

**U.S. Department of Health and Human Services**

**Centers for Disease Control and Prevention (CDC)**

**Report to Congress on Internal Laboratory Activities of CDC  
and Associated Funding Levels**

[Signed]

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Thomas R. Frieden, M.D., M.P.H.

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“CDC’s laboratory scientists are at the heart of our work to protect America on a 24/7 basis. CDC could not succeed without them. State and local public health departments, health care professionals, and many others rely on our laboratory scientists for specialized testing, consultation, and new technologies to address a wide and growing spectrum of health threats. CDC is the de facto reference laboratory for the United States and for the entire world, an invaluable and indispensable resource.”

— Thomas R. Frieden, MD, MPH  
Director, Centers for Disease Control and Prevention

In Senate Report 112-84, which accompanied the Fiscal Year (FY) 2012 appropriations bill for the U.S. Departments of Health and Human Services, Labor, Education, and related agencies, the Senate Committee on Appropriations stated,

“The Committee requests a report to Congress no later than 120 days after the enactment of this act that details CDC’s various internal laboratory activities and associated funding levels.”

The Centers for Disease Control and Prevention (CDC) has prepared this report in response to the committee’s request. The body of the report is organized into 21 sections that correspond with the standard format of the CDC budget documents with which the Committee is familiar. Each section addresses a specific CDC budget activity and its associated internal laboratory activities. The report encompasses the majority of CDC’s laboratory activities. Relevant definitions and descriptions of laboratory activities not addressed appear in the Explanation and Definition of CDC’s Laboratory Activities section that follows.

### **Overview of CDC Laboratories**

CDC is committed to keeping America safe from threats to its health, safety, and security, whether foreign or domestic. CDC promotes health and quality of life domestically and globally by preventing and controlling disease, injury, and disability. Achieving excellence in laboratory science and in delivering laboratory services is key to fulfilling CDC’s mission.

CDC’s laboratories are integral elements of its prevention and control programs that address infectious and chronic diseases, birth defects and developmental disabilities, and environmental and occupational health. These programs cannot succeed without the actionable information and knowledge generated by CDC’s laboratory scientists, many of whom are nationally or internationally recognized as preeminent experts in their fields.

Thanks in part to the laboratories it operates, CDC has been able to

- identify and take action to address new disease threats (e.g., the influenza strain that erupted into the 2009 pandemic influenza A [H1N1] and the novel virus that triggered severe acute respiratory syndrome [SARS] in 2003);

- track the emergence of drug-resistant infections and develop new ways to counter these threats;
- confirm the sources of foodborne disease outbreaks (e.g., those associated with cantaloupes in 2011 and eggs in 2010), and advise industry, the Food and Drug Administration (FDA), and states on corrective actions;
- serve as World Health Organization (WHO) Collaborating Centers (e.g., for influenza, malaria, tularemia, rotavirus, rabies, poxviruses, and viral hemorrhagic fevers) and participate in global health networks;
- address priorities in human immunodeficiency virus (HIV) diagnosis, prevention, and treatment to reduce HIV-related illness and death in the United States and internationally;
- determine and address the causes of flare-ups of vaccine-preventable diseases (e.g., the spike in U.S. measles cases that appeared in early 2011 after 15 years of low incidence);
- examine suspicious substances to determine if they pose any threats and report findings so that appropriate actions to protect the public can be taken (e.g., the 2001 anthrax attacks);
- test for potential health dangers stemming from toxic releases (e.g., the Deepwater Horizon oil spill in 2010) and provide scientifically based information on their health implications to the public and to decision makers;
- collect objective data for use in designing interventions to prevent and control disease and disability (e.g., through the National Health and Nutrition Examination Survey [NHANES], the only U.S. collection of biologic samples related to nutrition and health on a populationwide basis);
- ensure accuracy of the tests state public health laboratories use to screen newborns in the United States for medical conditions that can lead to lifelong disability or death if not detected; and
- develop and disseminate authoritative public health guidelines (e.g., for the respirators that protect millions of health care professionals, first responders, and industrial workers from airborne viruses and pollutants).

CDC's laboratories are distinct from the many commercial, hospital, and physician-office laboratories that perform tests related to individual patients. CDC has the unique ability to develop and perform highly sophisticated, cutting-edge tests important for monitoring population health and to serve as the last-resort reference laboratory, able to confirm or rule out a new virus or other pathogens. Some of this work is performed in high-containment laboratories where scientists work with especially dangerous infectious and chemical agents. CDC is also uniquely capable of establishing definitive standards for laboratory testing, including tests used in both public health and clinical settings. In addition, CDC's laboratory scientists focus multiple,

complementary disciplines on solving complex public health problems. A recent example is the effort to develop and validate new mass spectrometry test methods for detecting human exposure to botulinum toxin — a result of collaboration between CDC’s Environmental Health Laboratory, which specializes in assessing chemical exposures, and Foodborne Disease Laboratory, which specializes in biologic testing. The new test methods will support responses to biologic or chemical terrorist attacks and foodborne illness outbreaks, as well as investigations of potentially contaminated cosmetic products.

CDC laboratory scientists work closely with their programmatic partners within CDC, including epidemiologists and other colleagues across a wide spectrum of disciplines. In turn, CDC relies on the work its laboratory scientists conduct across multiple domains that are crucial to the agency’s priorities and to its vital contribution to national security. Examples include the following:

- **Surveillance** — Testing to track trends in diseases and other health threats, monitor national health status, and evaluate the effectiveness of vaccines, treatments, infection control programs, and other public health and medical strategies.
- **Emergency Response** — Testing for rapid identification of the causes of disease outbreaks from natural or human-made biologic threats (BT), chemical threats (CT), or radiologic threats (RT) to ensure rational treatment decisions are made.
- **Standards Setting** — Establishing technical and scientific standards for public health and clinical laboratory tests (e.g., for the millions of cholesterol tests performed annually in our nation’s hospitals and clinical laboratories, and for antimicrobial susceptibility testing).
- **Quality Assurance** — Developing, promoting, and evaluating standards and guidelines for public health and clinical laboratories, and providing technical assistance and reliable reference materials to support test validation, quality control, and proficiency testing.
- **New Product Development** — Applying research findings to develop new types of tests, new vaccines, and other products, many of which are licensed to private companies to manufacture and make available through the commercial marketplace.
- **Health System Support** — Providing scientific, technical, and financial assistance to help state and local public health agencies, health care providers, nonprofit groups, federal agencies, and other partners improve their laboratory practices and strengthen their laboratory systems.

## Partnerships

CDC relies heavily on collaboration with other federal agencies, state and local public health departments, health care organizations, and other domestic and international partners to accomplish its mission. The agency’s laboratory scientists partner closely with public health

laboratory professionals and scientists in other U.S. Department of Health and Human Services operating divisions, the U.S. Department of Homeland Security, the U.S. Department of Defense, the Federal Bureau of Investigation, the U.S. Agency for International Development (USAID), and the U.S. Department of Agriculture (USDA), among other federal agencies; WHO and ministries of health worldwide; and industry and nongovernmental organizations (e.g., the Association of Public Health Laboratories).

State and local public health laboratories protect health in their jurisdictions and partner closely with CDC as critical parts of the nation's public health laboratory safety net. Among other services, state and local public health laboratories perform many public health reference tests, confirming or ruling out patient diagnoses, advising providers on the significance of patient test results, and simultaneously using test results to monitor community health trends. Of special note are the critical roles they play in detecting the onset of threats at the front line and in providing surge capacity, helping to manage the high number of tests required during public health emergencies (e.g., the 2009 influenza A H1N1 pandemic).

CDC provides critical support to state and local public health laboratories by designing, developing, and transferring high-quality testing practices to them and by providing technical consultation, training, financial assistance, and high-priority supplies not available from other sources. In addition, CDC has sponsored creation and operation of national networks for disease cluster detection and investigation, rapid communication, and test result validation during foodborne disease outbreaks (e.g., PulseNet) and in response to BTs or CTs or other public health emergencies (i.e., the Laboratory Response Network [LRN]). PulseNet enables state and local public health agencies to detect clusters of illnesses in one or many states rapidly by comparing DNA fingerprints of bacteria from ill patients through the use of an online pattern database maintained by CDC. These disease clusters often represent silently developing foodborne disease outbreaks that can be controlled if detected early. More importantly, PulseNet-detected outbreaks provide industry and regulators the information they need to fix problems in our food supply that would otherwise go unnoticed. LRN — comprising 162 laboratories, most of which can confirm the detection of BT agents and a subset of which have additional capacity to do CT testing — expands and leverages the capacity of the public health laboratory system to respond to public health threats and emergencies. An estimated 85% of the U.S. population lives within 100 miles of an LRN member laboratory, ensuring broad access to testing during public health emergencies. Other federal agencies (e.g., the U.S. Department of Defense, the Federal Bureau of Investigation, FDA, USDA, the U.S. Department of Energy, and the U.S. Environmental Protection Agency), collaborate with the network and coordinate response activities through the Integrated Consortium of Laboratory Networks. Public health laboratories in Australia, Canada, Mexico, and the United Kingdom also participate in LRN.

University- and industry-based scientists and members of scientific and professional associations also are valuable partners for CDC's laboratory scientists. They bring important viewpoints from relevant disciplines and contribute new knowledge from research and front-line industry and clinical experience. In turn, CDC's laboratory scientists use multiple channels to disseminate information to these partners about the new tests, improved testing methods, and laboratory best practices CDC develops. These channels include the electronic Health Alert Network and

Laboratory Outreach Communication System and CDC's *Morbidity and Mortality Weekly Report*, among others. In addition, CDC maintains and continually expands its invaluable collections of unique biologic specimens that CDC scientists and colleagues in universities and other settings use for research into the causes of disease and for development of new medical and public health interventions.

### **Explanation and Definition of CDC's Laboratory Activities**

For the purposes of this report, *internal laboratory activities* are defined as laboratory-related activities that CDC employees and contractors conducted during FY 2011 in the United States, primarily at CDC facilities, and which were funded by the budget activities that appear in the accompanying table. Those facilities are located in the Atlanta, Georgia, metropolitan area and in Anchorage, Alaska; Ft. Collins, Colorado; Cincinnati, Ohio; Pittsburgh, Pennsylvania; San Juan, Puerto Rico; Spokane, Washington; and Morgantown, West Virginia.

This report addresses testing and applied research activities, as well as selected scientific, technical, and laboratory support services. In general, support services include activities such as oversight and implementation of CDC's policy on dual-use research of concern; management of CDC's central collection of more than 6 million biologic specimens for use by CDC and extramural researchers; laboratory security and worker safety protection services; provision of bioinformatics and information technology services; and provision and maintenance of physical facilities. They also include assistance in complying with federal regulatory mandates (e.g., the Clinical Laboratory Improvement Amendments, diagnostic device regulations, and the Select Agents and Toxins regulations). The Emerging Infectious Diseases, Public Health Scientific Services, and Public Health Preparedness and Response sections of this report include information regarding laboratory support services funded from these three appropriations.

This report also addresses domestically based CDC laboratory activities that support external partners, including laboratories operated by ministries of health in other countries. Support for external partners includes provision of laboratory technical support and training, program administration, and cooperative agreement management. Many of these activities advance CDC's global health priorities. Several sections of this report (e.g., the Global Health sections) include descriptions of domestic CDC laboratory activities that support overseas activities.

