC began helping PulseNet laboratories throughout the nation use AMD methods on foodborne bacteria, increasing the speed at which labs can detect outbreaks and identify contaminated food sources. By getting contaminated food off of store shelves and out of people’s homes faster, we can prevent additional illnesses.

Foodborne Illness by the Numbers

1 in 6 Americans get sick from foodborne disease each year

~128,000 hospitalizations

~3,000 deaths

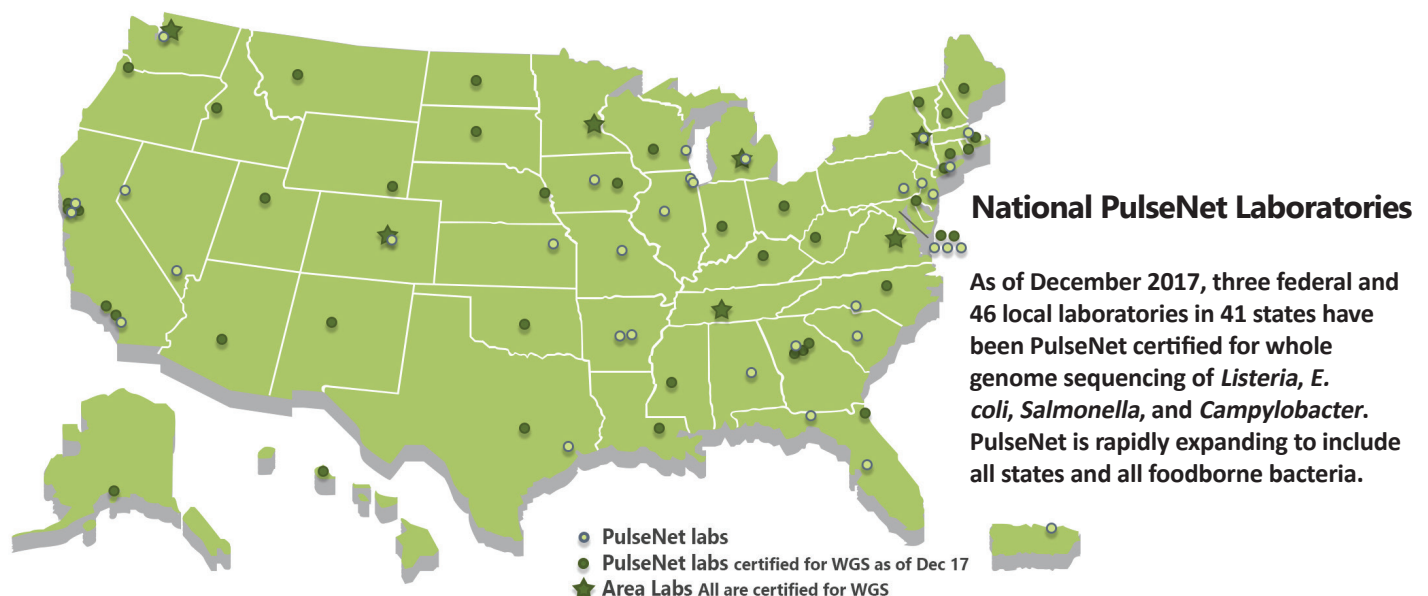
~\$15.6 Billion in direct and indirect costs to the U.S. economy

