

**THE ANNUAL REPORT
OF THE STATE OF THE
NATIONAL
VACCINE PLAN**



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

2014

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ACRONYMS AND ABBREVIATIONS

ACV	Advisory Commission on Childhood Vaccines
ACF	Administration for Children and Families
ACIP	Advisory Committee on Immunization Practices
ACOG	American Congress of Obstetricians and Gynecologists
ACS	American Cancer Society
AEFI	Adverse Event Following Immunization
AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired Immunodeficiency Syndrome
AIM	Association of Immunization Managers
AIRA	American Immunization Registry Association
APhA	American Pharmacists Association
AITF	Adult Immunization Task Force
ASH	Assistant Secretary for Health
ASPR	Assistant Secretary for Preparedness and Response
ASTHO	Association of State and Territorial Health Officials
BARDA	Biomedical Advanced Research and Development Authority (within the Office of the Assistant Secretary for Preparedness and Response or ASPR)
BMGF	Bill & Melinda Gates Foundation
BPHC	Bureau of Primary Health Care (within the Healthcare Research and Services Administration)
BSL	Biosafety Level
CBER	Center for Biologics Evaluation and Research (of the Food and Drug Administration)
CICP	Countermeasure Injury Compensation Program (within the Healthcare Research and Services Administration)
CDC	Centers for Disease Control and Prevention
CISA	Clinical Immunization Safety Assessment
CME	Continuing Medical Education credit
CMS	Centers for Medicare & Medicaid Services
CRS	Congenital Rubella Syndrome
CSTF	Council of State and Territorial Epidemiologists
DHS	U.S. Department of Homeland Security
DoD	U.S. Department of Defense
DoJ	U.S. Department of Justice
DPT	Diphtheria-Pertussis-Tetanus vaccine
DTaP	Diphtheria-Tetanus-Pertussis vaccine
EHR	Electronic Health Record
EIND	Emergency Investigational New Drug
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
FIC	Fogarty International Center (within the National Institutes of Health)
FQHC	Federally Qualified Health Center
FY	Fiscal Year
GAP	Global Action Plan for Influenza Vaccines
GAVI	The GAVI Alliance
GBS	Guillain-Barré syndrome
GPEI	Global Polio Eradication Initiative
HCP	Health Care Professional or Health Care Personnel
HCV	Hepatitis C Virus
HepA	Hepatitis A
HepB	Hepatitis B
HepC	Hepatitis C
HHS	U.S. Department of Health and Human Services
Hib	Haemophilus influenzae type b
HIE	Health Information Exchange
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HRSA	Health Resources and Services Administration
HSV	Herpes Simplex Virus
ICT	Information and Communication Technologies

ACRONYMS AND ABBREVIATIONS

IHS	Indian Health Service
IIS	Immunization Information Systems
IIV	Inactivated Influenza Vaccine
IOM	Institute of Medicine
ISTF	Immunization Safety Task Force
JE	Japanese Encephalitis
LTC	Long-Term Care
MCV	Meningococcal Vaccine
MD	Medical Doctor
MenB	Meningococcal serogroup B
MMR	Measles, Mumps, and Rubella vaccine
MPH	Master of Public Health
MSF	Médecins Sans Frontières International (Doctors Without Borders)
NAIIS	National Adult and Influenza Immunization Summit
NAIP	National Adult Immunization Plan
NCIRD	National Center for Immunization and Respiratory Diseases (within the Centers for Disease Control and Prevention)
NFID	National Foundation for Infectious Diseases
NIAID	National Institute of Allergy and Infectious Diseases (within the National Institutes of Health)
NIH	National Institutes of Health
NNDSS	National Notifiable Disease Surveillance System
NVAC	National Vaccine Advisory Committee
NVPO	National Vaccine Program Office
OGA	Office of Global Affairs
ONC	Office of the National Coordinator for Health Information Technology
OPV	Oral Polio Vaccine
PAHO	Pan American Health Organization
PCP	President's Cancer Panel
PCV	Pneumococcal conjugate vaccine
PHAC	Public Health Agency of Canada
PhD	Doctor of Philosophy
PRISM	Post-Licensure Rapid Immunization Safety Monitoring (a component of the Food and Drug Administration's Sentinel Initiative)
PSA	Public Service Announcement
R&D	Research and Development
RePORT	Research Portfolio Online Reporting Tools (of the National Institutes of Health)
RSV	Respiratory Syncytial Virus
SMART Vaccines	Strategic Multi-Attribute Ranking Tool for Vaccines
STI	Sexually Transmitted Infection
TB	Tuberculosis
Td	Tetanus-diphtheria vaccine
Tdap	Tetanus-diphtheria-pertussis vaccine
TIV	Trivalent Influenza Vaccine
UKHPA	United Kingdom Health Protection Agency
UN	United Nations
UNICEF	United Nations Children's Fund
U.S.	United States
USAID	U.S. Agency for International Development
VA	U.S. Department of Veterans Affairs
VAERS	Vaccine Adverse Event Reporting System
VCWG	Vaccine Confidence Working Group (of the National Vaccine Advisory Committee)
VFAP	Vaccine Facts and Policy
VFC	Vaccines for Children program
VHA	Veterans Health Administration (with the Department of Veterans Affairs)
VIS	Vaccine Information Statement
VLER	Virtual Lifetime Electronic Record
VSD	Vaccine Safety Datalink
WHO	World Health Organization

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DIRECTOR'S NOTE

If only one word could be used to describe vaccines, it would have to be: transformative. From Edward Jenner's observations and experiments ultimately leading to the eradication of smallpox, to Louis Pasteur's development of vaccines for anthrax and rabies to Jonas Salk's creation of the first polio vaccine, the planet and the health of its people, have been positively impacted in innumerable ways by the tireless efforts of the many people and organizations who create and provide vaccines that not only protect individuals but also the communities in which they live and work.

Here in the United States, we seldom see the harsh realities of infectious diseases experienced just a generation ago. Vaccines have safely and effectively prevented many once common infections and their often devastating sequelae. Still, as the diseases that vaccines prevent have disappeared from our schools, hospitals and communities, ironically, some vaccines have lost their perceived need and value. There has been a small, but worrisome trend of some people, including parents of young children, delaying or opting-out of receiving recommended vaccines or immunizations. This, along with more traditional barriers to accessing vaccination services, has led to the resurgence of once common infectious diseases. The recent measles outbreak linked to a popular U.S. amusement park drew attention to these underlying issues.

With the National Vaccine Plan—which is the strategy that guides the National Vaccine Program—we continue our work to successfully accomplish five important goals. The first National Vaccine Plan was issued in 1994 and updated in 2010 to reflect new opportunities and challenges presented by the 21st century immunization landscape. In this Annual Report on the State of the National Vaccine Plan, you will find highlights of the work done by HHS agencies and their partners toward attaining the goals and objectives of the 2010 National Vaccine Plan. The accomplishments of each HHS agency in the realm of vaccines and immunizations are truly remarkable when considered individually, and even more impressive when seen collectively via the lens of the U.S. immunization system. In reviewing the year commemorating Jonas Salk's 100th birthday, we should look upon the immunization system with his words firmly in mind:

"I look upon ourselves as partners in all of this, and that each of us contributes and does what he can do best. And so I see not a top rung and a bottom rung - I see all this horizontally - and I see this as part of a matrix. And I see every human being as having a purpose, a destiny, if you like - the destiny that exists in each of us - and find ways and means to provide such opportunities for everyone."

Our 2014 report covers calendar year 2014 and provides a myriad of examples of collaboration, demonstrating the value of, and need for, a synergistic approach to maintaining and enhancing the immunization system of the United States.

DIRECTOR'S NOTE

Countless stakeholders, both federal and nonfederal, each providing their own set of specialized contributions, permit the successful functioning of our National Vaccine Program.

Of particular note is our own exemplary National Vaccine Advisory Committee (NVAC). NVAC is a chartered federal advisory committee composed of experts, across the national vaccine enterprise, involved in implementing the National Vaccine Plan by advising the Assistant Secretary for Health of HHS. Since its initiation nearly three decades ago, NVAC has provided essential expertise and guidance on HHS's work to improve the nation's immunization system and efforts.

This report also highlights and demonstrates the integrative mission of the National Vaccine Program Office (NVPO). NVPO brings expertise and stakeholders together and facilitates their collaboration to develop strategies that strengthen our national immunization system. By providing leadership and guidance and fostering partnerships and collaborations, NVPO helps identify and solve ongoing and emerging challenges confronting the U.S. vaccine enterprise. Part of this effort involves a continuous feedback process, where stakeholders share information about their respective activities toward the achievement of the five goals outlined in the National Vaccine Plan. In this way, NVPO ensures that affected and interested parties are included in the ongoing national strategic dialogue on vaccines and immunization.

Like the many people and organizations who have worked before us to foster widespread use of safe and effective vaccines, we recognize our efforts to achieve the eradication of vaccine-preventable diseases are an often challenging endeavor. Still, we remain steadfast in our purpose, and we forge ahead in passionate pursuit, because safe and effective vaccines prevent infectious diseases and their complications across the lifespan, across the U.S., and around the world.



A handwritten signature in blue ink, which reads "Bruce Gellin". The signature is fluid and cursive.

Bruce Gellin, MD, MPH

Deputy Assistant Secretary for Health
Director, National Vaccine Program Office

REPORT INTRODUCTION

Vaccination has single-handedly allowed Americans to enjoy healthier and longer lives—up to 30 years longer—with a 14-fold reduction in mortality from infectious disease in the last century.¹ Immunization becoming a part of routine preventive care has vastly improved the health of Americans and those in our global community. In the U.S. alone, approximately 33,000 lives are saved for every birth cohort vaccinated, preventing 14 million cases of disease, and saving \$43.3 billion in direct and indirect costs.^{2,3}

To ensure continued success, the National Vaccine Plan (NVP) was first created in 1994 to provide strategic direction and optimize the development, use, and evaluation of safe and effective vaccines.⁴ In 2010, the National Vaccine Plan was updated to reflect the priorities, opportunities, and challenges presented by emerging technologies, cutting-edge science, and a dynamic immunization infrastructure. The National Vaccine Plan is the United States' guiding vision for vaccines and vaccinations and the system in which they operate for the decade spanning 2010–2020.