### ***Exclusions***

Two types of laboratory-related activities that receive funds appropriated to CDC do not appear in this report, explained as follows:

**Domestic Laboratory-Related Activities Conducted by Grantees** — This report does not provide information on laboratory-related activities that state and local public health departments or extramural researchers conduct with funding they receive from CDC through cooperative agreements or other mechanisms. However, activities that CDC employees and contractors conduct in support of those grantees (i.e., managing cooperative agreements) are referenced where appropriate and as noted previously.

**Global Laboratory Activities** — CDC supports multiple laboratories located in other countries and also helps to build and operate global laboratory networks (e.g., the Global Polio Laboratory Network, which supports worldwide poliovirus surveillance). This report does not address these overseas activities or those of other CDC global laboratory networks. However, where appropriate, it provides information about CDC’s domestically based support for such activities, as noted previously.

### **FY 2011 Funding for CDC Internal Laboratory Activities**

The accompanying table indicates that CDC obligated \$412,029,029 to its internal laboratory activities during FY 2011. These funds derived from three sources, as follows:

- CDC direct budget authority (\$336,602,298 total);
- the U.S. Public Health Service Evaluation Fund (\$39,648,974 total); and
- the Public Health and Social Services Emergency Fund (\$35,777,757 total).

The table (next page) is organized according to the format of CDC’s FY 2011 operating plan.

Certain internal CDC laboratory activities are supported by funds that other federal agencies transfer to CDC. Such activities are not included in this report, with the exception of those supported by the U.S. Public Health Service Evaluation Fund and the Public Health and Social Services Emergency Fund. Also excluded are laboratory activities supported by no-year funds appropriated to CDC in fiscal years before FY 2011 but obligated to laboratory activities during FY 2011.

**FY 2011 Funding for CDC Internal Laboratory Activities**

<b><u>Budget Activity</u></b>		<b><u>Total</u></b>
Immunization and Respiratory Diseases		
Budget Authority (BA)	\$ 5,364,537	
Public Health and Social Services Emergency Fund*	\$ 35,777,757	
		<b>\$ 41,142,294</b>
HIV/AIDS, Viral Hepatitis, STD, and TB Prevention — BA		
Domestic HIV/AIDS	\$ 10,792,414	
Viral Hepatitis	\$ 3,304,900	
Sexually Transmitted Diseases (STDs)	\$ 4,154,881	
Tuberculosis (TB)	\$ 4,888,188	
		<b>\$ 23,140,383</b>
Emerging and Zoonotic Infectious Diseases — BA		
Vectorborne Diseases	\$ 8,970,182	
Lyme Disease	\$ 3,669,162	
Food Safety	\$ 6,979,036	
Chronic Fatigue Syndrome	\$ 3,362,953	
Emerging Infectious Diseases	\$ 55,335,645	
Other (Antimicrobial Resistance and Hantavirus/Special Pathogens)	\$ 7,963,416	
		<b>\$ 86,280,394</b>
Chronic Disease Prevention and Health Promotion — BA		<b>\$ 6,035,291</b>
Birth Defects, Developmental Disabilities, Disability and Health — BA		<b>\$ 2,540,629</b>
Environmental Health — BA		
Environmental Health Laboratory	\$ 32,422,706	
Healthy Homes/Childhood Lead Poisoning	\$ 781,512	
		<b>\$ 33,204,218</b>
Public Health Scientific Services		
Budget Authority	\$ 4,992,551	
Public Health Service Evaluation	\$ 3,752,455	
		<b>\$ 8,745,006</b>
Occupational Safety and Health		
Budget Authority	\$ 105,066,718	
Public Health Service Evaluation	\$ 35,896,519	
		<b>\$ 140,963,237</b>
Global Health — BA		
Global AIDS Program	\$ 9,769,770	
Global Immunization Program	\$ 4,064,530	
Global Disease Detection and Emergency Response	\$ 3,718,221	
Parasitic Diseases and Malaria	\$ 10,256,991	
		<b>\$ 27,809,512</b>
Public Health Preparedness and Response — BA		<b>\$ 42,168,065</b>
<b>CDC Total</b>		<b>\$ 412,029,029</b>
<i>BA subtotal</i>		<i>\$336,602,298</i>
<i>Public Health Service Evaluation subtotal</i>		<i>\$39,648,974</i>
<i>Public Health and Social Services Emergency Fund subtotal</i>		<i>\$35,777,757</i>

\* To support pandemic influenza laboratory-related activities.

## **BUDGET ACTIVITY — IMMUNIZATION AND RESPIRATORY DISEASES**

National vaccine programs and policies rely on a foundation of strong science, which is essential for vaccine policy decision making and for evaluating vaccination recommendations after they are implemented. A comprehensive immunization program requires national-level scientific expertise in laboratory sciences and services to monitor preventable disease rates, identify emerging new threats, track and respond to outbreaks, and evaluate vaccine effectiveness.

CDC efforts have helped reduce the occurrence and impact of multiple vaccine-preventable diseases, increased immunization coverage rates, and improved vaccine safety surveillance and research. Continual changes in influenza and other respiratory viruses require relentless tracking of emerging strains to ensure vaccines are effective as well as monitoring increasing importation of vaccine-preventable diseases that affect vulnerable populations.

### **Selected Laboratory Activities in FY 2011**

#### Vaccine-Preventable Diseases

For each annual U.S. birth cohort vaccinated against 13 diseases in accordance with the schedule adopted by CDC, approximately 42,000 lives are saved; 20 million cases of disease are prevented; \$13.6 billion in direct costs are saved; and \$68.9 billion in direct plus indirect (societal) costs are saved. CDC's Immunization Program aims to prevent vaccine-preventable diseases by achieving and maintaining high immunization rates. Since 2009, national policy recommendations have been in place in the United States to prevent a total of 17 diseases among young children, adolescents, and adults. These diseases include measles, mumps, rubella, varicella and herpes zoster, rotavirus, human papillomavirus (HPV), influenza and bacterial meningitis, whooping cough (pertussis), diphtheria, and others.

CDC laboratories

- provided data and analysis on which national immunization policies are based;
- developed new molecular diagnostic assays for measles and mumps and assisted with their implementation in state and local public health laboratories to detect and control outbreaks;
- provided outbreak assistance and performed testing to confirm vaccine-preventable disease occurrence;
- diagnosed and analyzed measles, rubella, and congenital rubella syndrome cases in the United States;
- assessed vaccine impact and changing epidemiology for new vaccine programs (e.g., rotavirus and pneumococcal prevention among children and meningococcal vaccine impact among adolescents);
- assessed effectiveness and duration of vaccine protection among individuals and across populations;

- monitored changes in bacteria and viruses that can cause vaccines to become less effective and identified new strains for use in vaccine development;
- provided evidence-based vaccine effectiveness and program impact results to demonstrate the need for a booster dose of meningococcal vaccine among adolescents;
- demonstrated impact of the childhood pneumococcal conjugate vaccine introduced in 2010 (the information is being used to formulate national policies on pneumococcal vaccine use among adults as well as pneumonia and meningitis treatment guidelines); and
- supported development and licensure of new vaccines through characterization of pathogen strains (e.g., meningococcus), development of standard antibody tests (e.g., pneumococcus and meningococcus), and monitoring trends during vaccine trials.

### Influenza

Influenza is a contagious respiratory illness caused by influenza viruses. It can cause mild to severe illness and death. During 1976–2006, estimates of flu-associated deaths in the United States range from a low of 3,000 to a high of 49,000 annually. Certain groups (e.g., older persons, young children, and those with certain health conditions) are at higher risk for serious flu-related complications. The CDC Influenza Program’s laboratory activities support detection, control, and prevention of influenza.

#### CDC laboratories

- provided year-round domestic surveillance for influenza;
- subtyped and characterized novel influenza viruses;
- studied global influenza trends and virus characteristics;
- identified potential candidate influenza vaccine virus strains through global surveillance activities;
- used cutting-edge technologies to engineer influenza vaccine candidate strains;
- provided weekly electronic reports of influenza activity to help doctors, public health officials, and the general public prevent influenza’s spread;
- helped guide development and deployment of medical countermeasures to prevent and treat persons affected by seasonal and future influenza pandemics;
- served as the National Influenza Center for the United States and as one of five WHO Collaborating Centers that received and tested thousands of influenza virus samples from around the world to monitor for emergence and spread of new variant viruses with epidemic and pandemic potential, including highly pathogenic influenza A (H5N1) viruses and other subtypes (e.g., H2, H7, and H9) that circulate in animal reservoir populations and pose a pandemic threat;

- characterized over 11,000 influenza viruses from domestic and international surveillance partner laboratories;
- participated with other WHO Collaborating Centers and National Influenza Centers in the yearly seasonal vaccine virus selection process for the Southern and Northern Hemispheres;
- sequenced and confirmed multiple novel influenza viruses, including H3N2v, which was confirmed in 12 cases in five states and has the potential to emerge as a circulating human strain;
- developed a vaccine candidate strain for H3N2v influenza virus and started work with manufacturers to develop a vaccine, in case large-scale production becomes necessary; and
- developed and piloted a new influenza risk assessment tool to assess the pandemic potential of novel influenza viruses, which will help prioritize virologic and epidemiologic studies and provide information on which selection of candidate novel influenza viruses for pandemic vaccines can be based.

#### **BUDGET ACTIVITY — HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION: DOMESTIC HIV/AIDS**

Despite major advances in prevention and treatment, HIV infection remains a substantial public health challenge. CDC estimates that approximately 1.2 million persons in the United States were living with HIV at the end of 2008 and that approximately 50,000 persons are newly infected each year.

CDC's laboratories help advance governmentwide efforts to reduce the burden of HIV and acquired immunodeficiency syndrome (AIDS) in the United States, as described in the *National HIV/AIDS Strategy*. The aims of the *Strategy* include

- reducing new HIV/AIDS infections;
- increasing access to care and improving health outcomes for persons living with HIV; and
- reducing HIV-related health disparities.

Early identification of HIV infection can improve access to life-saving treatment, reduce further transmission, and decrease health care costs.

#### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- served as worldwide reference laboratories for diagnosis and drug-resistance testing for HIV/AIDS by providing services to both domestic and international partners (see the Global AIDS Program section for additional activities);

- conducted state-of-the-art testing to advance HIV prevention, surveillance, and treatment (e.g., testing to support early diagnosis [facilitating referral to care, as well as counseling to help prevent transmission], evaluating disease prognosis and response to therapy, and identifying drug-resistant viruses);
- helped state health departments investigate cases of HIV transmission through organ transplantation;
- patented a novel HIV drug-resistance test that can identify hidden drug-resistant viruses in viral subpopulations within individual patients, including patients who respond to antiretroviral therapy (development of drugs that can target these hidden viruses might lead to a cure for HIV);
- developed and evaluated additional novel strategies and methods for HIV detection, isolation, and surveillance (e.g., strategies for identifying HIV infection at earlier stages of disease, increasing the number of persons who know their infection status and are referred for care, and facilitating simultaneous testing for infection with HIV and viral hepatitis);
- developed rapid, user-friendly tests that can be used in the field to identify recent HIV-1 infections and differentiate between HIV-1 and HIV-2 viruses;
- updated the national diagnostic algorithms for HIV testing and revised HIV screening guidelines for organ donations;
- conducted preclinical and clinical research on vaccines and methods for preventing HIV transmission;
- demonstrated that the dosage of an oral antiviral medication needed to prevent HIV infection might be reduced from the currently recommended daily dosing;
- evaluated the threat to the U.S. blood supply posed by human herpes virus type 8 (HHV-8) — the etiologic agent of Kaposi's sarcoma, the most common AIDS-associated malignancy worldwide — and transferred HHV-8 diagnostic technology to international laboratories in AIDS-endemic areas of Africa (also developed an HHV-8 assay appropriate for organ donor screening); and
- conducted research studies to determine if an association exists between a retrovirus — xenotropic murine leukemia virus-related virus — and chronic fatigue syndrome (CFS); no such association was identified and, consequently, two peer-reviewed journal articles from non-CDC investigators were retracted (see the Emerging and Zoonotic Diseases: Chronic Fatigue Syndrome section for additional activities).