Identifying the Source of *E. coli* in a Multistate Outbreak

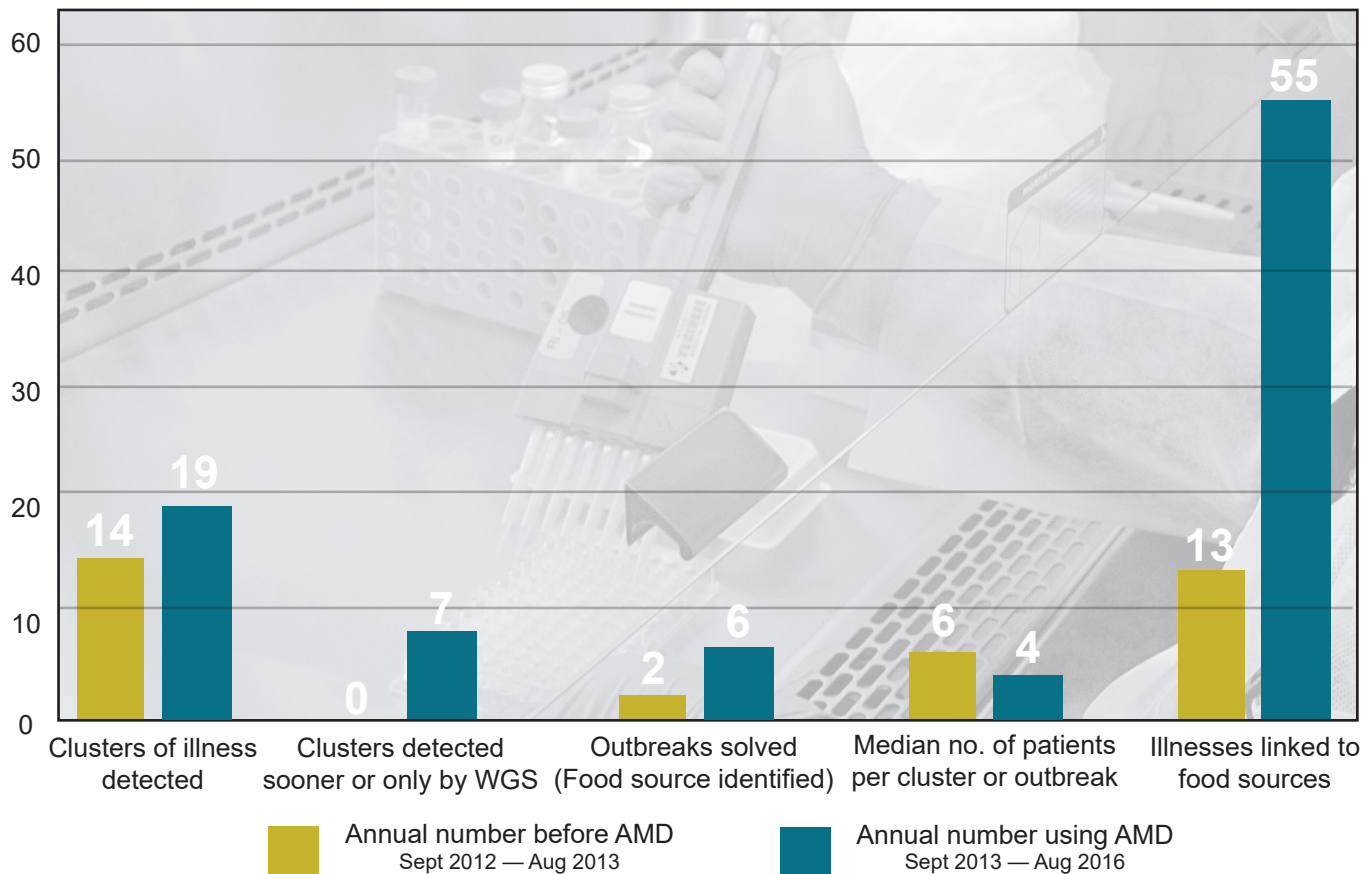
In 2016, an outbreak of *E. coli* infections made more than 60 people in 24 states sick and almost a third were hospitalized. Sick people reported eating raw dough or batter and several children played with raw dough at restaurants. The U.S. Food and Drug Administration (FDA) identified *E. coli* in bags of flour, which were produced at a single U.S. facility. Investigators used whole genome sequencing, an AMD method, to include ill people in the outbreak that would have been excluded using traditional methods and to confirm that the *E. coli* making people sick was closely related to the *E. coli* in the flour. The flour producer recalled more than 45 million pounds of flour.

Learning from *Listeria*

Every year, an estimated 1,600 people get sick from the bacterium *Listeria monocytogenes* and about 1 in 5 dies. Particularly vulnerable are the elderly, the immunosuppressed, pregnant women and their newborns. In 2013, CDC, in collaboration with the FDA, the U.S. Department of Agriculture, National Institutes of Health, and state and local health departments, began using AMD methods routinely in *Listeria* surveillance. Since that time, AMD methods have detected more clusters of listeriosis, linked more illnesses to food sources, and stopped more *Listeria* outbreaks while they are still small. Combined with good epidemiologic data, AMD gives a better understanding of how *Listeria* gets into our food system and how we can prevent it in the future.