Federal law (42 U.S.C. § 300aa-3) called for the establishment and implementation of the National Vaccine Plan. The Assistant Secretary for Health (ASH) serves as the Director of the National Vaccine Program, with support from the National Vaccine Program Office (NVPO) as the national coordinator of federal and non-federal activities described in the Plan.⁵ The National Vaccine Plan is composed of five broad goals, each oriented toward a facet of the national vaccine and immunization enterprise. This Annual Report of the State of the National Vaccine Plan details recent accomplishments and continued progress within the five goals of the Plan that speak to a wide breadth of immunization activity identified in the Plan.

- **Goal 1:** Develop new and improved vaccines.
- **Goal 2:** Enhance the vaccine safety system.
- **Goal 3:** Support communications to enhance informed vaccine decision-making.
- **Goal 4:** Ensure a stable supply of, access to, and better use of recommended vaccines in the United States.
- **Goal 5:** Increase global prevention of death and disease through safe and effective vaccination.

¹ American Academy of Pediatrics. (2009). Prologue. In L. K. Pickering (Ed.), *Red Book: 2009 Report of the Committee on Infectious Diseases* (28th ed.). Elk Grove Village, IL: American Academy of Pediatrics.

² Zhou, F., Santoli, J., Messonnier, M. L., Yusuf, H. R., Shefer, A., Chu, S. Y., Rodewald, L., & Harpaz, R. (2005). Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001. *Archives of Pediatric and Adolescent Medicine*, 159(12), 1136–1144. Retrieved from www.ncbi.nlm.nih.gov/pubmed/16330737

³ Schuchat, A. (2011). Human vaccines and their importance to public health. *Procedia in Vaccinology*, 5, 120–126. Retrieved from www.sciencedirect.com/science/article/pii/S1877282X11000269# (exit link disclaimer)

⁴ U.S. Department of Health and Human Services. (1994). *Disease prevention through vaccine development and immunization: The U.S. National Vaccine Plan - 1994*. Retrieved from http://archive.hhs.gov/nvpo/vacc_plan/1994plan/

⁵ Public Law (P.L.) 99-660 established the National Vaccine Program, and required the National Vaccine Program to focus on prevention of infectious diseases and adverse reactions to vaccines.

REPORT INTRODUCTION

Though tragic, the Ebola virus outbreak in West Africa poignantly illustrates how in a time of crisis the goals outlined in the National Vaccine Plan can provide a framework to aid in action and response regarding the role of vaccines in preventing infectious diseases and their spread. This episode demonstrates how the United States and the international community collaborate to ensure an effective anti-Ebola program—including but not limited to vaccination strategies. With extensive planning, strong leadership, and ongoing coordination, public health crises like Ebola can be contained, saving the lives of not just those in immediate danger but also the global populace.

This outbreak has accentuated the role that safe, effective and available vaccines can play in mitigating an infectious disease outbreak. Throughout this report, efforts of partners across the vaccine enterprise are highlighted, showcasing the critical work being done to advance the field of immunization. In the paragraphs that directly follow, the response to the Ebola outbreak serves as a case study of the call for and subsequent development and testing of a vaccine that is positioned to prevent life-threatening infections and their consequences

Research and Development

Several Ebola vaccine clinical trials are currently underway around the globe and are made possible through the diligent work of federal partners, such as NIH, CDC, FDA, DoD, and BARDA, as well as nonfederal partners, including the Gates Foundation, GSK, J&J, Wellcome Trust, the Public Health Agency of Canada, NewLink/Merck and many others.

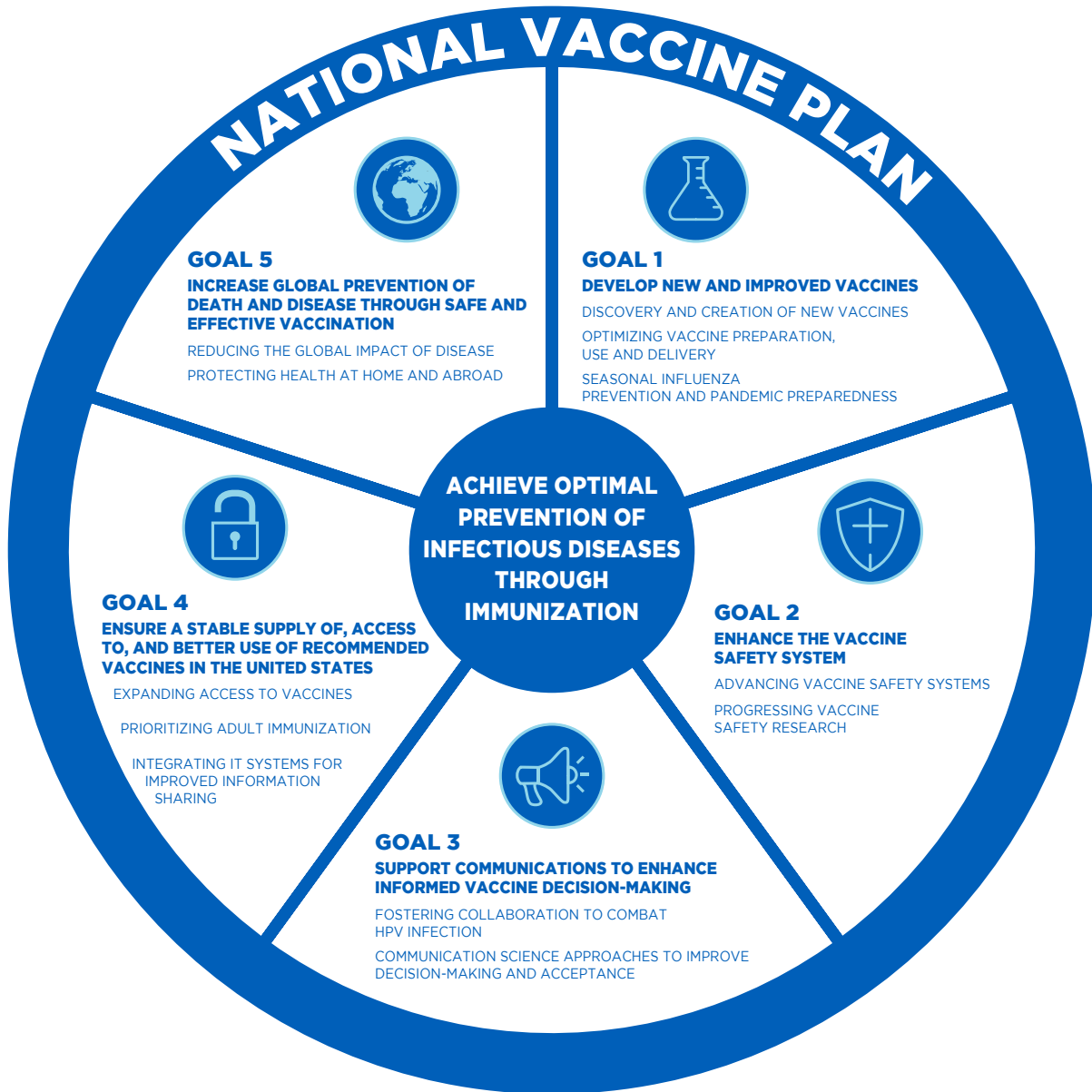
Vaccine Safety

Vaccine safety is a critical part of vaccine development and vaccine use in every setting. The vaccine trials touched upon above are conducted to evaluate immunogenicity, vaccine efficacy and vaccine safety. Side effects and more serious adverse events that may occur following vaccination are, and will continue to be, monitored, delineated and studied closely.

Communications and Decision-making

HHS and international partners, in concert with the West African countries affected by the Ebola outbreak, created and disseminated a host of culturally-appropriate communication materials, including videos, posters, PSAs, factsheets and brochures. Materials were carefully crafted to improve understanding of the disease, how it is spread and the role that vaccines might have in controlling the outbreak.

FIGURE 1: GOALS OF THE NATIONAL VACCINE PLAN



GOAL 1: DEVELOP NEW AND IMPROVED VACCINES

INTRODUCTION

Development of new vaccines, and the improvement of current ones, provides the foundation for a successful immunization system. Scientific and technological advancements can reduce health care costs, increase effectiveness, enhance vaccine safety and improve our ability to use vaccinations. The collective focus on the fundamentals of how well current vaccines work, and how new or more effective vaccines can be developed to better prevent infectious human diseases, guides the work toward achieving Goal 1 of the National Vaccine Plan. This chapter showcases select new vaccines, cutting-edge research, new vaccine technologies and advancements made in influenza vaccination. This chapter features a selection of examples that demonstrate the many sectors that come into play to develop and/ or improve needed vaccines. Ebola, bacterial meningitis (serogroup B), the SMART Vaccines tool, maternal immunization and seasonal and pandemic influenza are some of the topics covered. This chapter also highlights several aspects of basic and applied immunology that provide a deep foundation for developing a variety of vaccines in the future.



DISCOVERY AND CREATION OF NEW VACCINES

This past year saw numerous advancements on the vaccine research and development front, and several prominent outbreaks underscored the need to accelerate the development and testing of such vaccines. The examples of Ebola and meningitis B provided in this section reinforce the desire for vaccines to be a first line of defense in controlling outbreaks of communicable diseases. Developing vaccines to combat other infectious disease, such as hepatitis C and Herpes Simplex Virus, also advanced, as did a decision-support tool for helping to determine priority vaccines for particular populations.

SEARCH

CLINICALTRIALS.GOV

for publicly and privately supported clinical studies of human participants conducted around the world

Expediting an Ebola Vaccine in a Time of Crisis

In response to the historic and tragic 2014 Ebola outbreak in West Africa, a number of federal and nonfederal partners accelerated the development and clinical testing of several promising Ebola vaccine candidates. While the outbreak has stimulated a number of groups to apply their vaccine technologies to Ebola, as of the writing of this report in early 2015 the three vaccine candidates below are the most promising.