## **BUDGET ACTIVITY — HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION: VIRAL HEPATITIS**

Approximately 0.8–1.4 million persons in the United States are chronically infected with hepatitis B virus (HBV) and 2.7–3.9 million are infected with hepatitis C virus (HCV). Many persons are unaware of their infection, putting them at risk for cirrhosis or liver cancer and for transmitting infection to others.

CDC's laboratories help advance efforts across the government to reduce the U.S. burden of chronic viral hepatitis and associated cancers, as described in the U.S. Department of Health and Human Services' *Action Plan for the Prevention, Care and Treatment of Viral Hepatitis*.

### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- served as a worldwide reference laboratory for diagnosis of hepatitis A, B, C, and E;
- assisted U.S. states and cities and Veterans Administration medical centers in investigating 23 local outbreaks, including an outbreak of HCV infections in an outpatient clinic in Georgia, outbreaks of HBV infections in an assisted living facility and a psychiatric long-term care facility in Virginia, and outbreaks of HCV infections transmitted through transplanted organs and tissues in Kentucky;
- conducted state-of-the-art testing for detection of viral hepatitis antibodies and antigens and performed genomic and proteomic profiling of hepatitis viruses;
- assisted industry and academic researchers as well as health care partners by evaluating
  - rapid screening assays for detection of antibodies to HCV,
  - new methods for distinguishing acute from chronic HCV infection,
  - use of mass spectrometry methods to improve detection of HCV transmission,
  - the efficacy of existing vaccines in preventing HBV infections, and
  - candidate HCV strains that might be used to develop vaccines against HCV;
- conducted applied research on viral transmission and pathogenesis, including an assessment of host genomic factors associated with chronic viral hepatitis infection;
- provided technical assistance on disease detection to the U.S.–Mexico Border Infectious Disease Surveillance program; and
- conducted surveillance for hepatitis E viruses among animals to monitor the emergence of new strains.

## **BUDGET ACTIVITY — HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION: SEXUALLY TRANSMITTED DISEASES (STDs)**

Approximately 19 million new STD infections occur each year in the United States, approximately half of which are among young persons (those aged 15–24 years). STDs exact a tremendous economic toll. Direct medical costs associated with STDs are estimated to be more than \$15 billion annually.

CDC's laboratories support public health efforts to prevent and reduce STDs and associated medical complications (e.g., infertility resulting from pelvic inflammatory disease caused by chlamydia or gonorrhea; adverse pregnancy outcomes, including infant deaths or illness caused by neonatal herpes or congenital syphilis; and cervical cancer caused by chronic infection with HPV).

### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- served as worldwide reference laboratories for diagnosis of chlamydia, gonorrhea, syphilis, herpes simplex virus, *Mycoplasma*, chancroid, and HPV;
- monitored emergence of antimicrobial resistance (AR) in sexually transmitted pathogens and notified the health care and public health communities, as needed (e.g., about emerging resistance to cephalosporin antibiotics used to treat gonorrhea);
- provided reference services, diagnostic support, and staff proficiency training to state and local health laboratories, private laboratories, and FDA;
- developed and validated diagnostic tests, including new molecular tests, rapid point-of-care tests, and tests for molecular markers of drug resistance;
- provided expert consultation to physicians and physician groups, including national medical and nursing associations;
- updated the national laboratory testing guidelines for syphilis, gonorrhea, and chlamydia (to be published in 2012); and
- evaluated the impact of the HPV vaccination program by identifying HPV types in cancers, cervical precancers, and cervical specimens collected as part of NHANES (see the Public Health Scientific Services section for a more detailed description of NHANES).

## **BUDGET ACTIVITY — HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION: TUBERCULOSIS (TB)**

One third of the world's population is infected with TB. During 2010, approximately 9 million persons worldwide became ill with TB and 1.4 million died.

Although TB is declining in the United States — approximately 11,000 cases were reported in 2010 — the disease continues to affect disproportionately racial and ethnic minorities, persons infected with HIV, and persons who are foreign-born, including those from India, the Philippines, Vietnam, and Mexico. Moreover, emergence of multidrug-resistant TB (MDR TB) and extensively drug-resistant TB (XDR TB) is presenting new challenges for treatment and control. Prevention of a single case of MDR TB is estimated to save more than \$250,000.

CDC's laboratories focus on advancing TB elimination in the United States by reducing TB among populations at high risk and reducing TB's global impact, including HIV-associated TB, MDR TB, and XDR TB.

### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- served as worldwide reference laboratories for diagnosis and resistance testing for TB;
- managed cooperative agreements that provided technical and financial support for TB diagnosis, surveillance, and drug-resistance testing to all 50 states, the District of Columbia, select cities, and eight U.S. territories and freely-associated states;
- operated the Molecular Detection of Drug Resistance service, which identifies cases of MDR TB and XDR TB; the National Genotyping Program, which provides genetic bacterial fingerprints of TB cases reported in the United States; and the National Genotyping Information Management System, which analyzes laboratory and epidemiologic data to help identify TB cases that might be part of a widespread or multistate outbreak;
- provided test evaluation and guidance that increased use of rapid molecular tests by state and local public health laboratories, which
  - improved turnaround times for physicians (i.e., the time taken for a physician to receive a laboratory result) so that patients can be treated more quickly, and
  - facilitated public health efforts to interrupt disease transmission in communities;
- provided quality-assessment TB challenge samples to 40 public and private laboratories through the Model Performance Evaluation Program, which monitors and improves drug-susceptibility testing;

- provided reference testing services to the CDC Tuberculosis Trials Consortium, which includes 20 clinical sites, and conducted
  - applied research on drug resistance and human and bacterial genetics, and
  - operational research to determine optimal diagnostic methods and testing algorithms for use in high-burden and resource-limited settings;
- contributed to WHO guidance on use of a new test for detecting rifamycin-resistant TB, which can facilitate rapid isolation and specialized treatment of patients with MDR TB;
- issued recommendations on use of a new 12-dose regimen for TB preventive therapy that shortens and simplifies the course of treatment;
- served as a supranational reference laboratory in the STOP TB Partnership’s Global Laboratory Initiative Tuberculosis Network and worked with ministries of health and WHO to strengthen TB laboratory systems overseas, especially in countries that contribute to the burden of TB in the United States and countries that experience outbreaks of MDR TB or XDR TB; and
- led an international working group that is developing a strategy and organizational design for an international program of TB laboratory accreditation.

**BUDGET ACTIVITY — EMERGING AND ZOO NOTIC INFECTIOUS DISEASES:  
VECTORBORNE DISEASES**

CDC supports programs for prevention and control of diseases spread by mosquitoes, ticks, fleas, and other vectors in the United States and abroad (e.g., West Nile virus, dengue/dengue hemorrhagic fever, and Japanese encephalitis). These diseases cause tens of thousands of illnesses in the United States each year and millions of cases internationally, and they represent one of the most critical emerging threats to health in the United States. No human vaccines are available for the vast majority of these diseases.

These diseases can cause serious epidemics and ongoing endemic conditions. Two examples follow:

- Since 1999, West Nile encephalitis has been the most significant arthropodborne viral illness in the United States, causing an estimated 1.8 million infections and more than 12,700 severe illnesses. Outbreaks often have been severe locally, costing millions of dollars in vector control efforts.

- Dengue, the most important mosquitoborne viral disease in the world, threatens an estimated 2.5 billion persons in more than 100 endemic countries; 100 million infections occur annually. The ongoing risk for dengue is illustrated by endemic disease transmission in subtropical areas of the United States (e.g., Puerto Rico); sporadic outbreaks in Florida, Texas, and Hawaii; and thousands of ill travelers who acquire dengue in other parts of the world.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratories

- performed primary and confirmatory diagnostic testing to determine the etiology of suspected and previously unknown vectorborne (VB) human infections;
- evaluated commercially produced assays and advanced the development of new products and approaches for VB diagnostics — both optimization of existing and next-generation methods — and development of novel field-deployable, inexpensive bedside assays;
- advanced development and evaluation of innovative, effective tools for better prediction, prevention, and control of VB diseases;
- developed, successfully tested, and commercially licensed innovative pesticides derived from natural products and effective against mosquitoes, ticks, and other vectors that are increasingly resistant to existing pesticides (this work has been covered in national media and received CDC Innovation funding, an intramural seed grant for ideas that address CDC's public health priorities);
- conducted unique investigations on the immunology, molecular biology, and genetic aspects of viruses and their hosts and vectors;
- provided diagnostic laboratory testing, reference diagnostic services, and training to local, state, and international health laboratories in response to outbreaks, characterization of unknown specimens, and participation in field studies for VB investigations;
- provided training and proficiency testing for laboratory partners to improve recognition, response, and confidence in VB assay results;
- developed one of the first candidate vaccines effective against all four species of dengue virus;
- responded to dengue outbreaks in multiple Pacific Island nations and in East Africa; coordinated response to yellow fever in Uganda; and responded to a deadly tularemia outbreak in Louisiana; and
- completed validation and regulatory studies required for FDA 510(k) review of the first dengue molecular diagnostic test for use in the United States.

## **BUDGET ACTIVITY — EMERGING AND ZONOTIC INFECTIOUS DISEASES: LYME DISEASE**

CDC addresses the growing public health threat in the United States posed by *Borrelia burgdorferi*, the pathogen that is transmitted by *Ixodes* ticks that cause Lyme disease (LD). LD was the sixth highest incident reportable disease in the United States in 2010, with 30,158 cases reported to CDC. Since becoming nationally notifiable in 1991, LD has been increasing steadily in the United States, both in case numbers and in geographic distribution.

Laboratory activities support CDC's four-part strategy for LD prevention: (1) strengthen and refine national surveillance; (2) identify and validate effective prevention methods and approaches; (3) improve early and accurate diagnosis and treatment; and (4) leverage collaborative potential with external partners and stakeholders.

To combat this growing public health problem, CDC laboratories work to develop new prevention tools for persons and communities, better diagnostic tests to reduce misdiagnosis, and new vaccine candidates to replace the former LD vaccine for which production was discontinued in 2002.