The Impact of Advanced Molecular Detection: Investigating *Listeria* Outbreaks



The Future

PulseNet is expanding whole genome sequencing to its other pathogens under surveillance, including *Campylobacter*, *Shigella*, and *Salmonella*. CDC is working with PulseNet laboratories throughout the nation to help them use AMD methods on foodborne bacteria, which will improve outbreak detection.

Keeping Up with Culture-independent Diagnostic Tests

Culture-independent diagnostic tests (CIDTs) are the future of foodborne disease detection in hospitals and doctors' offices. These tests rapidly identify pathogens without the need to culture (grow) it first, yielding a faster diagnosis. But CIDTs pose a problem for public health investigators. The PulseNet surveillance system relies on isolates to identify outbreaks. Public health laboratories need isolates to determine the bacterium's DNA fingerprint and upload in PulseNet databases. Fortunately, CDC is developing tools to identify and extract disease-causing bacterial DNA from stool samples. These tools will continue to identify and isolate circulating strains of foodborne pathogens.

Why this is important: It is not enough to know which bacterium made someone sick. We also need to know which strain is making people sick and whether it is resistant to antibiotics. With genomic sequence data, we can identify specific features of a bacterium, link it to a food source, and know which antibiotics are likely to work against it.

Vaccine-preventable Diseases

Vaccines have helped eliminate many diseases in the United States, such as polio, but other vaccine-preventable diseases, like pertussis (whooping cough), remain common.

Pertussis (Whooping Cough) by the Numbers*

20,762 cases
1,103 hospitalizations
6 reported deaths

* Based on 2015 data

Flu by the Numbers

5–20% of people in the U.S. get the flu each year

~\$10.4 Billion in direct medical costs

~55,227 deaths from flu and pneumonia

Finding DNA Shifts in Pertussis

Despite the availability of vaccines against pertussis (whooping cough), the disease has rebounded to between 10,000 and 50,000 reported cases in the United States each year since 2010. Using AMD technology, CDC scientists have found shifts in the DNA of circulating *Bordetella pertussis* bacteria that could be contributing to the resurgence of pertussis. One bacterial component targeted by the vaccine, pertactin, is a protein believed to help the bacteria attach to cells in the throat. However, researchers have confirmed that the types of *B. pertussis* that cause the most illness in the United States are missing pertactin.

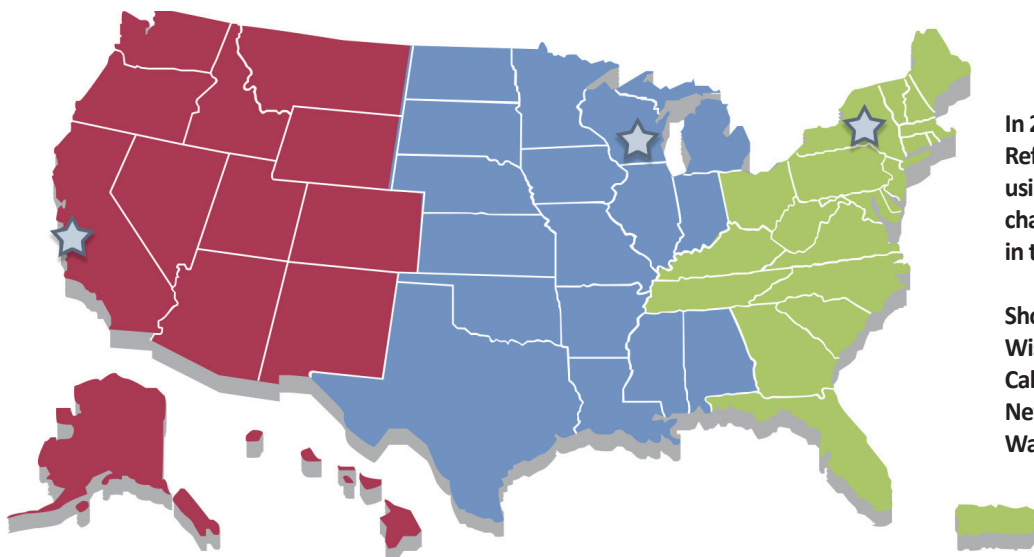
With AMD, investigators are mapping the complete genome of historical and currently circulating strains of *B. pertussis* to determine if these genetic changes are contributing to the reemergence of pertussis.

Improving Influenza Vaccines

Because influenza viruses rapidly mutate, CDC and global partners continually monitor circulating viral strains to develop the best formulation for each year's flu vaccine. Characterizing the thousands of co-circulating flu strains involves time-consuming, labor-intensive steps to grow the virus in the laboratory (culture), and then perform antigenic characterization, as well as other tests.