CAAd3-EBOZ is a non-replicating live virus vaccine candidate initially developed by the National Institutes of Health's Vaccine Research Center and currently licensed to GlaxoSmithKline (GSK) using an adenovirus vector. Protection was demonstrated in nonhuman primates who were challenged with lethal doses of Ebola virus following vaccination in NIH-supported studies.

Clinical Trials

Multiple dose-escalating Phase 1 clinical studies evaluating vaccine immunogenicity and safety started as early as September 2014. The published results of the NIH study showed that all dosages were well-tolerated and that a single dose at the highest dosage of this vaccine may provide protective immunity. Other Phase 1 studies evaluating other dosages and looking at a prime/boost approach using the MVA-EBOV vaccine as a booster are ongoing.

Manufacturing

Manufacturing of the vaccine for the clinical studies started at Advent (Italy) and transferred to GSK (Rixensart, Belgium), and is supported by the Wellcome Trust and the Bill and Melinda Gates Foundation and BARDA. GSK, along with support from BARDA, is moving forward with vaccine advanced development, including scaling up manufacturing from pilot to commercial scale, optimizing vaccine manufacturing processes, and addressing cold chain issues.

DISCOVERY AND CREATION OF NEW VACCINES

rVSV-ZEBOV-GP is a replicating live attenuated vector vaccine candidate initially developed by the Public Health Agency of Canada (PHAC) with several U.S. university laboratories using a vesicular stomatitis virus vector and support from the Department of Defense (DoD). Merck and NewLink Genetics Corporation entered into an exclusive license to research, develop, manufacture, and distribute the vaccine candidate. Protection was afforded to nonhuman primates immunized with this vaccine candidate and challenged with lethal doses of Ebola virus in PHAC- and DoD-supported studies. Animal studies also indicated that this vaccine candidate at high vaccine virus titers may provide post-exposure prophylaxis.

Clinical Trials

Dose-escalating Phase 1 clinical studies to evaluate vaccine immunogenicity and safety started as early as October 2014 at Walter Reed Army Institute of Research (WRAIR) and NIH/NIAID in the U.S.; other Phase 1 studies are ongoing in Germany, Switzerland, Canada, Gabon and Kenya. This vaccine candidate has been administered in emergencies under FDA's regulations for expanded access to investigational drugs in several Ebola-infected patients evacuated to the U.S. as a post-exposure prophylaxis indication. A Phase 2/3 randomized controlled trial with support from NIH/NIAID and a stepped-wedge clinical trial with support from CDC are expected to launch in early 2015.

THE VSV-EBOV TRIAL

was paused in Switzerland for three weeks during December, after temporary joint pain was experienced by some of the volunteers. The trial resumed in January 2015 in Geneva with more than 50 volunteers who will receive a lower dose of the vaccine.

Manufacturing

Manufacturing of vaccine clinical investigational lots at pilot scale is underway at IDT (Germany) for Phase 2 clinical studies and supported by the Department of Defense's Defense Threat Reduction Agency (DTRA) and BARDA. NewLink Genetics and Merck announced their partnership in further development and manufacturing of this vaccine candidate. BARDA is supporting scale-up development from pilot to commercial scale manufacturing and more thermostable vaccine formulations.

Ad26.ZEBOV/MVA-BN-Filo (MVA-mBN226B) is a prime-boost live virus vectored vaccine strategy in which one vaccine is used to prime and another to boost the immune response. The Ad26.ZEBOV vaccine candidate was developed initially by Crucell and later Janssen (Holland), a subsidiary of Johnson & Johnson (J&J) while the smallpox MVA EBOV vaccine candidate was developed by Bavarian Nordic (BN; Denmark). In October 2014 J&J and BN agreed to work together to develop the combination Ebola vaccine candidate with the adenovirus vector vaccine serving as the priming dose and the smallpox vector vaccine as the vaccine booster. Protection was afforded to nonhuman primates immunized with these vaccine candidates and challenged with lethal doses of Ebola virus. Multiple clinical trials are underway.

DISCOVERY AND CREATION OF NEW VACCINES

Clinical Trials

Dose-escalating Phase 1 clinical studies to evaluate vaccine immunogenicity and safety are planned in the U.K., the U.S. and Mali. Phase 2/3 efficacy study designs using a randomized controlled approach are being implemented for vaccination campaigns in West Africa that may begin in June 2015.

Manufacturing

Manufacturing of vaccine clinical investigational lots at Janssen and BN is completed for Phase 1 studies and Phase 2 clinical studies.

Combating Serogroup B Meningococcal Disease

The development and widespread use of quadrivalent vaccines against meningococcal serogroups A, C, Y and W, based on the polysaccharide outer capsule of the bacteria, have demonstrated the impact that these vaccines can have in preventing life-threatening diseases. However, the development of meningococcal serogroup B (MenB) vaccine has remained a distinctly different challenge since the outer capsule of the bacterium is poorly immunogenic and closely resembles other human cells. With the introduction of quadrivalent meningococcal vaccines, meningococcal serogroup B remains a leading cause of bacterial meningitis among certain groups, such as people living together in places like college residence halls. While these infections are uncommon they can occur in clusters or outbreaks and the outcomes can be quite serious, causing life-threatening illness. In 2013-2014, two U.S. universities, Princeton University and the University of California Santa Barbara (UCSB), experienced outbreaks of serogroup B meningococcal disease.

The severe threat of meningococcal disease across these academic institutions coincided with work already being done by Novartis and Pfizer, two large pharmaceutical companies, to develop MenB vaccines. The university outbreaks, based on epidemiologic assessment, warranted a quick response from the national vaccine program. To that end, the Food and Drug Administration (FDA) worked closely with the Centers for Disease Control and Prevention (CDC), the two affected universities and Novartis to expeditiously make Novartis' MenB vaccine, which was not yet licensed by the FDA, available to these at-risk populations. This was done via FDA's expanded access program for investigational products, which can be utilized



⁶ <http://www.cdc.gov/meningococcal/outbreaks/princeton.html>

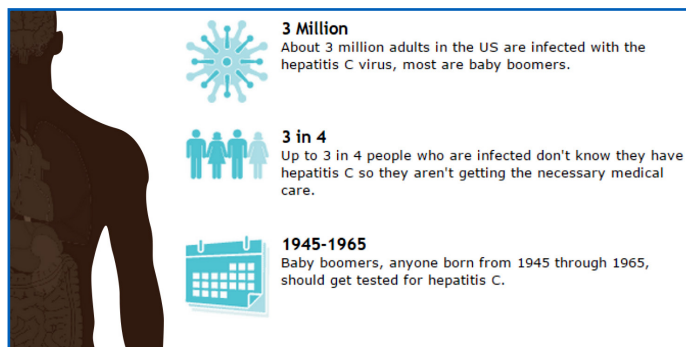
DISCOVERY AND CREATION OF NEW VACCINES

when there are no other comparable or satisfactory treatment options available and the use of an investigational vaccine is needed to prevent a serious or immediately life-threatening condition. Since that time, FDA has approved both the Pfizer and Novartis MenB vaccines.

Coordination between FDA, CDC, state health officials and the affected universities helped to secure a safer academic environment and protect these vulnerable communities of young adults. In fact, more than 13,000 (Princeton) and 17,000 (UCSB) doses of serogroup B vaccine were administered at the respective universities.⁶ The outbreaks resolved and there have been no unusual patterns of serious reactions associated with the vaccine.⁷

Progress Toward Preventing Hepatitis C Infection

With an estimated 3.2 million Americans chronically infected⁸, hepatitis C virus (HCV)⁹ represents a major health problem for which an efficient vaccination strategy would be highly beneficial. Chronic HCV is recognized as one of the major causes of liver cirrhosis, liver cancer and liver failure worldwide, and is the most common indication for liver transplantation, accounting for 40–50% of liver transplants.¹⁰ While progress has been made in the prevention of HCV transmission and antiviral treatment, it can cost many thousands of dollars for a 12-week course of treatment, so an effective vaccine could be a very cost-effective solution to prevent HCV-related hepatitis and to diminish the burden of HCV-related disease.



Based on an initial safety study of an HCV vaccine candidate conducted in Britain, a larger NIH/NIAID-funded efficacy study is underway with an enrollment goal of 450 subjects at the University of California San Francisco and Johns Hopkins University Bloomberg School of Public Health in Baltimore. This will be the first multi-center, double blinded, randomized, placebo-controlled trial of a vaccine to prevent hepatitis C infection. For more information on this study, or other clinical trials, visit ClinicalTrials.gov.

⁷ <http://www.cdc.gov/meningococcal/outbreaks/vaccine-serogroupB.html>

⁸ <http://www.hhs.gov/opa/reproductive-health/stis/hepatitis-c/>

⁹ <http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/hepatitis-c>

¹⁰ deLemos AS, Schmeltzer PA, Russo MW. Recurrent hepatitis C after liver transplant. World Journal of Gastroenterology : WJG 2014;20(31):10668-10681. doi:10.3748/wjg.v20.i31.10668.

DISCOVERY AND CREATION OF NEW VACCINES

Overcoming Challenges to Creating a Herpes Vaccine

Herpes simplex virus type 1 and type 2 (HSV-1 & HSV-2) infections are common.¹¹ According to the CDC, approximately 17% of adults in the U.S. have HSV-2, most often experienced as a genital herpes. While genital herpes is mainly caused by HSV-2 infections, over the past decade, there has been an increase in the number of genital herpes caused by HSV-1 infections in young adults. NIH/NIAID and their partners continued work on the development of HSV vaccine in 2014. Though this work has continued to be challenging, advancements have ensued.

Experts believe that developing an HSV vaccine is biologically feasible. Supportive evidence includes: (a) there is a safe and effective vaccine for varicella zoster virus (VZV), a virus closely related to HSV, (b) successful development of an HPV vaccine provides proof that intramuscular delivery of vaccine can be highly efficacious against genital viral pathogens, and (c) some success from the investigational Herpevac vaccine, tested in more than 8000 HSV-1/HSV-2 seronegative women and showed 58% vaccine efficacy for prevention of genital HSV-1 disease and 32% efficacy for prevention of HSV-1 infection.