### **Selected Laboratory Activities in FY2011**

CDC laboratories

- provided diagnostic and reference services for LD;
- developed a comprehensive LD serum panel for validation and use in FDA licensing of new diagnostic tests;
- distributed reference reagents to internal laboratories and external academic, clinical, and pharmaceutical laboratories;
- conducted research to test a novel, food-grade insecticide; evaluated a bait box with antibiotic bait plus a topical pesticide for mites and ticks targeting rodent reservoirs of LD; evaluated an oral, rodent-targeted vaccine; and tested a commercially available doxycycline cream as tick-bite prophylaxis;
- discovered a novel LD vaccine target for humans;
- furthered development of LD diagnostic tests that are simpler, more objective, more sensitive, and accurate in detecting early disease;
- identified biomarkers of active LD for potential use in novel diagnostics;
- initiated development of new tick diagnostic methods that included genetic tests for studying vector tick populations and for quickly detecting and characterizing tickborne pathogenic organisms;

- managed a cooperative agreement that funded tests and testing services in 19 state health departments in LD endemic and borderline endemic areas;
- initiated a study at one TickNet site to define the frequency of southern tick-associated rash illness that mimics early LD; and
- launched an enhanced communication plan and Internet-based prevention toolkit that includes information regarding laboratory testing for LD to improve public awareness and knowledge.

## **BUDGET ACTIVITY — EMERGING AND ZOOONOTIC INFECTIOUS DISEASES: FOOD SAFETY**

Every year in the United States, an estimated 1 in 6 U.S. residents experiences a foodborne illness, 128,000 are hospitalized, and 3,000 die from foodborne illnesses. The agents responsible for these outbreaks include bacteria such as *Escherichia coli* O157, *Salmonella*, *Shigella*, *Listeria*, and *Campylobacter*; parasites such as *Cryptosporidium*, *Entamoeba histolytica*, *Naegleria fowleri*, *Angiostrongylus cantonensis*, and *Plasmodium*; and viruses such as norovirus and hepatitis A.

Food recalls help stop foodborne disease outbreaks, thereby preventing additional illnesses, hospitalization, and deaths. Preventing a single fatal case of *E. coli* O157 saves up to \$7 million in direct medical costs. The CDC Food Safety Program’s laboratory activities support detection, control, and prevention of foodborne illness outbreaks.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratories

- led and coordinated the PulseNet system — a network of public health and food regulatory agency laboratories that includes 75 laboratories in the United States and 82 countries around the world (PulseNet member laboratories perform standardized molecular subtyping or fingerprinting of foodborne disease-causing bacteria and submit the results to CDC where the information is stored and made available online to other participants involved in foodborne disease investigations, upon request, allowing rapid comparison of fingerprints to link cases within a single outbreak);
- investigated outbreaks of foodborne illness and provided outbreak assistance by testing suspected outbreak samples and facilitating outbreak investigations onsite;
- led the public health and food safety systems in detecting, investigating, and controlling multistate outbreaks of foodborne infections, including

- listeriosis outbreak associated with Colorado cantaloupes, which resulted in the deadliest foodborne disease outbreak in the United States in approximately 90 years;
- multidrug-resistant *Salmonella* serotype Heidelberg outbreak associated with ground turkey;
- salmonellosis outbreak linked to papaya; and
- three *E. coli* O157 outbreaks linked to romaine lettuce, hazelnuts, and bologna;
- played a major role in the investigation of the German *E. coli* O104:H4 outbreak by confirming U.S. cases and linking international cases;
- coordinated the ongoing laboratory response to the cholera outbreak in Haiti, including testing of human and environmental samples and the training of Haitians in laboratory methods;
- led and coordinated CaliciNet — an electronic norovirus outbreak surveillance network that allows participants to compare fingerprints from norovirus outbreaks, often occurring on cruise ships, that have a common source, allowing for rapid comparison of fingerprints to link cases within a single outbreak;
- improved capacity at the state and local levels in conducting surveillance for foodborne diseases and in detecting, investigating, controlling, and reporting outbreaks;
- trained state and local laboratory personnel to assist in foodborne outbreak investigations;
- provided surge capacity testing for state health departments lacking the laboratory capacity crucial for rapid foodborne outbreak investigation and monitoring;
- provided worldwide reference laboratory support to address diagnostic testing for hepatitis A;
- developed and improved tests to detect and identify foodborne disease-causing agents (e.g., *Salmonella* molecular subtyping and *E. coli* genotyping test methods); and
- provided data and analysis to FDA and USDA on which to base food safety action and policy that led to recalls of ground turkey, ground beef, cantaloupes, imported papayas, and other contaminated foods.

## **BUDGET ACTIVITY — EMERGING AND ZOOONOTIC INFECTIOUS DISEASES: CHRONIC FATIGUE SYNDROME**

CFS is estimated to affect 1–4 million U.S. residents. The illness is long-lasting and debilitating, with a negative effect on health and quality of life similar to heart disease, multiple sclerosis, cancer, and AIDS. In the United States, the related annual loss in productivity is worth an estimated \$9 billion, with additional direct medical costs.

CDC supports an intramural multidisciplinary program that obtains and analyzes baseline information that will aid development of interventions for CFS and will improve measurement of clinical outcomes. Laboratory activities are directed at improving CFS diagnosis and attempting to identify groups responsive to specific therapies. These activities complement clinical research initiatives that focus on the causes, consequences, and treatment of CFS and related diseases.

### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- maintained the collection, processing, and archiving of serum, plasma, saliva, whole blood DNA, and RNA samples from CDC studies to form a biorepository linked to clinical and epidemiologic data for discovery and validation of biomarkers for CFS (materials have already been used for collaborative projects involving xenotropic murine leukemia virus-related virus, metagenomics for unknown pathogens, and for salivary biomarker discovery);
- conducted molecular analyses (e.g., gene expression profiling) and evaluated markers of inflammation in blood samples from case-control studies of stress-response as an approach to understanding the pathophysiology of CFS and to identifying CFS subgroups with targets for therapeutic intervention;
- analyzed functional magnetic resonance imaging case-control data to investigate the hypothesis that fatigue in CFS correlates with alterations in the brain;
- initiated studies to evaluate human herpesvirus-6 in CFS and to identify biomarkers of fatigue; and
- continued efforts to discover potential biomarkers and the underlying pathophysiology of CFS to validate the importance of the illness and to provide an impetus for new therapeutic strategies.

## **BUDGET ACTIVITY — EMERGING AND ZOOONOTIC INFECTIOUS DISEASES: EMERGING INFECTIOUS DISEASES**

The range of pathogenic organisms and infectious diseases covered by this budget activity is broad and includes viral, bacterial, fungal, and parasitic agents. The goals of CDC's emerging infectious disease activities are to build state and local public health laboratory capacity throughout the United States and to strengthen CDC's core infectious disease laboratories.

In addition to these activities, the Emerging Infectious Diseases funding line also provides cross-cutting laboratory services essential to the operation of all CDC infectious diseases laboratories. These laboratories have many functions, including but not limited to

- reference and diagnostic testing, technical assistance, consultation, and training for state, local, tribal, and other partners worldwide;
- testing in support of numerous surveillance programs;
- testing in support of outbreak response investigations;
- identification and characterization of novel, unusual or atypical pathogens;
- development, evaluation, and deployment of diagnostic tests and reagents;
- support for vaccine evaluation trials; and
- provision of proficiency testing programs for other laboratories.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratories

- provided worldwide reference laboratory support to address
  - health care–associated infections, including
    - investigating and responding to emerging infections, adverse events, and disease outbreaks associated with health care delivery in all settings, including health care–associated infections, which alone result in approximately 100,000 deaths and cost in excess of several billion dollars annually;
    - improving detection and characterization of health care–associated pathogens (e.g., *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus* [MRSA]);
    - detecting novel and emerging antimicrobial resistance in health care-associated bacteria; and
    - studying the importance of health care–associated disease pathogens in biofilms (e.g., on medical devices);
  - high-consequence pathogens, including anthrax, melioidosis, glanders, Ebola and Marburg hemorrhagic fevers, rabies, monkeypox, smallpox, and brucellosis, including
    - using molecular techniques to characterize high-consequence bacteria in clinical specimens referred to CDC by state and local public health departments;

- o serving as WHO Collaborating Centers for viral hemorrhagic fevers, for poxviruses, and for reference and research on rabies;
  - o serving as an international laboratory of the World Organization for Animal Health, providing diagnostic reference testing for human pathogens that are carried by animals;
  - o identifying and characterizing potential molecular targets for treating and preventing infections with high-consequence viruses;
  - o expanding the range of diagnostic capacity by improving molecular and serological assays to high-consequence viruses; and
  - o providing ongoing training and monitoring of partner nations on laboratory quality improvement, competency, and staff training in accord with Defense Threat Reduction Agency guidelines and goals.
- respiratory and enteric diseases (e.g., *Legionella*, Group A and B streptococcus, mycoplasma, respiratory syncytial virus, adenovirus, coronaviruses [SARS], and rotavirus), including
- o serving as a worldwide reference laboratory and training resource for diagnostic testing and antimicrobial susceptibility testing;
  - o developing new diagnostic tests, including a novel assay that can be used during an outbreak to test simultaneously for 21 different respiratory pathogens;
  - o conducting surveillance studies to determine the burden of respiratory disease in the United States; and
  - o supporting the global introduction of new vaccines against pneumococcal pneumonia and rotavirus (e.g., by providing reference services for measuring protective antibody responses to vaccination);
- waterborne and environmental pathogens, including
- o identifying pathogenic fungi and detecting antifungal resistance;
  - o responding to disease outbreaks associated with environmental transmission (e.g., through drinking water) and using molecular subtyping to match patient and environmental isolates;
  - o developing and implementing environmental microbiology techniques for detecting, recovering, and inactivating infectious pathogens; and
  - o providing public health and hospital laboratory staff training on mold identification;

- meningitis prevention, including supporting the development and introduction of a new meningitis vaccine in African countries that experience meningitis epidemics and leading development of the second edition of the WHO manual, *Laboratory Methods for Diagnosis of Meningitis caused by Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae*, a global resource for detection, isolation, and characterization of invasive bacterial vaccine-preventable disease agents;
- viral hepatitis and STDs, including
  - o diagnostic testing for acute and chronic hepatitis B and C;
  - o establishing a pathogen discovery program to investigate non-A-E viral hepatitis;
  - o serologic testing for HPV; and
  - o evaluation of the impact of HPV vaccination;
- laboratory support for field investigations of Rocky Mountain spotted fever and other rickettsial diseases;
- provided expertise to strengthen surveillance and applied research programs to improve detection and prevention of new and emerging infectious disease threats, including support for
  - development of pathogen discovery techniques to identify new and emerging lyssaviruses (the viruses that cause rabies);
  - identification of suitable targets for development of medical countermeasures for viral hemorrhagic fevers (i.e., high-consequence viruses);
  - development of integrated ecologic and epidemiologic studies for monkeypox and other orthopoxvirus diseases in the United States and globally, and improved diagnostic capabilities for orthopoxvirus disease worldwide (these studies focus on human disease, monkeypox disease ecology, and disease transmission dynamics and provide evidence for disease control efforts, including the use of vaccine);
- developed and enhanced critical infrastructure at CDC, including
  - high-containment laboratories (biosafety level-3 and -4) required for work with known high-consequence pathogens (e.g., anthrax, melioidosis, glanders, Ebola and Marburg hemorrhagic fevers, rabies, and brucellosis), and critical in the rapid identification of newly emerging pathogens associated with high-fatality disease outbreaks;
  - a pathology laboratory unit that provides state-of-the art diagnostic evaluation of tissue specimens to help identify previously unrecognized or new infectious diseases (e.g., H1N1 pandemic flu, SARS, and hantavirus pulmonary syndrome);