In 2014, CDC developed and put into operation a process, based on AMD technologies, to sequence influenza viruses directly from patient samples, without the need for culture. This new, more detailed, information allows CDC to prioritize samples for further characterization. This system has impacted vaccine decisions, providing critical data to support vaccine component selection.

Regional AMD Influenza Surveillance Laboratories

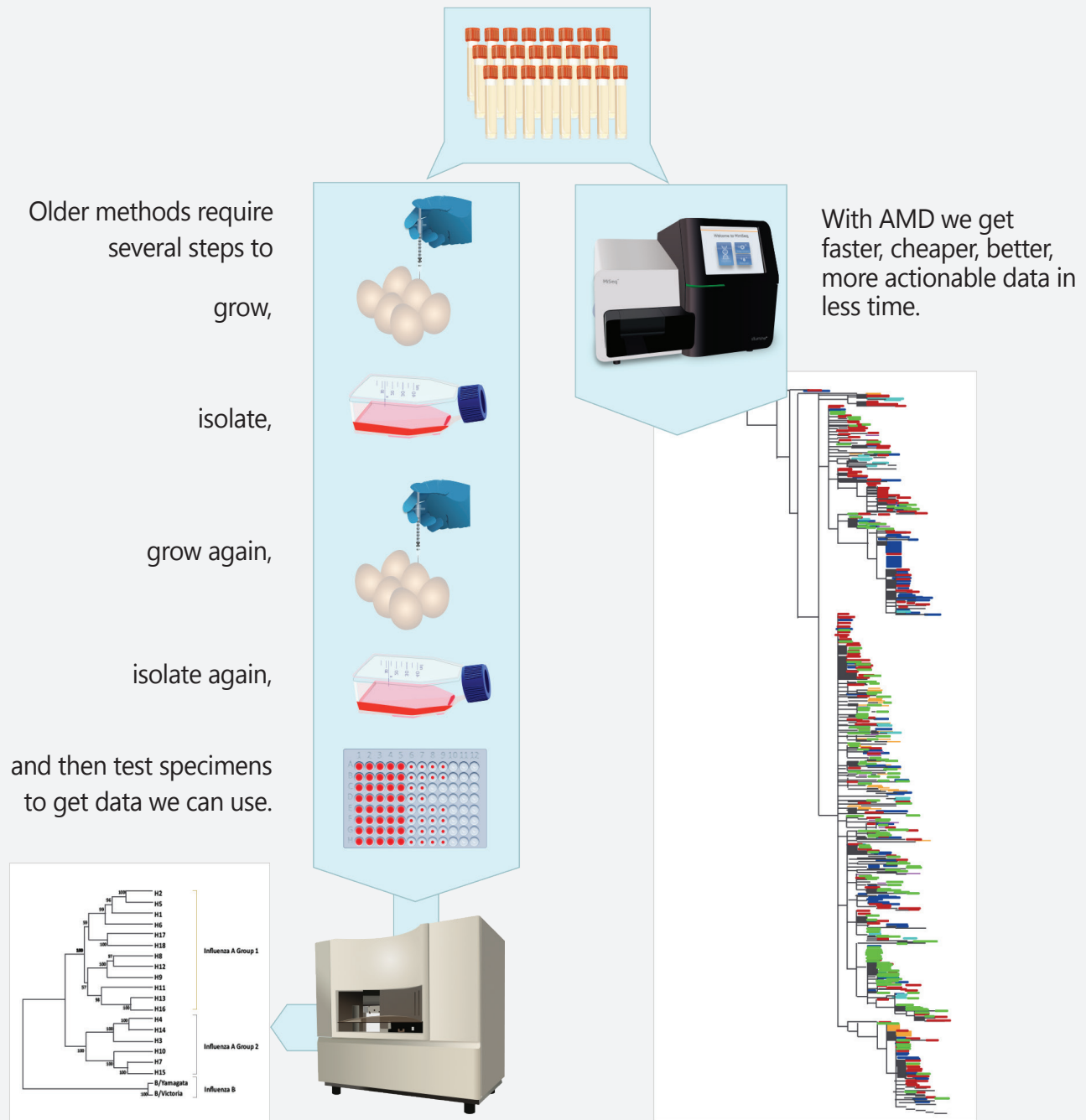


In 2016, three National Influenza Reference Centers (NIRCs) began using the “sequence first” approach to characterize influenza viruses circulating in the United States.