The most widely used approach in human clinical trials has been glycoprotein subunit vaccines. Glycoproteins are expressed on the viral surface and induce neutralizing antibodies, and provide an obvious vaccine target. The Herpevac trial, which used a vaccine candidate with glycoprotein and adjuvant, did not show efficacy against HSV-2 disease or infection. Further analysis showed that sera of those vaccinated neutralized HSV-1 3 times better than HSV-2, suggesting that the tested vaccine may be sufficient in preventing HSV-1 but not HSV-2 infection.¹² Results indicate that HSV-1 infection could be prevented with the vaccine and that there is an immune correlate of protection. Although the vaccine did not perform as expected, findings from the clinical trials represent new advances for the HSV vaccine field.

NIH/NIAID scientists are conducting a Phase 1 study of the safety of replication-defective HSV-2 vaccine in adults aged 18 to 40 with or without HSV infection. This vaccine, HSV529, was created by removing two essential genes from HSV. With these two deletions, the “replication defective” virus can infect, but not replicate, in normal cells. NIH/NIAID researchers are seeking to determine both the safety of HSV529 vaccine in persons with or without HSV infection, and the ability of the vaccine to elicit immune responses to HSV-2.

¹¹ Johnston C, Koelle D, Wald A. Current status and prospects for development of an HSV vaccine. *Vaccine* [serial online]. March 20, 2014;32 (Sexually transmitted infections: Vaccine development for global health):1553-1560. Available from: ScienceDirect, Ipswich,MA. Accessed February 20, 2015.

¹² Belshe, R. B., Leone, P. A., Bernstein, D. I., Wald, A., Levin, M. J., Stapleton, J. T., & ... Deal, C. D. (2012). Efficacy results of a trial of a herpes simplex vaccine. *The New England Journal Of Medicine*, 366(1), 34-43. doi:10.1056/NEJMoal103151



DISCOVERY AND CREATION OF NEW VACCINES

Shaping the Vaccine Priority Agenda

New and improved vaccines are needed for protection against emerging and re-emerging diseases. Given the number of diseases for which new and improved vaccines may be desired and the range of technological approaches that are available, decisions about which vaccines to prioritize can be daunting, especially when development timelines are long and costs of development are substantial.

A priority of the 2010 National Vaccine Plan is “to develop a catalogue of priority vaccine targets of domestic and global health importance” to aid decision-makers and invested stakeholders in selecting vaccine candidates and setting priorities for vaccine development and introduction targets. With this in mind, the Institutes of Medicine (IOM), with support from NVPO, developed a new vaccine decision-support tool called the Strategic Multi-Attribute Ranking Tool for Vaccines, or SMART Vaccines tool. In December, the IOM completed the third and final phase of this work.

The Phase I report, Ranking Vaccines: A Prioritization Framework, introduced an analytical model that employed multi-attribute utility theory, a specific version of the

TABLE 2: Choices of Attributes in SMART Vaccines 1.1	
Health Considerations	<ul style="list-style-type: none"> • Premature Deaths Averted per Year • Incident Cases Prevented per Year • QALYs Gained or DALYs Averted
Economic Considerations	<ul style="list-style-type: none"> • Net Direct Costs (Savings) of Vaccine Use per Year • Workforce Productivity Gained per Year • One-Time Costs • Cost-Effectiveness (\$/QALY or \$/DALY)
Demographic Considerations	<ul style="list-style-type: none"> • Benefits Infants and Children • Benefits Women • Benefits Socioeconomically Disadvantaged • Benefits Military Personnel • Benefits Other Priority Population
Public Concerns	<ul style="list-style-type: none"> • Availability of Alternative Public Health Measures • Potential Complications Due to Vaccines • Disease Raises Fear and Stigma in the Public • Serious Pandemic Potential
Scientific and Business Considerations	<ul style="list-style-type: none"> • Likelihood of Financial Profitability for the Manufacturer • Demonstrates New Production Platforms • Existing or Adaptable Manufacturing Techniques • Potential Litigation Barriers Beyond Usual • Interests from NGOs and Philanthropic Organizations
Programmatic Considerations	<ul style="list-style-type: none"> • Potential to Improve Delivery Methods • Fits into Existing Immunization Schedules • Reduces Challenges Relating to Cold-Chain Requirements
Intangible Values	<ul style="list-style-type: none"> • Eradication or Elimination of the Disease • Vaccine Raises Public Health Awareness
Policy Considerations	<ul style="list-style-type: none"> • Interest for National Security, Preparedness, and Response • Advances Nation's Foreign Policy Goals
User-Defined Attributes	<ul style="list-style-type: none"> • Up to Seven Attributes
Key: DALYs = disability-adjusted life years; NGOs = nongovernmental organizations; QALYs = quality-adjusted life years.	

DISCOVERY AND CREATION OF NEW VACCINES

general class of multi-criteria decision-analysis tools. The decision to use this approach signifies an important change from previous IOM approaches to prioritizing vaccines for development. This shift in approach was largely driven by stakeholder feedback indicating that the past studies limited the value of these decision-support tools to many in the global vaccine community. As part of Phase I, the SMART Vaccines Beta version was shared, which allowed users to specify which attributes are of highest importance and assign weighting to selected attributes. This, too, was a novel approach in a system that historically relied on priority lists.

In Phase II, the model was enhanced and extensive testing was conducted using additional data for hypothetical vaccines for the prevention of pneumococcal infection, HPV and rotavirus. A broad range of attributes were also embedded into the tool—28 attributes in total and 7 user-identified entries, as seen in the corresponding table. This software version was first made available for public use in September 2013 with specific guiding principles issued for the future development of the SMART Vaccines tool.

This past year proved to be pivotal in the development of the tool. The IOM's final report, Ranking Vaccines: Applications of a Prioritization Software Tool, was released in December 2014. There were three main tasks at hand: (1) the evaluation of the software in four user-based applications, (2) the development of a general data framework for the software, and (3) the definition of next steps that would increase the use and value of SMART Vaccines. The current SMART Vaccines software is available through National Academy of Science's website.

Three user groups were selected to explore three user case scenarios. The Public Health Agency of Canada (PHAC), one user which had a country-level goal of prioritizing new vaccine research and development, focused its initial efforts on use of the SMART Vaccines tool on tuberculosis and chlamydia. (See below for a more detailed look at PHAC's experience.) The New York State Department of Public Health, the second user, sought to use SMART Vaccines to help refine advice they provide to health care providers concerning which of two vaccines, already available, was best suited for vaccinating infants against rotavirus. The third user, the Serum Institute of India, which has a manufacturing focus on dengue and respiratory syncytial virus vaccines, looked to use the software to enhance their understanding of potential vaccine markets beyond India. In addition to the aforementioned user groups, two officials from Mexico's Ministry of Health served as advisory consultants in exploring the use of an early version of SMART Vaccines to compare the value of two existing influenza vaccines from a policy perspective. All users understood that they were testing the software and it was not meant to be used for actual decision-making.

DISCOVERY AND CREATION OF NEW VACCINES

In the Phase II report, key lessons learned and future R&D priorities were summarized. Emphasis was placed on the importance of outreach and communications efforts to achieve best use of SMART Vaccines, the need for a transition strategy to land on a permanent home for SMART Vaccines (which will be critical to its use and survival as a strategic planning resource), and the paramount importance of the community development model to facilitate further use of the tool, data development and software improvements. As a multi-stakeholder decision-support system, on both the domestic and international levels, the SMART Vaccines software has the potential to change the practices of many across the vaccine enterprise.

NVPO and NIH's Fogarty International Center (FIC) will continue to collaborate on development and execution strategies for Phase IV of the SMART Vaccines tool. and are looking into options for how best to make the tool available and useful to the public. In support of this overarching objective, a collaborative network of stakeholders and end-users may be established to implement an information gathering and information-sharing protocol to promote the ongoing evaluation and improvement of the tool, including the expansion of data. This network would likely be composed of individuals and institutions with experience in the development, regulation and implementation of vaccines, as well as those with experience in computational modeling, epidemiology, demography, database design, and data visualization.

DISCOVERY AND CREATION OF NEW VACCINES***Public Health Agency of Canada's Review of the SMART Vaccine Tool***

Great interest remains in SMART Vaccines as a thinking tool to guide vaccine priorities of public health importance for the Public Health Agency of Canada (PHAC). The software supplies multiple attributes to choose from, some quantitative but most qualitative, and suggests an initial comparison of ranking scores with a comparative bar chart. The software also provides an option to change the attribute weights in slider bars, which will subsequently re-rank the priority scores. PHAC tested three hypothetical diseases, with corresponding vaccine characteristics in a Canadian population and compared results by moving the attribute weights, emphasizing:

- premature deaths averted
- incidence cases prevented
- net direct cost (savings) of vaccines used per year (millions)
- workforce productivity gained
- cost-effectiveness
- benefiting infants and children
- benefiting women
- possible elimination of disease

In each scenario, the program gave very different ranking scores and priority lists. While committee members would have likely gone through the same thinking process without the software, in complex scenarios, it would be difficult to track verbal arguments and consistency. Sensibly used, the SMART Vaccines tool tells a story, and does not just provide numbers of ranking scores; a story which orders the thoughts and sharpens the intuitive notions in the discussions.

The software is strong in the application of the optimization algorithm from management sciences, but weaker on the insight of epidemiology. An illustrative example of this would be for a vaccine against TB when “new incident cases prevented per year” is the only attribute and a comparison is made for targeting vaccines for the elderly versus for those younger than age 65 years. SMART Vaccines suggested targeting the vaccine to those older than 65 years, because the incidence rate of active TB is the highest in this age group. Since TB is a chronic disease with long latency period (decades), the higher incidence rates of active TB observed in the elderly are due to infections taking place in younger

DISCOVERY AND CREATION OF NEW VACCINES***Public Health Agency of Canada's Review of the SMART Vaccine Tool, continued***

persons. As vaccines are designed to prevent new infections, and there is no reliable estimate for annual incidence of new infections as input to the software, caution may be required in using the program for chronic infectious diseases such as TB, viral hepatitis, and HIV.