- an environmental microbiology laboratory activity that develops and implements diagnostic and disinfection techniques to enhance food and water safety;
- a field laboratory in Alaska with a diverse portfolio of activities that supports surveillance, studies in antimicrobial resistance, vaccine evaluations, outbreak response, applied laboratory research, and preparedness activities; and
- a biotechnology core laboratory that performs high-throughput, next-generation sequencing of bacterial, viral, and fungal genomes; associated genomic assembly; and advanced bioinformatics for infectious, and importantly, outbreak and unknown pathogen identification; proteomic analyses of the functions, structures, and interactions of proteins, primarily by mass spectrometry and protein sequencing; chemical synthesis of complex oligonucleotides and peptides critical for molecular technologies used by CDC laboratories and LRN; as well as evaluates and develops new, cutting-edge technologies (these functions and the expertise that supports them continue to provide the data and the knowledge needed by CDC scientists and physicians rapidly, particularly during emergencies, to keep the agency at the forefront of public health in an expanding and evolving world);
- provided laboratory infrastructure services to all CDC infectious disease laboratories, including
  - developing an infectious disease laboratory database — a comprehensive and cross-linked source of information regarding CDC laboratories for stakeholders and leadership and to aid in meeting anticipated FDA requirements for laboratory-developed tests;
  - supporting uniform information management systems for infectious disease laboratories that enhance capacity for tracking, reporting, and analyzing samples received for testing, surveillance, and outbreak investigations, as well as providing enterprise capacity for interoperability (i.e., data sharing) through technologic advances, shared resources, and strategic alignment with external partners;
  - enhancing a quality management system across CDC’s infectious diseases laboratories to strengthen regulatory compliance and adherence to quality standards for these laboratories;
  - supporting cutting-edge public health bioinformatics through a new centralized bioinformatics core consisting of highly skilled bioinformatics scientists who collaborate with CDC program scientists to facilitate faster pathogen identification, development of better diagnostics, and improved analysis of laboratory data for epidemiologic surveillance and outbreak investigations;
  - purchasing and distributing laboratory supplies and personal protective equipment;
  - producing, managing, and shipping biologic products, diagnostic kits, cell cultures, and high-quality specialized reagents;

- providing animal care services (maintained at multiple laboratory sites), with ongoing veterinary care, guidance, and oversight to ensure the welfare of laboratory animals (unique services that include maintenance of insect and tick colonies for work with VB pathogens [e.g., dengue and LD]);
- managing specimens (including triage, processing, and distribution) and maintaining a serum bank used in studies of different pathogens;
- decontaminating biologic waste, monitoring autoclaves, and maintaining laboratory water systems; and
- providing the Laboratory Outreach Communication System for CDC's Emergency Operations Center and urgent communications during response events to public health laboratories and the 25 largest associations for laboratory professionals.

## **BUDGET ACTIVITY — EMERGING AND ZOO NOTIC INFECTIOUS DISEASES: OTHER**

This budget activity provides funding for activities related to controlling and preventing AR and for detecting and controlling diseases for recognized and emerging high-consequence threats known as special pathogens.

### Antimicrobial Resistance

AR is one of the world's most pressing public health threats and is increasing in scope. Infections with resistant bacteria have become more common in health care and community settings. Patients infected with drug-resistant microbes are more likely to require hospitalization, remain in the hospital longer, and have a poor prognosis. In a 2008 study of hospital-acquired antimicrobial-resistant infections, the medical costs attributable to AR ranged from \$18,588 to \$29,069 per patient; hospital stays were extended by 6.4–12.7 days; and the mortality attributable to AR was 6.5%. Using the most conservative estimates, the total cost of the resistant infections was \$13.35 million dollars for the 188 patients in that study alone.

In efforts to identify, control, and prevent new AR, CDC laboratories set an ultimate standard for laboratory testing for state health departments and hospital laboratories, CDC surveillance and outbreak control, and analysis of AR transmission and risk factors.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratories

- provided gold-standard testing services to state health departments, clinical diagnostic laboratories, and academic researchers and collected and maintained a repository of AR isolates;

- supported CDC surveillance systems by testing organisms of public health importance, including *Streptococcus pneumoniae*, Group A and B streptococcus, *Neisseria meningitidis*, MRSA, *Haemophilus influenzae*, *Neisseria gonorrhoeae*, *Helicobacter pylori*, and *Candida*;
- monitored resistance rates and informed, guided, and evaluated prevention efforts;
- provided outbreak response and technical assistance to state health departments (e.g., collaborated with seven state health departments and Puerto Rico to stop outbreaks of carbapenem-resistant Enterobacteriaceae, and also provided susceptibility testing for state and hospital laboratories);
- tested more than 5,000 samples of microbes, including *Salmonella*, *Shigella*, *Campylobacter*, *E. coli*, and *Vibrio*, to document the emerging genetic mechanisms of resistance to antimicrobial drugs;
- conducted strain typing and additional molecular characterization of multiple AR pathogens, including carbapenem-resistant Enterobacteriaceae, MRSA, *C. difficile*, and multidrug-resistant *Acinetobacter* species;
- detected emergence of antibiotic resistant *N. gonorrhoeae* and developed molecular assays for detecting cephalosporin-resistant *N. gonorrhoeae* in the United States;
- used culture and molecular techniques to detect and identify mechanisms of AR for all respiratory and vaccine-preventable bacterial diseases, including *S. pneumoniae*, *N. meningitidis*, and Group A and B streptococci;
- developed new assays for surveillance of resistant hepatitis C strains by predicting resistance to combined interferon/ribavirin therapy among patients chronically infected with hepatitis C virus; and
- detected the emergence of a strain of antibiotic-resistant pneumococcus not covered by the PCV7 pneumococcal vaccine that was recommended by the Advisory Committee on Immunization Practices (ACIP) in 2000 (this helped guide the inclusion of this strain in the new pneumococcal vaccine, PCV13, which was recommended by ACIP in 2010).

### Hantavirus/Special Pathogens

Hantavirus pulmonary syndrome is a severe, sometimes fatal, respiratory disease among humans caused by infection with a hantavirus. CDC provides continuing surveillance and epidemiologic studies of hantaviruses in the United States and globally. CDC also provides reagents, technical advice, response teams, and epidemiologic investigations to improve diagnostic and reagent capability for hantaviruses and related hemorrhagic fever viruses. Through its laboratory work, CDC has developed more sensitive assays for detection of hantaviruses and emerging hemorrhagic fever viruses, and for evidence of their infection among humans and animal hosts, that will enhance the ability to respond to outbreaks of these diseases domestically and globally.

## **Selected Laboratory Activities in FY 2011**

### CDC laboratories

- provided laboratory support to all state health departments for hantavirus pulmonary syndrome diagnostics and consultations regarding case management and surveillance;
- provided consultations on hantavirus small animal reservoir populations in North and South America;
- conducted basic research to understand further the natural history and pathogenicity of hantaviruses for improved diagnostics and vaccine development;
- completed successful vaccine trials of a live-attenuated Rift Valley fever recombinant virus for use among livestock; and
- discovered a novel phlebovirus associated with two Missouri cases of severe febrile illness with thrombocytopenia.

## **BUDGET ACTIVITY — CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION**

Chronic diseases are the leading cause of preventable death in the United States. Prevention and control of chronic diseases are among CDC's highest priorities. Annually, U.S. residents suffer more than 2 million heart attacks and strokes. An estimated 443,000 persons die prematurely from smoking or exposure to secondhand smoke. Cigarette smoking accounts for more than \$96 billion a year in health care-related costs and \$97 billion a year in lost productivity. Deficiencies in micronutrients (e.g., iron, iodine, vitamin A, folate, and zinc) affect a third of the world's population.

CDC's related laboratory activities center on developing and applying accurate, high-quality methods to (1) improve detection, diagnosis, treatment, and prevention of cardiovascular disease; (2) reduce individual and population exposure to addictive and toxic substances in tobacco products; and (3) improve nutrition through reductions in micronutrient deficiencies.

## **Selected Laboratory Activities in FY 2011**

### Lipid Standardization Program and Reference Lipid Testing

#### CDC laboratories

- developed and maintained highly accurate and precise methods, including two new mass spectrometry reference methods, to measure total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides;

- operated an internationally recognized reference laboratory to calibrate and monitor accurately, over time, cholesterol and lipid measurements used in patient care, public health, and research;
- served as the only U.S. laboratory that provides technical assistance on cholesterol and lipid assessment through reference measurements, training, and professional education activities;
- conducted research to identify and better address problems with current cholesterol and lipid measurements;
- provided quality-control materials to 84 laboratories, including 43 research (academic) laboratories, 38 commercial laboratories performing patient-care testing and clinical trials, and three assay manufacturers to ensure accuracy of lipid measurement for ongoing U.S. and international studies of cardiovascular disease; and
- assigned reference values to proficiency testing survey materials used in assessing the performance of patient care, public health, and research tests (in collaboration with the College of American Pathologists).

### Tobacco Testing

#### CDC laboratories

- maintained the only federal laboratory that measures addictive and toxic substances in tobacco products and smoke, as well as in the urine and blood of persons who use tobacco or are exposed to secondhand smoke;
- studied the effects of chemical additives, constituents, and design on the toxicity and addictiveness of tobacco products;
- documented the impact that different types of cigarettes and smoking styles have on exposure to carcinogenic tobacco-specific nitrosamines (TSNAs) and used these laboratory findings to shape future CDC NHANES surveys, which will track cigarette types and smoking behaviors to monitor how changes in cigarette composition affect human exposure (see the Public Health Scientific Services section for a more detailed description of NHANES);
- assessed U.S. residents' exposure to the harmful chemical constituents of tobacco smoke, including measuring a highly specific biomarker of the most carcinogenic TSNA (the first assessment of exposure to tobacco carcinogens among the U.S. population) and serum cotinine, a marker of nicotine and secondhand smoke exposure, thereby determining that nonsmokers' exposure to tobacco carcinogens increases with their exposure to secondhand smoke;
- collaborated in health studies examining the association of secondhand smoke exposure with cancer, asthma, sudden infant death, birth defects, and other diseases;

- demonstrated that roll-your-own cigarettes deliver as much as or more mainstream smoke as manufactured cigarettes, potentially increasing a smoker’s exposure to toxic and addictive chemicals;
- collaborated with FDA’s southeastern regional laboratory to establish standard methods to measure tobacco product constituents and to enhance FDA laboratories’ capability to conduct tests in support of regulatory standards; and
- supported global laboratory capacity to analyze addictive and toxic substances in tobacco through shared development of testing methods and test validation (in collaboration with the World Health Organization’s Tobacco Laboratory Network).

### Quality Assurance and Training for Micronutrient Testing

#### CDC laboratories

- improved laboratory measurements to detect micronutrient deficiencies so that national nutrition surveys in developing countries can efficiently and reliably assess nutritional status; and
- provided full laboratory support, including technical assistance, in-country planning and training, external quality assessment, and technology transfer to ensure accurate assessment of nutritional status in national nutrition surveys in the Democratic Republic of Congo, the Dominican Republic, Iraq, Kenya, Kyrgyzstan, and Malawi.