Shown here:
Wisconsin State Laboratory of Hygiene
California Department of Health
New York Department of Health,
Wadsworth Center

Better Flu Surveillance

Health organizations collect thousands of influenza samples from patients.



Vector-borne Diseases

Virtually everyone on earth is at risk of becoming ill from bacteria and viruses transmitted through the bites of mosquitoes, flies, ticks, and other insects, known as vectors.

Battling Malaria on Two Fronts

Malaria is a life-threatening disease caused by *Plasmodium* parasites. People are infected by mosquitoes carrying the *Plasmodium* parasites. Recently, both the parasites and mosquitoes have become resistant to most front-line treatments. To combat the emergence and spread of resistance, CDC is developing AMD tools to track and study the spread of resistance and help guide prophylaxis and treatment guidelines both in the United States and globally.

Malaria by the Numbers*

~214 Million malaria cases worldwide

~438,000 deaths, mostly children in the African Region

~1,500 U.S. malaria cases, mainly in travelers returning from countries with malaria

* Based on 2015 data

1 Recognizing drug resistance in the malaria-causing parasites

Since the 1960s, the *Plasmodium* parasites have continually evolved resistance to different antimalarial drugs, making malaria difficult to control. AMD methods are helping identify and track genetic markers of resistance more rapidly than ever before. CDC is using this technology to build an integrated surveillance system that can identify and track drug-resistant *Plasmodium* parasites. This will directly help guide accurate treatment and prophylaxis of malaria, limiting the spread of resistant parasites.



2 Investigating insecticide-resistant mosquitoes

Due to decades of unmanaged insecticide use, many malaria vector populations are now resistant to certain insecticides, including pyrethroids, the most cost-effective class of public health insecticides currently available. Using AMD, CDC scientists can identify genetic markers of pyrethroid resistance in mosquitoes. Armed with this information, communities can choose the most effective way to control malaria vectors in their area while managing insecticide resistance among mosquito populations.

Zeroing in on Zika Virus

In 2015, Zika virus arrived in South America bringing with it a terrifying birth defect, microcephaly. CDC scientists were able to quickly adapt AMD methods developed for other mosquito-borne viruses, such as chikungunya and dengue, to this new invader. Within 3 weeks of receiving the first Zika virus-positive sample, CDC scientists developed, validated, and distributed a new, faster molecular testing protocol for use in laboratories throughout the Western Hemisphere. This process would have required 3-4 months with older laboratory methods. In addition, studying the genome of Zika strains helped scientists map the spread of the virus, which appears to have come from the Asian-Pacific region, where outbreaks occurred previously. And understanding the genomic make up of the three viruses helped CDC develop a test that can differentiate between chikungunya, dengue, and Zika in a single patient sample.

Previously Unknown Pathogens

AMD gives us the power to discover infectious agents we have not seen before. CDC scientists use AMD to discover several new bacteria and viruses and solve complex medical puzzles.

Uncovering a Tickborne Virus

In 2014, while researching the tickborne Heartland virus, CDC scientists stumbled upon something unexpected: evidence of a different virus. The keen eyes of a CDC microbiologist recognized something unusual in samples obtained from a person in Kansas who had recently died of a suspected tickborne illness.

Using AMD to sequence the virus genome, CDC researchers identified it as a member of a different genus, and the first of its kind to cause human disease in the Western Hemisphere. Named after the county in Kansas where it was collected, Bourbon virus is still being investigated.

Revealing Novel Bacterial Tickborne Pathogens

In 2016, Mayo Clinic and CDC scientists described a novel cause of Lyme borreliosis in North America, the bacterium *Borrelia mayonii*. Using AMD, CDC scientists sequenced the full genome of the newly discovered bacterium, providing a critical foundation for diagnostic development. AMD methods are also being used to broadly detect bacteria that may be causing illness in patients with suspected tickborne disease. This approach has already led CDC researchers to discover additional novel tickborne bacterial pathogens not associated previously with human infection.



Researchers knew blacklegged ticks carry *Borrelia burgdorferi*, the pathogen that causes Lyme disease. In 2016, a new bacterial species that also causes Lyme disease, *Borrelia mayonii*, was found in blacklegged ticks in Minnesota and Wisconsin.