Chlamydia was also used in PHAC's test case. Morbidity and costs differ between infected males and females, and between infants and adults; the software offered little option to make separate entries by age. In addition, some individuals can fall into more than one category of morbidity over the course of their infection, so the percentage of all morbidities is greater than 100, which required an artificial forcing to 100% to meet the software requirement for the calculation of scores. In addition, the software could not perform the calculation if the outcome did not include death, even for diseases with zero fatality.

The last software version tested was also weak in linking the disease with the population groups in which it spreads, allowing for only country-level population data with a predefined age-structure. In the TB example, preference would be to separate Canadian North and South as two exclusive populations, each with their own demographic characteristics, annual incidence rates and vaccination coverage rates. While the northern Canadian population is very small, the TB incidence rates are very high, thus a TB vaccine might be scored more favorably against other candidate diseases in southern Canada. The PHAC looks forward to evaluating the next version of the SMART Vaccine software.

OPTIMIZING VACCINE PREPARATION, USE AND DELIVERY

The impact of immunizations has been notable. While our earliest vaccines were developed with a very limited understanding of the human immune system, the maturation of the scientific understanding of immunity has accelerated vaccine development and provides new opportunities for vaccine design. Therefore, the vignettes in this section highlight some of the work being done to better understand the human immune system and its relevance to vaccine research and development.

Studying Vaccine Adjuvants

The use of adjuvants, or substances that enhance the body's immune response to an antigen, are important in the continued development of safe and effective vaccines. NIH spurred a number of research efforts in this research area, including awarding seven new vaccine adjuvant discovery contracts this year. Total funding for these contracts could reach \$70 million over five years. Dr. Anthony Fauci, the Director of NIH/NIAID, describes the potential impact of this research as novel and exciting because "such adjuvants could be used to improve current vaccines, extend the vaccine supply or enhance vaccine efficacy in people with immature or weakened immune systems, such as infants and the elderly."¹³

This new research, led by NIH/NIAID, focuses on enhancing acquired immunity, thus expanding our understanding of the role of adjuvants to indirectly and directly stimulate adaptive immunity. The first stage of research uses experimental and computer-based approaches to screen more than one million molecules and identify those capable of enhancing the adaptive or acquired immune responses. In the next stage of research, the investigators will determine which adjuvant candidates show the greatest promise to work. Next, structural changes will be made to the molecules to augment their ability to safely enhance protective immune responses without causing undesirable side effects. Finally, in the last stage of research, scientists will test vaccines formulated with the optimized adjuvant candidates for safety and effectiveness in animals.¹⁴

¹³ www.niaid.nih.gov/news/newsreleases/2014/Pages/vaccineadjuvantawards.aspx

¹⁴ *ibid*

OPTIMIZING VACCINE PREPARATION, USE AND DELIVERY***A Deeper Dive into Adjuvants for Mucosal Immunity***

Approximately 95% of current vaccines are administered by intramuscular routes and elicit circulating antibody and cellular responses that together provide protective immunity. However, the protection at mucosal sites (e.g., the lining of the airways, the intestine, and genitourinary tract), where most pathogens initiate infection, may not be optimal. Mucosal epithelium covers approximately 400 m² of surface in humans and is protected by specialized antibodies and resident immune cells.

To optimize vaccine/adjuvant combinations for mucosal immunization, NIH/NIAID is funding two promising approaches at the pre-clinical stage. A major goal of these approaches is to develop vaccines that are administered intranasally, sublingually, or orally to elicit protective cellular immune responses at these sites.

First, an influenza vaccine combined with an innate immune activating adjuvant was given sublingually to mice and was found to induce high levels of protective antibody responses. Second, a vaccine candidate for Herpes Simplex Virus (HSV)-2 co-delivered intranasally with a novel nanoemulsion adjuvant elicited greater than 90% protection against an HSV-2 vaginal challenge infection in guinea pigs. The same nanoemulsion adjuvant combined with a test vaccine for Respiratory Syncytial Virus (RSV) protected nonhuman primates from challenge infection with RSV. A similar na-

noemulsion/vaccine approach is currently being evaluated in monkeys to enhance protection to whooping cough caused by the bacteria *Bordetella pertussis* and to reduce the amount of bacteria carried in the respiratory tract of asymptomatic infections. These studies are at an early stage and additional work will be needed to demonstrate the effectiveness of mucosal administration of vaccines for particular diseases.

Adjuvants Targeting Novel Innate Immune Receptors

A major goal of adjuvant research is to develop a “toolbox” of different adjuvants that could be employed to elicit optimal vaccine immunity to different types of infections. One approach is to target different receptors of the immune system that trigger immune responses best suited to a particular pathogen. Alum, the most widely used adjuvant, may activate several pathways. The adjuvant component of the FDA-approved Cervarix (GSK’s bivalent HPV vaccine), and many promising adjuvants in development, target a class of innate immune receptors (toll-like receptors). In order to identify new adjuvants that target additional pathways, researchers supported by NIH/NIAID, among others, are studying a molecule present in most cells and tissues, termed RIG-I, that recognizes infections by RNA viruses such as influenza virus, West Nile Virus or hepatitis. Saponin-derived adjuvants such ISCO Matrix and Matrix M are under investigation for several pandemic influenza vaccines with promising results from Phase 2 studies.

OPTIMIZING VACCINE PREPARATION, USE AND DELIVERY

The Promise of Maternal Immunization

Maternal immunization continues to exemplify an effective vaccination strategy by protecting the woman, her developing fetus and her infant against infectious disease. Maternal immunization yields this trifecta of protection by enhancing antibody levels against particular infections. These antibodies are transferred to the fetus by the placenta or to the baby via breast milk. Studies have established the benefits of maternal influenza vaccination. In a randomized controlled trial based in Bangladesh, pregnant women vaccinated against influenza were significantly less likely to develop febrile respiratory illness and had fewer clinical visits than pregnant women in the control group who received pneumococcal vaccine only. Also, infants whose mothers had been immunized with inactivated influenza vaccine during pregnancy had a 63% reduction in laboratory-confirmed influenza and a 29% reduction in respiratory illness with fever compared with infants whose mothers had only received the pneumococcal vaccine.¹⁵

In a prospective study, spanning 3 consecutive influenza seasons (November 2002 to September 2005), there was a 41% reduction in laboratory-confirmed influenza and a 39% reduction in hospitalizations due to influenza-like illness in infants born to mothers who were vaccinated against influenza during pregnancy compared with infants of unvaccinated mothers.¹⁶ Further, during the 2009 H1N1 influenza pandemic, it was reported that the monovalent 2009 H1N1 flu vaccine produced a protective antibody level in 97% of vaccinated mothers and 89% of newborns.¹⁷ These findings collectively aid in building support for maternal immunization strategies and help to support the World Health Organization's recommendation that all pregnant women receive a flu vaccine regardless of trimester.

Pertussis (commonly known as whooping cough), like influenza, can cause serious and potentially life-threatening illness that affects both children and adults. In 2012, the CDC reported 48,277 cases of pertussis in the U.S., with many more cases going undiagnosed and unreported. This is the highest number of cases reported in the U.S. since 1955, when 62,786 cases were reported.¹⁸ Infants are at greatest risk, as illustrated by the graph to the right, with those less than three months of age, too young to have completed the recommended vaccination series, being the group most at-risk from severe pertussis infection. Hospitalizations and mortality rates from pertussis are highest in this group, with pertussis hospitalization rates climbing to over 50% in infected infants less than 1 year of age, compared to the adult

¹⁵ Zaman K, Roy E, Arifeen SE, Rahman M, Raqib R, Wilson E, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* [Internet]. 2008 Oct 9 [cited 2013 Oct 3];359(15):1555-64. Available from: www.ncbi.nlm.nih.gov/pubmed/18799552

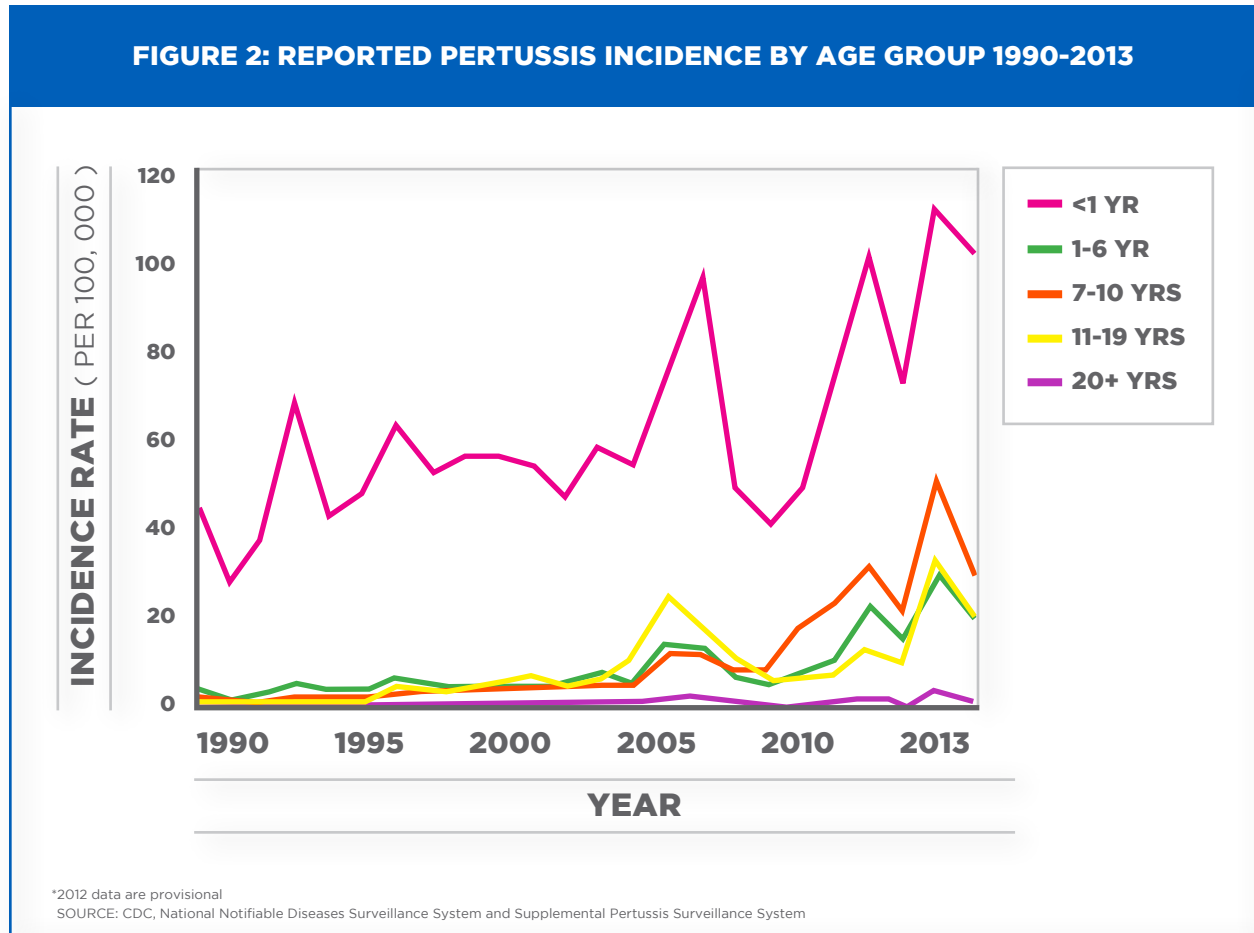
¹⁶ Eick AA, Uyeki TM, Klimov A, Hall H, Reid R, Santosham M, et al. Maternal influenza vaccination and effect on influenza virus infection in young infants. *Arch Pediatr Adolesc Med* [Internet]. 2011 Feb [cited 2013 Oct 8];165(2):104-11. Available from: www.ncbi.nlm.nih.gov/pubmed/20921345