## **BUDGET ACTIVITY — BIRTH DEFECTS, DEVELOPMENTAL DISABILITIES, DISABILITY, AND HEALTH**

Birth defects and blood disorders place a considerable burden on persons, families, and society. Approximately 1 in 33 babies (or about 130,000 annually) is born with a birth defect. Birth defects account for more than 20% of infant deaths and result in more than \$2.6 billion annually in hospital costs. Nonmalignant blood disorders affect millions of U.S. residents each year. Direct health care costs for hemophilia alone exceed \$1 billion per year and might approach \$3–\$4 billion if complications are considered.

CDC’s internal laboratory activities to address birth defects and blood disorders focus on (1) preventing and reducing the adverse consequences of birth defects by conducting studies to identify genetic factors that contribute to the causes of these complex diseases and (2) preventing death and disability by reducing the complications associated with blood disorders.

## Selected Laboratory Activities in FY 2011

### CDC laboratories

- served as the central laboratory for the National Birth Defects Prevention Study (NBDPS), the largest population-based case-control study in the United States that collects genetic samples and information regarding environmental exposures; in collaboration with eight grantees,
  - tested the quality of more than 5,500 biologic specimens collected at NBDPS sites;
  - developed, validated, and performed genetic tests for research studies on selected birth defects;
  - investigated and applied optimal methods for DNA collection, processing, and quality assessment and provided guidance on the long-term storage of biologic specimens;
  - provided quality-assurance materials and technical assistance to ensure that collaborating NBDPS laboratories perform highly accurate measurements;
  - performed pilot projects to evaluate new technologies for the collection, processing, genotyping, and storage of biologic specimens; and
  - evaluated collection methods and provided guidance to increase the effectiveness of NBDPS sample use;
- monitored for infectious agents in the U.S. blood supply to prevent the transmission of infectious diseases to persons undergoing treatment for bleeding disorders and thalassemia (the only laboratory in the world that conducts such active infectious disease surveillance);
- monitored and adapted new technologies for surveillance of blood products;
- performed genetic and other related research on coagulation inhibitor (antibody) formation, a serious complication among hemophilia patients;
- compiled and maintained a national database of genetic information to help providers diagnose and prevent disease complications associated with hemophilia and coagulation inhibitors;
- maintained the largest collection in the world of DNA samples from persons of African descent in the United States who have had a venous thrombosis event (a critical resource for defining risk factors among this population); and
- performed ABO Blood Group type testing during the 2011 Haiti cholera outbreak to assess the severity of disease.

## **BUDGET ACTIVITY — ENVIRONMENTAL HEALTH**

Public health action to protect the nation's health includes promoting a healthy environment and preventing premature death, avoidable illness, and disability caused by noninfectious, nonoccupational, environmental, and related factors. CDC's Environmental Health Laboratory provides unique laboratory science to improve detection, diagnosis, treatment, and prevention of (1) diseases that result from exposure to environmental chemicals, (2) treatable congenital disorders among newborns, and (3) nutrition-related diseases and selected other diseases requiring advanced laboratory measurement for accurate diagnosis.

### **Environmental Health Laboratory**

#### **Selected Laboratory Activities in FY 2011**

##### Biomonitoring of Chemical Exposures

In the United States and internationally, persons come into contact with thousands of chemical substances in the environment, both naturally occurring and manufactured. The Environmental Health Laboratory conducts biomonitoring — the direct measurement of environmental chemicals, or their products, in human blood and urine — to assess population and individual exposure to environmental chemicals.

##### CDC laboratories

- conducted the nation's only comprehensive assessment of U.S. residents' exposure to more than 300 chemicals in the environment through biomonitoring of persons who participate in the ongoing NHANES survey (see the Public Health Scientific Services section for a more detailed description of NHANES);
- updated the *Fourth National Report on Human Exposure to Environmental Chemicals* to include new biomonitoring results for 66 environmental chemicals, including cotinine, bisphenol-A, phthalates, triclosan, and perfluorchemicals;
- provided laboratory measurements for 50 studies that examined the exposure of vulnerable groups to environmental chemicals or investigated associations between exposures and adverse health effects;
- served as the world's sole or primary source for high-quality laboratory tests in human blood or urine for bisphenol-A, trans fatty acids, speciated arsenic, uranium, speciated mercury, volatile organic compounds, phthalates, triclosan, selected radionuclides (e.g., polonium-210, cesium-134, cesium-137, and iodine-131), and other substances;

- developed, evaluated, and applied innovative laboratory methods to
  - improve response to public health emergencies, including emergencies that involve disease and death from unknown causes; and
  - measure and analyze priority environmental chemicals;
- provided technical support, training, quality assurance, and technology transfer to state and local laboratories during investigations of known and potentially unsafe chemical exposures; and
- demonstrated the impact of voluntary discontinuation of the use of perfluorooctane sulfonic acid (PFOS) by documenting a substantial reduction in human exposure to PFOS after the end of production in 2002.

### Newborn Screening

Each year, more than 4 million newborns — nearly every newborn — in the United States are screened for such disorders as congenital hypothyroidism and sickle cell disease. These conditions often can be treated to prevent serious complications if detected early in life. State public health laboratories — which test 98% of U.S. infants for birth defects every year — rely on CDC to ensure the accuracy of testing and to develop methods for detecting congenital disorders that are not apparent at birth.

#### CDC laboratories

- operated the nation’s only quality-assurance program to ensure the accuracy of newborn screening tests to detect treatable diseases that cause malformation, mental retardation, and death;
- provided newborn screening quality-assurance materials, proficiency testing, and technical assistance to more than 500 laboratories in all 50 U.S. states and in 67 countries;
- developed new methods to detect newborn diseases; and
- conducted laboratory studies that supported the addition of severe combined immunodeficiency (SCID), better known as “Bubble Boy Disease,” to the U.S. Department of Health and Human Services Secretary’s Recommended Uniform Newborn Screening Panel — the first new condition added to the original panel of 29 conditions (SCID affects an estimated 1 in 100,000 to 1 in 40,000 newborns and leads to death during infancy if not treated early).

## Nutrition-Related and Selected Other Chronic Diseases

Prevention and treatment of nutrition-related and selected other chronic diseases require accurate laboratory measurement to detect and diagnose disease and to assess the effectiveness public health interventions.

CDC laboratories

- conducted the nation's only comprehensive assessment of the nutritional status of the U.S. population by measuring more than 50 nutritional indicators among persons who participate in NHANES (see the Public Health Scientific Services section for a more detailed description of NHANES);
- developed new and improved methods for measuring nutritional and dietary bioactive compounds, including a method to monitor vitamin D blood levels among populations; and
- standardized and improved the accuracy of clinical measurements for cholesterol, related lipids, testosterone, estradiol, and selected other diagnostic tests for chronic diseases.

## **Healthy Homes/Childhood Lead Poisoning**

### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- conducted the nation's only comprehensive assessment of U.S. residents' exposure to lead through biomonitoring of persons who participate in the NHANES survey, determined the prevalence of persons (including children aged 1 year and older) with lead exposures higher than toxicity levels, and reported elevated exposures to ensure effective treatment and exposure interventions (see the Public Health Scientific Services section for a more detailed description of NHANES);
- provided laboratory measurements for 11 studies (including the National Children's Study) that examined the exposure of vulnerable groups to lead;
- provided blood lead quality assurance to nearly 70 U.S. laboratories through CDC's Lead and Multi-Element Proficiency Program;
- provided portable blood lead instruments, quality assurance, training, and laboratory assistance to the investigation of an outbreak of lead poisoning in two mining villages in Nigeria, where CDC staff used the portable lead instrument to identify exposed children rapidly onsite, enabling life-saving medical treatment.

## **BUDGET ACTIVITY — PUBLIC HEALTH SCIENTIFIC SERVICES**

This budget activity provides funding for activities related to support services for CDC's laboratories and for selected laboratory testing as part of CDC's unique NHANES survey.

### Laboratory Support Services

The success of CDC's laboratory scientists and laboratories depends on their access to a spectrum of scientific, technical, policy, and other services provided by multiple CDC offices. These essential support services extend from coordination of national CDC laboratory initiatives to assistance in complying with multiple federal regulatory mandates. They also include technical training, laboratory worker safety, and availability of suitable equipment and facilities, among other services.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratory-support services

- assessed implications for the agency's laboratories if state and local public health laboratories — the majority of which operate under intense fiscal and other pressures — continue to lose capacity to conduct critically important tests (this led to creation of the new Laboratory Efficiencies Initiative to help them maintain testing capacity and achieve long-term sustainability through the adoption of alternative high-efficiency management practices);
- provided consultation to CDC laboratory directors regarding compliance with federal regulatory requirements related to disease agents that have potential to pose severe threats to human, animal, and plant health and to animal and plant products;
- coordinated formulation and implementation of a uniform, agencywide policy to assist CDC laboratories in complying with the federal Select Agents and Toxins regulations (the regulations are available at [http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr73\\_main\\_02.tpl](http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr73_main_02.tpl));
- enhanced management of CDC's central collection of more than 6 million biologic specimens and delivered more than 700,000 specimens to CDC and extramural scientists for research into the causes and prevention of disease;
- trained more than 450 CDC scientists in dual-use research awareness and policies (based on recommendations of the National Science Advisory Board for Biosecurity) to prevent release of research findings that can be misused intentionally to pose a biologic or chemical threat to public health or national security;
- provided advanced training through the National Laboratory Training Network to state and local public health laboratory professionals, preparing them to respond to biologic and chemical terrorism, infectious disease outbreaks, disasters, and other public health threats and emergencies;

- provided training in safe handling practices and in specialized microbiology testing for BT agents;
- managed CDC’s technology transfer program to facilitate commercialization of inventions generated by CDC laboratory scientists and other researchers;
- licensed 51 inventions by CDC laboratory scientists for production and sale by private-sector firms and maintained an additional 1,116 patents based on CDC inventions consistent with U.S. Patent and Trademark Office requirements;
- managed CDC’s cooperative agreement with the Association of Public Health Laboratories to assist CDC’s scientists in conducting research, developing informatics applications, delivering training, and implementing other high-priority projects with extramural partners; and
- supported agencywide plans to review and comply with FDA regulatory requirements for *in vitro* diagnostic devices.

#### The National Health and Nutrition Examination Survey

Data from NHANES have been the cornerstone for national health and nutrition policy and surveillance activities — the surveys are the only collection of biologic samples related to nutrition and health on a populationwide basis in the United States. Each year, tens of thousands of specimens from NHANES participants are processed and shipped to multiple CDC programs for laboratory analysis of nutritional biochemistries, environmental exposures, infectious diseases, and other health indicators. Approximately 250 different types of laboratory tests are performed. Those CDC programs provide funding for the laboratory tests they need, with the following exception, which is supported by the Public Health Scientific Services funding line.

#### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- received, processed, and tested more than 4,500 blood samples for a complete blood count, a panel of tests used to screen for such disorders as anemia, presence of infection, and other diseases.

#### **BUDGET ACTIVITY — OCCUPATIONAL SAFETY AND HEALTH**

Workers typically spend a quarter of their lives and up to half of their waking hours at work, making the workplace a key location for health problems. During 2010, employers in the private sector reported approximately 2.9 million nonfatal work-related injuries and approximately 200,000 cases of occupational illness. On average, 14 workers in the United States die each day from an injury sustained at work (approximately 4,500 workers during 2010), and another 134 die from work-related disease. The total estimated direct and indirect costs for work-related

diseases and injuries are approximately \$250 billion. CDC maintains unique laboratory capacity for conducting multidisciplinary occupational safety and health research and provides global leadership in areas of evidence-based information to prevent work-related illness, injury, disability, and death.