Solving an Unusual Cancer Case

In 2013, doctors in Colombia asked CDC to help diagnose unusual tumors from a man infected with HIV. While the tumors resembled cancer, their cells were much smaller than human cancer cells. After performing dozens of tests, CDC identified the cancer-like cells as being from the dwarf tapeworm, *Hymenolepis nana*, and AMD proved the mutations were in the tapeworm genome. This is the first time scientists have seen a tapeworm's cancer cells take root in a person. Researchers suspect the cancer transferred to the patient because his immune system was weakened by HIV infection. Because HIV is a global threat and the dwarf tapeworm is found worldwide, similar cases may occur. Thanks to work through AMD, clinicians will be aware and able to spot additional cases of this rare disease.

HIV and TB

HIV and TB remain persistent problems in the United States and are complex and costly to treat. Vigilant surveillance and targeted treatment are needed to reduce transmission.

Stopping TB Transmission

To prevent the transmission of TB, timely diagnosis and intervention are critical, especially before people show symptoms of active disease. Public health professionals use surveillance and genotyping of *Mycobacterium tuberculosis* bacteria to look for possible outbreaks and transmission networks. With AMD technology, we can acquire genomic data on TB that lead to more effective epidemiologic field investigations and help us focus limited public health resources and interventions where they will have the greatest impact.

TB by the Numbers*

9,557 cases in the U.S.

\$18,000 per person to treat TB

\$154,000 per person to treat multidrug-resistant (MDR) TB

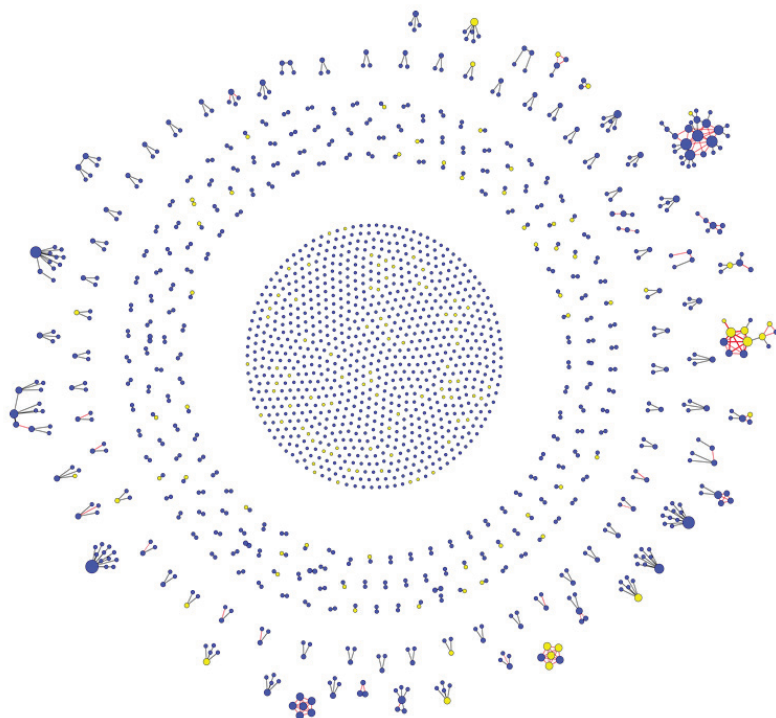
\$494,000 per person to treat extensively drug-resistant (XDR) TB

\$450 Million in total costs to the U.S.

* Based on 2015 data

Connecting HIV Cases

When a small, rural Indiana community saw a dramatic spike in the number of people infected with HIV-1 and hepatitis C virus in 2015, CDC scientists used AMD methods to identify connections between those infected. By using high-performance computing capacity built through the AMD program, investigators were able to combine laboratory and case demographic data with genetic sequences for each infected person's viral strains. Analyses of these combined data sets identified recent, local HIV transmission clusters in persons with pre-existing hepatitis C virus infections. Information provided by this work helped focus prevention efforts and provided reassurance the HIV outbreak was geographically limited in its spread.



Developing Tools to Trace Rapidly Expanding HIV Outbreaks

Through the AMD program, CDC bioinformatics professionals have developed the Microbial Transmission Network Analytics Platform (MTNAP).