¹⁷ Jackson LA, Patel SM, Swamy GK, et al. Immunogenicity of an inactivated monovalent 2009 H1N1 influenza vaccine in pregnant women. *J Infect Dis* 2011; 204:854-863.

¹⁸ www.cdc.gov/pertussis/fast-facts.html

OPTIMIZING VACCINE PREPARATION, USE AND DELIVERY

pertussis hospitalization rate of 3% for the rest of the population.¹⁹ Partners across HHS seek to further understand how to prevent pertussis disease, particularly in this high-risk neonate population and is looking toward the concept of maternal immunization for guidance.



Recently, FDA scientists reported results of an animal model study they conducted with pregnant and infant baboons. In this study, baboons were vaccinated with licensed acellular-pertussis vaccines to investigate how effective maternal and neonatal immunization is for the prevention of pertussis. Study results demonstrated that infant baboons born of mothers that had been vaccinated during pregnancy were protected against pertussis when exposed to it at five weeks after birth. Evidence also showed that the newborn baboons from mothers that had not been vaccinated were protected after receiving either a single vaccination given at two days of age or at two days and 28 days of age.²⁰ The results of the FDA study establish an important proof-of-concept in a primate model. Maternal vaccination may confer

¹⁹ www.cdc.gov/pertussis/clinical/complications.html

²⁰ Warfel, JM, PapinJF, Wolf RF, Zimmerman, LI, Merkel TJ. Maternal and Neonatal Vaccination Protects Baboons from PertussisInfection Journal of Infectious Diseases March 2014, [Epub ahead of print], accessed at: www.fda.gov/BiologicsBloodVaccines/ScienceResearch/ucm387180.htm

OPTIMIZING VACCINE PREPARATION, USE AND DELIVERY

immunity to infants against severe pertussis during the first months of life, before the infant can benefit from individual vaccination as s/he is too young to have completed this vaccination series.

Research has also been conducted on the safety of pertussis vaccination in human patient practice. A 2014 observational study from the U.K., published in the *British Medical Journal*, found that pregnant women given an acellular-pertussis-containing vaccine during their third trimester had no evidence of increased risk of adverse events related to pregnancy, and in particular, no increased risk of stillbirth.²¹ Moving beyond this observational safety study, findings from a recent clinical trial, published in the May 2014 issue of *Journal of the American Medical Association*, further substantiated that vaccinating pregnant women with the tetanus, diphtheria and acellular pertussis (Tdap) vaccine is safe, induces an immune response in the mother and is likely to protect their newborn against whooping cough.²² This study was conducted through a national network supported by NIH and led by investigators at Baylor College of Medicine. These data are suggestive of the effectiveness of maternal pertussis vaccination, as well as the safety of pertussis vaccine during pregnancy on birth outcomes.²³

Public-private partnerships have also been leveraged to further maternal immunization strategies. For example, the Bill & Melinda Gates Foundation (BMGF) has been working to identify and address scientific, technical, regulatory, policy and operational challenges to broadening maternal immunization efforts in low income countries (LIC). Influenza and RSV were the initial pathogens of focus, which expanded in 2014 to include GBS and Pertussis. Working in-sync with the maternal immunization pipeline, BMGF is also supporting efforts in the development of a maternal respiratory syncytial virus (RSV) vaccine and GBS vaccine, as no vaccines are currently available to prevent these diseases.

Alternatives to Needles

While vaccines are crucial for preventing the onset and spread of a myriad of potentially deadly diseases, delivery by needle and syringe puts vaccination in the hands of a trained health care professional and may be a constraint to vaccine access in many settings. Additionally, those who are afraid of needles or injections may avoid vaccination by the traditional syringe-and-needle delivery method. New developments in vaccine administration techniques, including but not limited to oral or mucosal delivery, may appeal to those with a needle phobia or a low threshold for pain, and simultaneously improve vaccine coverage. CDC, NIH and FDA lead efforts to broaden administration options to boost vaccine uptake.

²¹ FM Munoz et al. Safety and immunogenicity of tetanus, diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: A randomized clinical trial. *Journal of the American Medical Association* DOI: 10.1001/jama.2014.3633 (2014).

²² FM Munoz et al. Safety and immunogenicity of tetanus, diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: A randomized clinical trial. *Journal of the American Medical Association* DOI: 10.1001/jama.2014.3633 (2014).

²³ Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, Donegan K, Fry NK, Miller E, Ramsay M. Effectiveness of maternal pertussis vaccination in England: An observational study. *Lancet*. 2014;384(9953):1521-28

OPTIMIZING VACCINE PREPARATION, USE AND DELIVERY

CDC, in partnership with industry and academia, demonstrated that novel microneedle technologies can deliver rotavirus vaccine to animals. A microneedle patch has also been developed and tested to deliver measles and rubella vaccine.²⁴ Likewise, other studies were conducted this year to investigate the use of other novel devices to deliver polio vaccine.

Meanwhile, NIH-supported researchers are developing an influenza patch that uses microneedles, which could be sent by mail for patients to administer themselves. This low cost, single-use patch is designed to be applied easily and quickly and should not require refrigeration. The researchers recently completed an acceptability and usability test of nearly 100 adults and plan to conduct a clinical trial in 2015.²⁵

In addition to these emerging technologies, FDA approved the use of one specific jet injector device supported by BARDA for the administration of an influenza vaccine. This is the first needle-free delivery system approved by the FDA for the administration of an inactivated influenza vaccine. Only one influenza vaccine is approved for use with the PharmaJet Stratis Needle-free Injection System, AFLURIA®, a three strain, or trivalent, influenza vaccine. It provides protection against an influenza A (H1N1) virus, an influenza A (H3N2) virus and one influenza B virus. FDA approved Afluria for use with the PharmaJet Stratis Needle-free Injection System in adults 18 through 64 years of age. While data demonstrated that vaccination with this method provided a similar level of immune protection compared to the same flu vaccine administered via a traditional needle,²⁶ This technology provides another option for delivering vaccine without a needle and helps to prevent needle stick injuries in health care professionals.



A jet injector is a medical device used for vaccination that uses a high-pressure, narrow stream of fluid to penetrate the skin instead of a hypodermic needle. Jet injectors may be powered by compressed gas or springs. The devices were invented in the 1960s and were used successfully in mass vaccination efforts to eradicate smallpox and other diseases.

*Definition from
CDC at www.cdc.gov/flu/protect/vaccine/jet-injector.htm*



*Administering measles vaccine with a microneedle patch is expected to be much easier than getting a shot. c/o CDC
Photo Credit: Gary Meek, Georgia Tech*

²⁴ Edens, C (07/25/2013). "Measles vaccination using a microneedle patch". *Vaccine* (0264-410X), 31 (34), 3403.PMID: 23044406 DOI: 10.1016/j.vaccine.2012.09.06

²⁵ Norman, J. J. (2014-04-01). Microneedle patches: usability and acceptability for self-vaccination against influenza. *Vaccine*, 32(16),1856-1862.doi:10.1016/j.vaccine.2014.01.076

²⁶ www.cdc.gov/flu/protect/vaccine/jet-injector.htm

SEASONAL INFLUENZA PREVENTION AND PANDEMIC PREPAREDNESS

Collaborative efforts across the federal government and the private sector have led to influenza vaccine technologies that may better prepare the Nation for seasonal flu and potential influenza pandemics. Despite these preparedness gains, influenza viruses readily mutate, creating the potential for severe influenza seasons or even pandemics as new strains emerge for which the public has little or no immunity. This point is illustrated by the poor match, due to antigenic drift, of one of the A strains (H3N2) in the 2014-2015 seasonal flu vaccine. This left the public with suboptimal protection from certain circulating flu strains. The 2014-2015 seasonal flu vaccine mismatch also underscores the need for a universal influenza vaccine, which would offer broad protection and prolonged immunity from a wide range of both seasonal and pandemic influenza threats.