### **Selected Laboratory Activities in FY 2011**

#### Assessment of Mining Health and Safety Hazards and Disaster Prevention

CDC laboratories

- conducted full-scale experiments before testing interventions at working mine sites;
- developed a new award-winning LED cap lamp to prevent injuries by enhancing the illumination of underground mines and associated hazards, including uneven and cluttered surfaces, areas of unstable rock, and other obstacles integral to mining operations;
- improved understanding of mine explosions, designed explosion and fire suppression strategies, and developed approaches for minimizing or preventing massive rock failures by using the unique capabilities of the Lake Lynn Laboratory and the Mine Roof Simulator;
- simulated underground coal mining conditions at active production zones and conducted research that addresses health hazards (e.g., coal dust);
- identified inadequate coal mine dusting standards, which led the U.S. Department of Labor to issue an Emergency Temporary Standard for all coal mines to prevent coal dust explosions; and
- conducted research on hearing loss prevention for mine workers using large-scale mining equipment.

#### Improved Personal Protective Equipment and Technologies

CDC laboratories

- conducted research to advance technology to improve protection, comfort, fit, and the use of personal protective equipment and to examine exposures to inhalation, dermal, and other occupational hazards;
- conducted firefighter turnout gear investigations and research in personal protective equipment anthropometrics and aerosols/filtration by using capabilities that exist in only a few laboratories in the world (e.g., human metabolic response simulation and chemical protective clothing penetration);
- administered the respirator certification program to ensure a level of standard filter efficiency for all respirators used in U.S. workplaces by using the only full-size respirator testing facility in the United States; and

- improved the quality and quantity of respiratory protection for workers through 588 certified respirator decisions (including 356 new approvals) and 248 complete respirator audit activities.

### Industrial Hygiene

#### CDC laboratories

- developed and evaluated methods used worldwide to sample and analyze contaminants in workplace air and in the blood and urine of workers who are exposed occupationally;
- designed and tested aerosol sampling equipment prototypes to evaluate exposure to ultrafine and nanoparticles in field studies;
- identified, evaluated, developed, and implemented technology to prevent worker exposure to workplace health hazards; and
- developed a portable, free-standing airborne isolation system capable of producing airborne infection isolation in harsh environments.

### Applied Toxicology

#### CDC laboratories

- used diverse laboratory disciplines (e.g., exposure generation and assessment, pulmonary toxicology, cardiovascular toxicology, and neurotoxicology) to answer critical questions about workplace hazards and how they affect workers on a biologic and physiological level;
- conducted aerosol generation and animal inhalation exposure research for work-related hazards (e.g., multiwalled carbon nanotubes, carbon nanofibers, welding fumes, and artificial flavorings);
- conducted research by using animal models and published a series of reports on the health effects of the oil dispersant used in the Deepwater Horizon emergency response;
- used a biosafety level-3 adaptable laboratory with simulated patient examination room complete with a coughing and breathing mannequin to monitor health care workers' potential aerosol exposure to an infected patient; and
- demonstrated aerosolized transmission of influenza virus in laboratory studies and hospital settings and characterized viral particle size and quantity in coughs from influenza patients.

### Safety Engineering

#### CDC laboratories

- developed engineering controls and safe work practices to prevent work-related deaths and injuries;

- researched human behavior, physical responses, and decision-making skills under simulated conditions of work at elevated heights by using unique virtual reality capacity;
- researched interactive effects of biomechanics, physiological load, and psychological stress on workers; and
- registered and quantified human body size and shape of various occupational groups for use in developing improved equipment designs (e.g., developed and disseminated a comprehensive database of truck driver anthropometrics to major truck manufacturers who are using the data to improve truck cab design for increased safety).

## **BUDGET ACTIVITY — GLOBAL HEALTH: GLOBAL AIDS PROGRAM**

Thirty years since the onset of the HIV/AIDS epidemic, technical advances and improved knowledge of disease epidemiology have led to investments in prevention and treatment that are helping to reduce new infections, save lives, and achieve an AIDS-free generation.

U.S.-based CDC laboratories provide technical assistance and expert consultation to advance the U.S. Global Health Initiative and the President’s Emergency Plan for AIDS Relief (PEPFAR) by improving disease prevention and treatment and care for persons living with HIV/AIDS.

### **Selected Laboratory Activities in FY 2011**

CDC laboratories

- served as worldwide reference laboratories for diagnosis and drug-resistance testing for HIV/AIDS, providing services to both domestic and international partners (see the Domestic HIV/AIDS section for additional activities);
- provided laboratory support to address public health priorities in HIV diagnosis, prevention, care, and treatment, as well as in cross-cutting areas (e.g., HIV/TB co-infection, health systems strengthening, public health training, and laboratory biosafety and biosecurity);
- helped developing countries’ laboratories implement improved methods for diagnosis of HIV and AIDS-related opportunistic infections, including co-infection with TB; for HIV and TB drug-resistance testing; for measurement of blood CD4<sup>+</sup> levels and HIV viral loads to monitor disease progression and treatment effectiveness; and for HIV incidence testing to monitor the effect of disease prevention and control efforts;
- assisted ministries of health in 45 countries in developing national laboratory strategic plans that strengthen the laboratory component of national health systems (e.g., by implementing quality laboratory services and systems, strengthening laboratory biosafety and biosecurity, and developing national laboratory networks that optimize the use of local resources);

- provided support for hands-on training to 865 laboratory professionals in 283 laboratories in 22 countries to improve accreditation preparedness, and helped to establish the African Society for Laboratory Medicine, which will administer a regional laboratory accreditation program;
- strengthened HIV/AIDS prevention and control programs by
  - providing support for training and diagnostic assistance to developing country public health laboratories that collectively tested 9.8 million pregnant women for HIV, leading to prevention of mother-to-child transmission and allowing an estimated 200,000 infants to be born HIV-free;
  - providing testing panels to 120 laboratories in 40 PEPFAR countries to facilitate training in drug-resistance testing by using the low-cost dried blood spot assay developed at CDC; and
  - evaluating the quality of HIV rapid tests considered for inclusion in the USAID waiver list, which authorizes local procurement of goods and services under PEPFAR (use of these rapid tests allows prompt referral for care and treatment); and
- conducted operational research to
  - evaluate field use of rapid point-of-care tests in resource-limited settings (e.g., to accelerate the entry into care of HIV-positive pregnant women);
  - implement widespread use of molecular tests for early diagnosis of HIV among infants (e.g., to allow early determination of the HIV status of infants born to HIV-positive mothers); and
  - scale up collection and analysis of laboratory data for measuring the impact of HIV prevention efforts, facilitating faster translation of research findings into local practice.

## **BUDGET ACTIVITY — GLOBAL HEALTH: GLOBAL IMMUNIZATION PROGRAM**

Vaccination against serious infectious diseases (e.g., polio and measles) is one of the most effective of all global public health interventions. Globally, cases of polio have decreased by over 99% since 1988. Polio vaccination in the United States has yielded net economic benefits that exceed \$180 billion, not counting the intangible benefits associated with eliminating endemic polio in the United States. Globally, measles deaths declined by 78% during 2000–2008, although the disease continues to affect more than 20 million persons each year. Measles vaccination is one of the most cost-effective health interventions available today for preventing deaths.

However, much remains to be done. U.S.-based CDC laboratories are helping to advance the Global Polio Eradication Initiative by providing critical diagnostic services and genomic sequencing of polioviruses to track local and global transmission pathways and help guide

disease control efforts in multiple countries. The CDC Polio Laboratory serves as a WHO global specialized laboratory, a high-level facility that provides technical and programmatic assistance to the Global Polio Laboratory Network. CDC also is helping to advance the Global Measles Initiative, which aims to accelerate the reduction of measles deaths worldwide. Moreover, increased use of a combined measles and rubella vaccine is also reducing birth defects caused by congenital rubella syndrome. The CDC measles and rubella laboratories are WHO global specialized laboratories within the WHO Measles and Rubella Laboratory Network.

In addition, CDC laboratories support global efforts to prevent children's deaths from other vaccine-preventable diseases by increasing access to vaccines in low-resource countries and by helping to strengthen surveillance capacity.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratories

- served as worldwide reference laboratories — and as regional reference laboratories for the Pan American Health Organization — for diagnosis of polio, measles, and rubella, as well as for other vaccine-preventable diseases (i.e., infections with *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, *Neisseria meningitidis*, and pertussis);
- provided proficiency testing, technical assistance, and training and consultation regarding best practices to expand and enhance the WHO Global Polio Laboratory Network (145 laboratories) and the WHO Global Measles and Rubella Laboratory Network (700 laboratories);
- developed, evaluated, and deployed state-of-the art tests for diagnosis, genotyping, and subtyping of polio, measles, and rubella; these tests support outbreak investigations and disease-tracking and guide polio and measles prevention strategies;
- used global genotyping data to track and contain over 200 domestic cases of measles;
- conducted applied research to develop, evaluate, and implement new prevention approaches (including vaccines) and treatments (including antiviral drugs) (e.g., the CDC Polio Laboratory has evaluated new inactivated polio vaccines, oral polio vaccines, and novel vaccine delivery technologies);
- developed and validated disease surveillance tools, including
  - a global measles DNA sequence database, developed in collaboration with WHO, that provides critical information for controlling measles at home and abroad; and
  - a molecular diagnostic assay for poliovirus that will help guide decision-making and outbreak response in countries where polio has not yet been eliminated.
- provided support for hands-on laboratory training and assistance, including developing and publishing laboratory guidelines, for the WHO Invasive Bacterial/Vaccine-Preventable Diseases Surveillance Network of laboratories in six WHO regions; and

- provided support for hands-on laboratory training and sentinel site assistance to ministries of health in three central African countries (Cameroon, Central African Republic, and the Democratic Republic of Congo) for laboratory-based surveillance of vaccine-preventable diseases as part of the Projet de Renforcement de la Surveillance en Afrique Centrale project.

## **BUDGET ACTIVITY — GLOBAL HEALTH: GLOBAL DISEASE DETECTION AND EMERGENCY RESPONSE**

CDC’s U.S.-based infectious disease laboratories support the overseas laboratory operations of the CDC Global Disease Detection (GDD) regional centers whose goal is to strengthen global health security by ensuring (1) prompt identification and reporting of new threats and (2) rapid response to public health threats, including public health emergencies of international concern reported to WHO under the International Health Regulations (IHR).

The GDD Regional Centers — located in China, Egypt, Guatemala, India, Kenya, Thailand, and South Africa — work closely with U.S.-based CDC laboratories and with the GDD Operations Center in Atlanta.