MTNAP allows for the rapid integration, exploration, and visualization of data from existing bioinformatics, laboratory, clinical, and epidemiologic sources. This will allow state and local health departments to visually identify rapidly expanding clusters of HIV-1 transmission. HIV-1 sequences are color-coded, yellow circles represent very recent HIV infection and blue represent established HIV infections. Large groups of connected yellow circles suggest recent and rapid transmission.

This image represents a clinical study conducted at multiple sites across three public health jurisdictions—San Francisco, CA; New York City, NY; Raleigh, NC—from 2011–2013.

Meningitis and Pneumonia

Bacterial meningitis and Legionnaires' disease can be life-threatening conditions. People can get these bacterial infections from the environment, food or water sources, or from one another.

Identifying the Cause of Bacterial Meningitis

Bacterial meningitis is serious and can be deadly. *Neisseria meningitidis* and *Haemophilus influenzae* are two of the leading causes of bacterial meningitis. Vaccines are available for some, but not all, types of these bacteria. During outbreaks, public health officials need to quickly know what type of bacterium is responsible so they can determine whether or not people who are at increased risk should be vaccinated to help prevent additional cases.

Meningitis by the Numbers

~4,100 cases reported in the U.S. each year

~500 U.S. deaths each year*

*While most people with meningitis recover, permanent disabilities such as brain damage, hearing loss, and learning disabilities can result from the infection.

Using AMD, CDC has developed faster identification tests for *N. meningitidis* and *H. influenzae*. Additionally, CDC designed web-based software using AMD bioinformatics that can accurately identify strains when comparing closely related bacterial samples. State public health departments have access to this software for outbreak investigations, helping them rapidly identify the cause of meningitis, provide appropriate interventions, and prevent further illnesses.

Locating the Source of Legionnaires' Disease

In 2015, New York City public health officials saw a spike in reported cases of Legionnaires' disease from clinics and hospitals in the Bronx. Legionnaires' disease is a serious type of pneumonia (lung infection) caused by inhaling small droplets of water that contain *Legionella* bacteria. To stop outbreaks, public health officials must identify the environmental source, such as plumbing or cooling towers, and ensure adequate disinfection.

In the Bronx, investigators mapped where all the patients lived and worked. They identified cooling towers as the most likely source of the bacteria. City, state, and CDC laboratories used multiple AMD methods to compare the *Legionella* DNA from patients' samples to the DNA of *Legionella* found in one of the cooling towers, confirming the tower as the source of the outbreak.

Environmental health specialists collect water samples from a cooling tower in the Bronx during the summer 2015 Legionnaires' disease outbreak.



Improving Testing and Detection

Expanding CDC's Library of Rare Pathogens

MicrobeNet is an online database that helps hospitals, public health labs, and other diagnostic labs rapidly identify rare and emerging infections. Beginning in 2013 with a DNA sequence search module, researchers expanded MicrobeNet to include high-quality reference genomes on available strains. They continue adding reference data on new strains, including many rare and unusual species from CDC's collection of pathogens.

Through AMD, CDC scientists have expanded MicrobeNet to include 2,400 species of microorganisms—more than tripling the number available when MicrobeNet started. In addition, they partnered with Bruker Corp. and bioMérieux to give labs additional ways to search and compare bacteria to rare pathogens in CDC's library. Adding this module greatly expanded MicrobeNet's user base to more than 1,400 users worldwide.

Developing an Environmental Testing System for Valley Fever

Valley fever is caused by a microscopic fungus called *Coccidioides* that lives in parts of the western United States. People get Valley fever when they inhale the fungus blown into the air by wind. Using AMD technology, CDC has developed a test that can detect *Coccidioides* DNA in air and soil samples. The data from these tests will help us understand where and when people are most likely to come in contact with *Coccidioides*, which will help patients and physicians know when to suspect Valley fever and get the right treatment.

CDC is also working with the Department of Homeland Security to determine whether air monitoring for *Coccidioides* can provide an early warning to the public when dangerous levels of the pathogen are present.



Brugia malayi is one parasitic organism responsible for the disease lymphatic filariasis.

Detecting Parasites with a Comprehensive Test

Diseases caused by parasites are notoriously difficult to identify. Even when scientists can acquire sequence data, parasitic genomes are so large that they require specialized computer programs to decipher. But AMD is helping CDC scientists explore the complex parasitic genome in new and faster ways.