Many partners across HHS and the vaccine enterprise, like the World Health Organization, and vaccine manufacturers, played critical roles in prioritizing flu prevention and preparedness on the global-level. Both pandemic and seasonal influenza threats require planning, evaluation and research and a number of efforts detailed below were conducted this past year in an effort to improve our ability to combat a variety of pandemic influenza threats and improve options and uptake of seasonal influenza vaccine. While the information here is focused on influenza, other pathogens considered to be potential global threats are discussed in Goal 5.

Expanding Seasonal Influenza Vaccines

In recent years, new influenza vaccines created more vaccine choices for senior citizens, those with egg allergies and those who fear needles. While typical seasonal flu vaccine delivery has included intramuscular injection or nasal spray, a growing variety of influenza vaccine options became available for the 2014-2015 influenza season. Both intramuscular injections and nasal delivery remain, but with specific preparations that protect against three (two Type As

FLU.GOV Know what to do about the flu.

Flu Season Is Here Get Vaccinated Today

Who should get the vaccine?

EVERYONE 6 MONTHS AND OLDER | **PEOPLE AT HIGH RISK**

Everyone **6 MONTHS OF AGE AND OLDER** should get the flu vaccine. Seasonal flu vaccines have a very good safety track record.

It is especially **IMPORTANT TO GET THE VACCINE IF YOU, SOMEONE YOU LIVE WITH, OR SOMEONE YOU CARE FOR IS AT HIGH RISK** of complications from the flu.

- ✓ Children & Infants
- ✓ Pregnant Women
- ✓ Seniors
- ✓ People with Disabilities
- ✓ People with Health Conditions
- ✓ Travelers & People Living Abroad

Can I get the flu from the vaccine?

NO, YOU CAN'T GET THE FLU | **MILD REACTIONS**

NO, YOU CAN'T GET THE FLU from the flu vaccine. The flu vaccine protects you from the flu, not the common cold. But you may experience some side effects.

MILD REACTIONS such as soreness, headaches, and fever are common side effects of the flu vaccine.

How should I get the vaccine?

There are **TWO TYPES** of vaccine, the flu shot and the nasal spray. Both protect against the same virus strains.

FLU SHOT | **NASAL SPRAY**

Made with inactivated (killed) flu virus | Made with weakened live flu virus

Given by needle | Given with a mist sprayed in your nose

Approved for use in healthy people older than 6 months and people with chronic health conditions | Approved for healthy people between the ages of 2 and 49, except pregnant women

When should I get the vaccine?

Get your flu shot or spray **TODAY**. Flu season usually peaks in January or February, but it can occur as late as May. **EARLY IMMUNIZATION IS THE MOST EFFECTIVE**, but it is not too late to get the vaccine in December, January or beyond.

Where can I get the vaccine?

Visit **FLU.GOV** and use the **FLU VACCINE FINDER**.

Flu Vaccine Finder Just the vaccine you need.
Everyone six months of age and older needs a flu vaccine.
Enter Zip Code [] [GO]
powered by HealthMap
www.flugov.gov

FLU.GOV A federal government website managed by the U.S. Department of Health & Human Services
200 Independence Avenue, S.W. - Washington, D.C. 20201

SEASONAL INFLUENZA PREVENTION AND PANDEMIC PREPAREDNESS

and one Type B) or four (two Type A and two Type B) strains of influenza, known respectively as trivalent and quadrivalent vaccines.

Historically, most influenza vaccines have been produced in chicken eggs. While there has been a long history of success with these vaccines, they have several limitations. They may not be appropriate for those with severe egg allergies, and vaccine production in eggs can result in additional viral mutations as the virus adapts to this substrate.

To solve this inherent issue, CDC scientists used advanced molecular detection technology to examine the genetic sequences of ten generations of H3N2 influenza viruses as they evolve in embryonated eggs. Once the desirable genetic changes are identified, CDC will use advanced genetic techniques to select specific H3N2 strains with the properties that can be used to make vaccine candidates that better represent viruses that are likely to circulate in humans in the upcoming influenza season and therefore may offer better protection against H3N2 viruses.²⁷

Advancing Pandemic Preparedness

Historic steps have been taken in the past several years to combat the deadly threat presented by avian influenza with the FDA's approval of the first adjuvanted avian influenza vaccine in 2013. Manufactured by ID Biomedical Corporation, a subsidiary of GlaxoSmithKline, in partnership with the Biomedical Advanced Research and Development Authority (BARDA), this vaccine protects against avian influenza H5N1.

To complement advances in the approval of the H5N1 vaccine, FDA continues to advance our vaccine preparedness for a potential pandemic by preparing and distributing potency reagents needed in the development of vaccines for clinical trials. For example, in the past year, new reagents were needed for vaccines being developed for the emerging H7N9 viruses in China. FDA was the lead agency in production and calibration of the first H7 reference reagent and to date, FDA is the only regulatory agency that has been able to produce an H7-specific antiserum that works with the H7N9 candidate vaccines. To produce this potency antiserum FDA utilized a novel method of immunization with H7 virus-like particles that was developed a few years ago as an alternative technique should such an emergency arise.

HHS has truly made great strides since the H1N1 pandemic in 2009 to strengthen the Nation's preparedness for mild to severe pandemics. HHS has afforded greater pandemic preparedness with regard to vaccines through vaccine development using modern cell-and recombinant-based manufacturing platforms, use of antigen- and dose-sparing adjuvants that provide longer lasting cross-protection, pre-pandemic vaccine stockpiling, and building modern vaccine manufacturing facilities in

²⁷ www.cdc.gov/amd/project-summaries/influenza-vaccines.html

SEASONAL INFLUENZA PREVENTION AND PANDEMIC PREPAREDNESS

the U.S., resulting in enhanced 4-5 fold domestic influenza vaccine manufacturing capacity to meet the U.S. demands for pandemic influenza vaccines. Pre-pandemic H5N1 and H7N9 influenza vaccine and adjuvant stockpiles were established and maintained by BARDA to address the needs of the Nation's critical infrastructure and other high risk populations. Research and development efforts led by HHS through the Influenza Vaccine Manufacturing Improvement I initiative incorporated technological improvements (e.g., synthetic biology) to speed production of pandemic influenza vaccines during the H7N9 outbreak in 2013.

Evaluating Potential Pandemic Influenza Threats

Designed to assist a range of stakeholders in understanding the potential threats posed by individual strains of potentially pandemic influenza, the Influenza Risk Assessment Tool (IRAT) was developed by CDC to evaluate novel influenza viruses. HHS uses the IRAT to annually assess potential influenza pandemic risk, based on two different domains: "emergence" and "public health impact." Ten scientific criteria are used to measure the potential pandemic risk associated with each of these domains. Each of the ten criteria is then statistically weighted, based on significance, to test each scenario. A composite score for each influenza virus is then calculated. Composite scores provide a system to rank and compare emerging, novel influenza viruses (H5N1, H7N9) to each other in terms of their potential pandemic risk. These results inform NIH, CDC, and BARDA on the need to develop new pandemic influenza vaccines and BARDA on what actions are needed to update the national pre-pandemic influenza vaccine stockpiles.

CDC also conducted studies evaluating vaccines against influenza subtypes with pandemic potential for their ability to provoke an effective immune response. CDC collaborated with academic and industry partners to evaluate the preclinical effectiveness of several novel adjuvants and non-traditional delivery methods, such as vector-based vaccines.

NIH/NIAID also conducted several clinical trials to assess the safety and immunogenicity of 2009 H1N1 pandemic vaccines and stockpiled H5N1 influenza vaccines. These NIH/NIAID-sponsored trials evaluated inactivated vaccines given alone or mixed with an adjuvant prior to administration. NIH/NIAID also conducted clinical trials to test inactivated vaccines against other influenza viruses with pandemic potential, including H7N9 and a novel variant strain of an H3N2 virus (H3N2v). The H7N9 vaccine candidate administered with an adjuvant generated a significantly higher immune response than doses of the vaccine given alone.²⁸ These trials were done in collaboration with HHS/BARDA, which provided the vaccines and the AS03 and MF59 adjuvants, demonstrating a highly coordinated and successful public health response across agencies.

²⁸ MJ Mulligan et al. Serological responses to an avian influenza A/H7N9 vaccine mixed at the point-of-use with MF59 adjuvant: a randomized clinical trial. JAMA DOI: 10.1001/jama.2014.12854 (2014).

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Working Toward a Universal Influenza Vaccine

The promise of a universal influenza vaccine has been attracting considerable attention due to its potential to impact public health. According to the WHO, flu epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 250 000 to 500 000 deaths each year.²⁹ In the US alone, each year on average, more than 200,000 people are hospitalized from seasonal flu-related complications. Flu season severity can also be unpredictable, with estimates of annual flu-associated deaths in the U.S. ranging from 3,000 -49,000.³⁰ A universal influenza vaccine that provides safe, effective and long-lasting immunity against a broad spectrum of influenza viruses, including seasonal and pandemic influenza, is the goal.

Development of a universal influenza vaccine was highlighted as a priority in 2014 in the President's proposed Opportunity, Growth, and Security Initiative as part of the 2015 fiscal year budget. The budget proposes a total investment of \$170 million in the Public Health and Social Services Emergency Fund to support pandemic flu activities, of which \$73 million will enable BARDA to support the advanced development of a universal influenza vaccine designed to be effective against all strains of influenza.

A study published in the June issue of *Journal of Virology* underscores that progress is being made toward a universal flu vaccine. There, FDA scientists reported that a potential universal influenza vaccine candidate protected animals from lethal infection with several different influenza A viruses, and also reduced transmission of other strains of flu.³¹ These findings suggest that a universal influenza vaccine for humans could offer both disease protection and reduction in the spread of infection. This would be especially important early in a pandemic, before a conventional vaccine matching the circulating virus would be available.