### **Selected Laboratory Activities in FY 2011**

The U.S.-based CDC infectious disease laboratories provided guidance, technical support, and management services to GDD regional centers that

- served as regional resources for
  - technical assistance, training, and rapid coordination of diagnostic testing during public health emergencies; and
  - strategic planning for IHR implementation;
- detected seven pathogens that were new to the world, new to their geographic region, or for which testing capacity now exists (e.g., a *Bartonella vinsonii* subspecies, *Streptococcus difficilis*, metapneumovirus, and a Crimean-Congo hemorrhagic fever variant);
- worked with ministries of health in China, Guatemala, Kenya, and Thailand to strengthen national public health laboratory systems that optimize the use of local resources;
- worked with the ministries of health of China and Thailand to advance IHR implementation by developing and customizing laboratory system assessment tools for IHR compliance and conducting assessments in 29 laboratories in Guangdong Province, China, and 13 regional medical centers and clinical laboratories in Thailand;
- advanced development of the WHO Laboratory Quality Management System and distributed the system handbook, which is based on training sessions and modules provided by CDC and WHO in more than 25 countries; and

- disseminated two diagnostic tests to laboratories in GDD host countries, including a real-time diagnostic platform for use in identifying causes of unexplained respiratory disease outbreaks.

## **BUDGET ACTIVITY — GLOBAL HEALTH: PARASITIC DISEASES AND MALARIA**

Parasitic infections are responsible for a major disease burden throughout the world. Malaria affects 250–300 million persons annually, resulting in approximately 700,000 deaths, primarily among children. Approximately 1,500 cases of malaria are diagnosed each year in the United States, primarily from returning travelers and immigrants. Other parasitic diseases — sometimes called “neglected tropical diseases” — affect more than 1 billion persons, including certain diseases that are endemic to the United States (e.g., neurocysticercosis, toxocariasis, and toxoplasmosis).

The U.S.-based CDC infectious disease laboratories focus on advancing the U.S. Global Health Initiative, the President’s Malaria Initiative, and the Neglected Tropical Diseases Initiative and on improving diagnosis and control of parasitic diseases in the United States.

### **Selected Laboratory Activities in FY 2011**

#### CDC laboratories

- served as a worldwide reference center for
  - diagnosis of malaria, neglected tropical diseases, and other parasitic diseases; and
  - evaluation of commercially available rapid diagnostic tests for malaria;
- provided assistance, training, and consultation to state and local public health departments in diagnosing, investigating, preventing, and controlling parasitic diseases; and
- provided first-line and reference diagnostic testing services for physicians, hospitals, clinical laboratories, and government partners;
- conducted over 15,000 diagnostic tests, including microscopic evaluation for over 100 medically important parasites, immunodiagnostic testing for 14 diseases, and molecular detection for over 20 agents;
- operated an Internet-based telediagnostic service for parasitic diseases;
- developed molecular assays for use in malaria case management and surveillance, as well as new methods for diagnosis of other parasitic diseases, including filariasis, cyclosporiasis, strongyloidiasis, and infections with free-living amoebas;

- improved neglected tropical disease diagnoses through validation of laboratory tests, including rapid tests and assays to detect multiple diseases from a single drop of blood;
- provided training and consultation to domestic and global partners on surveillance for drug resistance (e.g., CDC offered training to investigators in endemic countries regarding use of molecular markers to detect and track drug-resistant parasites);
- provided technical support to ministries of health and WHO — thus helping to strengthen malaria prevention and control programs — by providing a resident advisor to assist with implementing the President’s Malaria Initiative in 15 African countries; and
- conducted applied research on antimalarial drugs and on drug resistance mechanisms in parasite and vector populations.

## **BUDGET ACTIVITY — PUBLIC HEALTH PREPAREDNESS AND RESPONSE**

CDC’s laboratories are critically important to America’s national security. CDC helps the nation prepare for and respond to urgent public health threats by providing strategic direction, support, and coordination for emergency preparedness and response activities across the agency, as well as with local, state, tribal, national, territorial, and international public health partners.

CDC also works with other federal agencies and intelligence authorities to ensure that authorities are apprised of all novel threats (engineered and natural) and retains world-class expertise in detecting, preventing, and controlling BT, CT, and RT agents.

To meet these goals, CDC supports LRN, an integrated network of state and local public health, federal, military, and international laboratories that operates 24/7 to respond to BT and CT and other public health threats and emergencies. LRN protects the health and security of U.S. citizens and armed forces, providing essential information on human and animal exposures to enable health officials to react appropriately to threats, including deployment of medical countermeasures. LRN identifies the threat agents, who has been exposed and how severely, and the geographical extent of exposure to facilitate reactive and preemptive actions. CDC also promotes laboratory biosafety and biosecurity by administering the HHS Select Agent Program (42 CFR Part 73, available at [http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr73\\_main\\_02.tpl](http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr73_main_02.tpl)), which regulates throughout the United States the possession, use, and transfer of BT and toxins that can pose a severe threat to public health and safety. In the absence of these critical programs, the use, movement, and presence of these BT threat agents would be unmonitored and could allow their intentional use as a biologic weapon to go undetected.

### **Selected Laboratory Activities in FY2011**

CDC laboratories

- strengthened the biologic component of LRN by

- developing reagents and assays for BT and emerging threats, including a mass spectrometry method for detecting anthrax lethal factor (a component of anthrax toxin) that detects disease 24 hours before symptoms; methods to quantify clinically relevant levels of botulinum neurotoxins in serum and feces; methods to determine botulinum toxin subtypes A and B (used to identify a previously unknown subtype); a rapid point-of-care test for plague and other BT agents;
  - providing consultation and confirmatory testing for the U.S. Department of Homeland Security BioWatch program, which detects environmentally dispersed BT agents, including the bacterium that causes anthrax;
  - ensuring safe and secure working conditions within biosafety level-4 containment facilities for scientists working with high-consequence pathogens and VB agents;
  - enhancing preparedness to respond to outbreaks of high-consequence pathogens through test development and demonstration of efficacy for prophylaxis or postexposure treatments, including various therapeutic interventions for treatment of orthopoxvirus infections (e.g., attributable to vaccine-related adverse events or to smallpox);
  - providing instruction to more than 3,000 sentinel laboratory personnel from local public health, hospital and clinical laboratories in Rule-Out-and-Refer protocols and in laboratory safety and security protocols, including safe handling, packaging, and shipping of potentially dangerous specimens;
  - conducting intensive, hands-on trainings for 28 LRN reference laboratories in rapid detection and identification of BT agents;
  - ensuring laboratory performance and timely response to a biologic terrorism incident by conducting BT response team exercises, developing and distributing quality-control materials, providing quality-assurance and performance testing to laboratories, and coordinating with federal partners through the Integrated Consortium of Laboratory Networks; and
  - processing 1,530 individual test results reported by 143 laboratories (out of 162 LRN laboratories) participating in the LRN BT proficiency testing program and certifying that LRN BT laboratories are qualified to measure biologic threat agents during a public health response.
- strengthened the chemical component of LRN by
    - maintaining round-the-clock laboratory response capability, expanding surge capacity, and upgrading the Rapid Toxic Screen that can evaluate up to 150 CT agents within 24–36 hours;

- ensuring laboratory performance and timely response to a chemical terrorism incident by conducting CT response team exercises, developing and distributing quality-control materials, providing quality-assurance and performance testing to laboratories, and coordinating with federal partners through the Integrated Consortium of Laboratory Networks;
- processing 11,500 individual test results reported by 46 state public health laboratories participating in the LRN proficiency testing program and certifying that LRN laboratories are qualified to measure CT agents during a public health response;
- developed new analytic methods for the urine radionuclide screen, thereby strengthening CDC laboratory capacity to assess radiologic exposure of persons during RT events, including exposures to low-grade nuclear bombs, industrial unintentional incidents, thermonuclear devices, and radionuclides that cannot be detected by Geiger counters or by clinical assessment (e.g., exposures to uranium-235, strontium, plutonium-238, and radium);
- investigated and identified low levels of radiation exposure among U.S. residents working in Japan after release of radiation from the Fukushima Daiichi Nuclear Power Plant by using the urine radionuclide screen;
- executed regulatory and statutory responsibilities for the HHS Select Agent Program (42 CFR Part 73, available at [http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr73\\_main\\_02.tpl](http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr73_main_02.tpl)), the CDC Import Permit Program (42 CFR Part 71.54, available at <http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=d53e3b1b73bd80865fb0a044f8be8c1d&rqn=div8&view=text&node=42:1.0.1.6.59.6.19.4&idno=42>), the Foreign Quarantine Regulations, the Bioterrorism Response Act of 2002, and the PATRIOT Act. CDC regulates more than 325 entities that use, possess, or transfer Select Agents within the United States and processes more than 1,500 import permits per year to prevent bioterrorism events within the United States (e.g., the anthrax attacks of October 2001).
- improved analysis and messaging of BT, CT, and RT data by
  - assisting states in implementing laboratory information management systems that increase the speed and accuracy of data transfer;
  - disseminating customized software that promotes use of common definitions of BT events by all LRN laboratories; and
  - developing a communications channel for addressing delays and difficulties in disseminating test information (e.g., results, test specifics, and specimen types) within the public health community;

- supported a cross-cutting program that provides infrastructure, diagnostic, reference, research, reagent production, and surveillance programs to CDC laboratories; the unique services provided are essential to the daily operations of the laboratories and include veterinary and animal husbandry, centralized specimen management, and support to CDC scientists in genomics, proteomics, bioinformatics, chemical synthesis, and other scientific disciplines;
- confirmed exposures among Alaska residents to saxitoxin, a neurotoxin located in shellfish exposed to toxic algal blooms;
- helped identify the source of the 2011 cholera outbreak in Haiti by using next-generation whole genome sequencing data;
- produced biologic products, reagents, kits, and cell cultures to provide immediate readiness to meet the needs of CDC laboratories, ongoing influenza surveillance projects, and LRN (e.g., test kits for anthrax and botulism detection, as well as influenza serotyping); and
- managed a memorandum of understanding established with the Office of In-Vitro Diagnostic Device Evaluation and Safety at FDA for the 1-year assignment of a CDC scientist to FDA to learn about regulatory 510(k) requirements for laboratory-developed tests and *in vitro* diagnostics, and to assist CDC laboratories in meeting these requirements.

## List of Abbreviations Used in This Report

ACIP	Advisory Committee on Immunization Practices
AIDS	acquired immunodeficiency syndrome
AR	antimicrobial resistance
BA	budget authority
BT	biologic threat
CDC	Centers for Disease Control and Prevention
CFS	chronic fatigue syndrome
CT	chemical threat
FDA	Food and Drug Administration
FY	Fiscal Year
GDD	Global Disease Detection
HBV	hepatitis B virus
HCV	hepatitis C virus
HDL	high-density lipoprotein
HHV-8	human herpes virus type 8
HIV	human immunodeficiency virus
HPV	human papillomavirus
IHR	International Health Regulations
LD	Lyme disease
LDL	low-density lipoprotein
LRN	Laboratory Response Network
MDR TB	multidrug-resistant tuberculosis
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
NBDPS	National Birth Defects Prevention Study
NHANES	National Health and Nutrition Examination Survey
PEPFAR	President's Emergency Plan for AIDS Relief
PFOS	perfluorooctane sulfonic acid
RT	radiologic threat
SARS	severe acute respiratory syndrome
SCID	severe combined immunodeficiency
STD	sexually transmitted disease
TB	tuberculosis
TSNAs	tobacco-specific nitrosamines
USAID	U.S. Agency for International Development
USDA	U.S. Department of Agriculture
VB	vectorborne
WHO	World Health Organization
XDR TB	extensively drug-resistant tuberculosis