A new detection method developed by CDC scientists has the potential to revolutionize parasitic testing by selectively detecting all parasite DNA without interference from human DNA in blood samples. This will make it easier to identify not just which parasite made someone sick, but also important genetic information about it; all of this in one test. Once the test is validated, CDC scientists will make it available to other researchers, who could apply it to additional pathogens and disease processes.

Building Workforce and Lab Capacity

Developing the National AMD Workforce

For AMD to be successful, the nation needs a workforce adept in pathogen genomics. As the AMD program began, many in the public health laboratory workforce in the United States had completed their training before genomics was such a prominent field within microbiology. To address this knowledge gap, the AMD program partnered with the Georgia Institute of Technology to bring CDC's laboratory staff members up to speed on sequencing and bioinformatics. As the program expands beyond CDC, the agency has begun to provide funding through the Epidemiology and Laboratory Capacity (ELC) Cooperative Agreement to establish regional training networks at state and local health departments. This approach is designed to boost genomics expertise in these departments while strengthening their ties with local universities. At the same time, the AMD program is bringing scientific talent into the U.S. public health system, particularly through recruitment of bioinformaticians. The AMD program partnered with the Association of Public Health Laboratories (APHL) to create a bioinformatics fellowship program, which is successfully attracting a new generation of public health scientists to both CDC and state health departments.



CDC's ELC program strengthens the nation's capacity to respond to domestic infectious disease threats.

Investigating Outbreaks in the Genomic Era

Epidemiologists are used to analyzing and interpreting data, but before AMD, few had experience incorporating genomic data into outbreak investigations. Through the AMD program, CDC professionals developed a course to introduce epidemiologists to AMD, with a focus on how to work with DNA data obtained through NGS. In 2016, CDC began training its epidemiology staff through the one-day Molecular Epidemiology for Epidemiologists course. In 2017, CDC partnered with Cornell University and the Food Safety Centers of Excellence to develop an online version for state and local epidemiologists and work one-on-one with those epidemiologists. In addition, CDC partnered with the Council of State and Territorial Epidemiologists (CSTE) to offer this course at its annual meeting.

Building the Bioinformatics Base

Because bioinformatics is a specialized field, CDC competes against biotechnology companies for graduates with extensive training and experience in bioinformatics. But CDC partnered with APHL to create a fellowship program to encourage these high-demand professionals to spend 1 – 2 years working on AMD projects. And many recent masters- and PhD-level graduates have jumped at the opportunity to apply their skills to real-world public health problems.

Through this multi-pronged approach of developing internal staff and recruiting external professionals, CDC increased the number of bioinformaticians from fewer than a dozen before 2013 to almost 60 after just three years.

60
in 2016


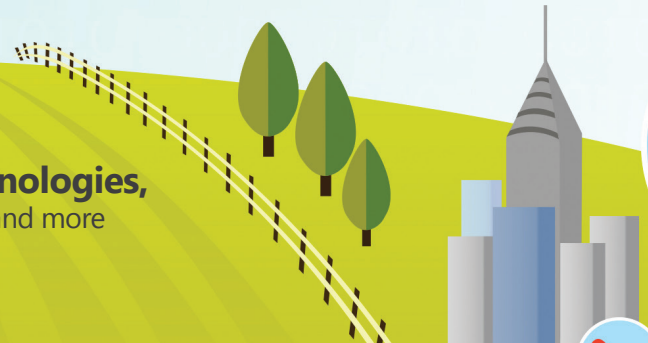


10
in 2013





WHAT'S NEXT *for* AMD



Prior to the AMD program, federal and state health agencies were behind in the adoption of next-generation sequencing, bioinformatics, and related technologies; now they are leading. But it is essential to keep up with technology and maintain AMD infrastructure to prevent CDC and state and local public health laboratories from falling behind in a technological realm that continues to evolve at a breakneck pace.






Keeping pace with rapidly advancing sequencing technologies, which are cheaper, more automated, and more reliable than ever before.



Opening CDC's data on microbial DNA to the outside world speeds research and innovation. The AMD program is committed to ongoing efforts to provide DNA sequence data, databases, and tools available whenever possible.



Transforming the workforce of microbiologists and epidemiologists addresses gaps in existing expertise. The AMD program supports state partnerships with local academic institutions to provide training in basic microbial genomics and the interpretation of data.



Finding new ways to apply advancing technology to real-world problems including using portable nanopore sequencers to identify emerging pathogens in the field and developing robust, sequence-based diagnostic tests with the potential to greatly improve and customize clinical care.