Researchers interested in a universal flu vaccine have also identified a region of the viral hemagglutinin (HA) protein called the stem or stalk, which is more conserved than the HA head region on which current licensed influenza vaccines are based. Vaccination strategies that induce immune responses to the HA stalk may provide protection against a variety of flu strains. NIH/NIAID-supported researchers immunized human volunteers against the avian flu virus H5N1 which contains a HA that is not currently circulating in the United States and to which the volunteers had not been exposed. The result of vaccination with novel HA was that these participants developed antibodies—indicators of protection—against the conserved stalk region

²⁹ www.who.int/mediacentre/factsheets/fs211/en/

³⁰ <http://www.cdc.gov/flu/about/qa/disease.htm>

³¹ Price G, Lo C, Misplon J, Epstein S. Mucosal immunization with a candidate universal influenza vaccine reduces virus transmission in a mouse model. *Journal Of Virology* [serial online]. June 2014;88(11):6019-6030. Available from: MEDLINE Complete, Ipswich, MA.

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of the viral HA protein. In comparison, volunteers immunized with standard seasonal trivalent vaccines containing HA proteins against which the volunteers were previously exposed had undetectable levels of antibodies to the conserved HA stalk, instead developing most of their antibodies against the more variable head region of the HA. The results of this study were published in the August 2, 2014, Proceedings of the National Academy of Sciences. The quest for a universal influenza vaccine which provides increased breadth and duration of protection against seasonal and emerging influenza viruses is a high public health priority for NIH/NIAID.³²

³² Ellebedy A, Krammer F, Ahmed R, et al. Induction of broadly cross-reactive antibody responses to the influenza HA stem region following H5N1 vaccination in humans. Proceedings Of The National Academy Of Sciences Of The United States Of America [serial online]. September 9, 2014;111(36):13133-13138. Available from: Academic Search Premier, Ipswich, MA.

GOAL 2: ENHANCE THE VACCINE SAFETY SYSTEM

INTRODUCTION

Ensuring the safety of vaccines is paramount. Since vaccines are recommended for use among healthy populations, they undergo rigorous safety assessment and monitoring throughout their lifecycle: during preclinical and clinical development, as part of the evaluation undertaken by FDA, and after they are granted licensure and in use by the public. A robust network of safety checks, including extensive research and a variety of active and passive monitoring systems, has proven to work well in identifying safety “signals,” or health events that occur following immunization and may or may not have been associated with vaccination, and determining whether adverse events that follow immunization may be caused by immunization. These many assessments throughout vaccine development and use ensure that vaccines are among the safest medical products available.

Manufacturers have the responsibility to evaluate vaccines’ safety prior to and following licensure. However, vaccine manufacturers, independent researchers, several agencies within HHS, the Department of Defense and the Veterans Administration work to monitor vaccines’ safety. HHS also works to develop, enhance, and maintain safety monitoring systems, conduct research related to vaccine safety, and develop new strategies to quickly detect and evaluate adverse events following immunization (AEFI). Given the commitment to vaccine safety, there has been tremendous dedication and progress made in 2014 toward enhancing the vaccine safety system—Goal 2 of the National Vaccine Plan.



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Vaccines are exceptionally safe and effective, with the majority of AEFIs being minor and resolving within days. Serious adverse events following vaccination are extremely rare. The United States vaccine safety system is a large, multifaceted system. The goal of this system is to identify, in a timely manner, and minimize the occurrence of AEFI. As with any system, opportunities to expand and improve the system always exist. The following sections highlight some of the major advancements to have occurred in 2014—from defining the vaccine safety scientific agenda to improving procedures for the monitoring and reporting of safety signals.

Coordinating Safety Efforts to Develop a Vaccine Safety Scientific Agenda

HHS prioritizes assessing vaccine safety during discovery and development, regulatory evaluation, recommendations for use, and subsequent post-marketing surveillance. In the U.S., vaccine safety evaluation is overseen by the Director of the National Vaccine Program (the ASH), with the FDA’s legal authority in determinations of vaccine safety and efficacy, and coordinated by federal departments and agencies represented on the Immunization Safety Task Force (ISTF).

The ISTF was established in 2008 at the request of the Secretary of HHS to ensure that all federal efforts relevant to immunization safety were coordinated and integrated and that opportunities to enhance synergies across the federal government in immunization safety are identified. The ISTF includes HHS representatives from CDC, FDA, HRSA, NIH, CMS, BARDA, IHS, AHRQ, DoD and the VA.

Highlighting the importance of vaccine safety, the National Vaccine Plan called for the development of a vaccine safety scientific agenda to summarize the contributions and particular research focus of federal partners to the overall safety of vaccines in the U.S. These contributions cover the roles that the federal agencies play, in concert with vaccine developers and manufacturers, in safety testing of vaccines across their lifespan, from development through post-administration. Safety testing is categorized into the following:

1. Pre-licensure (Discovery/Research and Development) Safety Activities
2. Regulatory Review and Licensure Safety Activities
3. Post-Licensure Vaccine Safety Activities

One focus of the ISTF in 2014 centered on articulating the scientific agenda for vaccine safety-related activities to be undertaken by the main federal agencies leading particular systems and groups within the broad vaccine safety system. This exercise was guided by both the National Vaccine Plan and the NVAC White Paper on the United States Vaccine Safety System (2011). The three tables below outline the vaccine safety activities that federal partners lead and the scientific agenda items for which they are responsible within the broader vaccine safety system. The variety of agencies, activities and priorities provide a foundation of checks and balances across the expansive vaccine safety system, in place to identify any potential

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vaccine safety issues. Having a more transparent view of such activity and priority areas within the safety system underscores the rigorous safety testing performed, yielding vaccines that are safe, effective and crucial to maintaining and improving the health of the American public.

Table 3: Pre-Licensure Vaccine Safety Scientific Activities		
Leading Institution	Vaccine Safety Activity	Scientific Agenda
NIH	Identification and development of vaccine candidates	Develop and provide resources to facilitate basic and applied research including the ability to assess vaccines for safety and immunogenicity http://www.niaid.nih.gov/about/organization/vrc/Pages/default.aspx http://www.niaid.nih.gov/labsandresources/labs/aboutlabs/lid/Pages/default.aspx http://www.niaid.nih.gov/about/organization/dmid/Pages/default.aspx
NIH	Design of novel vaccine strategies	Support research to explore novel vaccine technologies and strategies to improve the immunization profile http://www.niaid.nih.gov/about/organization/dait/programs/Pages/basicImmunology.aspx
NIH	Investigate the variability in human immune responses	Support research to understand the range of variability in the human population that impacts responses to vaccines and potential associations with AEFIs
NIH	Improving vaccine immunomodulators, administration, and formulations	Discover and develop novel adjuvants, alternative routes of administration, and formulations
FDA	Vaccine development	Develop pre-clinical models, and vaccine efficacy and safety screening methodology http://www.fda.gov/BiologicsBloodVaccines/default.htm http://www.fda.gov/AboutFDA/CentersOffices/OrganizationCharts/ucm350562.htm http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/ucm133096.htm
FDA	Study of pathogenicity	Study molecular mechanisms of pathogenicity and determine biomarkers of virulence that might improve the safety profile

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Table 4: Routine Vaccine Safety Monitoring and Research Systems		
Leading Institution	Safety System	Objectives
CDC and FDA	Vaccine Adverse Event Reporting System (VAERS)	Receives reports of possible adverse events from a variety of sources, including parents, providers, manufacturers, pharmacists, and the military, and rapidly detects “signals”: possible adverse events for follow up. http://vaers.hhs.gov/about/index
CDC	Vaccine Safety Datalink (VSD)	Rapidly tests, and confirms or rejects VAERS-generated signals. It links databases, including vaccination and medical records and allows for near real-time surveillance. http://www.cdc.gov/vaccinesafety/Activities/vsd.html
CDC	Clinical Immunization Safety Assessment (CISA)	Addresses vaccine safety issues, conducts high quality clinical research, and assesses complex clinical AEFIs. http://www.cdc.gov/vaccinesafety/Activities/cisa/cisa_studies.html
FDA	Post-Licensure Rapid Immunization Safety Monitoring Program (PRISM)	Monitors the safety of vaccines post licensure using a national large, linked electronic healthcare database and a variety of observational study designs, including near-real time surveillance. http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/default.htm
DoD	Defense Health Agency-Immunization Healthcare Branch (DHA-IHB)	Researches adverse events using electronic health records and can contact individuals when consultation for follow-up or care is needed. Can follow up on VAERS signal detections. https://www.vaccines.mil/
DoD	Armed Forces Health Surveillance Center (AFHSC)	Supports post-marketing database studies. http://www.afhsc.mil/home
VA	Adverse Drug Event Reporting System (ADERS)	Reports, tracks and monitors adverse events caused by medications and vaccines across the entire VA health care system using a passive surveillance system comparable and linked to VAERS. http://www.pbm.va.gov/PBM/vacenterformedicationsafety/vacenterformedicationsafetyadverseeventtrackingtools.asp
VA	Center for Medication Safety (VAMedSAFE)	Obtains data from VA ADERS and VA Integrated Databases to track the safety of vaccines administered in the VA healthcare system. http://www.pbm.va.gov/vacenterformedicationsafety/vacenterformedicationsafetyaboutus.asp

ADVANCING VACCINE SAFETY SYSTEMS**Table 5: Post-Licensure Vaccine Safety Research of Special Interest**

Leading Institution	Vaccine Safety Research Topic	Research Plan
CDC and FDA	Vaccine recipient's individual risk factors	(1) improve safety monitoring and assessment by defining which sub-populations should be monitored, (2) identify individuals at increased risk for AEFIs, (3) improve the clinical approaches to treating AEFIs, (4) develop advanced vaccines with a decreased likelihood of AEFI occurrence, and (5) enhance risk communication about the safety of vaccines, particularly with regard to groups identified at higher risk for AEFIs.
FDA	General vaccine safety studies	Research potential safety concerns of newly licensed products such as auto-immune diseases or anaphylaxis
FDA	Concomitant and multiple dose vaccine administration	Study potential AEFIs that may arise after administering concomitant vaccine doses and multiple dose vaccines given at recommended intervals
FDA	Study of vulnerable populations	Vaccine safety research on special populations such as pregnant women
FDA	Safety evaluation methodology testing	Improve sensitivity and eliminate analytic bias when studying vaccine administration outcomes
CDC	Prevention of AEFI	Assessment of vaccine products, dosing and administration to identify factors that could be modified to avoid AEFIs
CDC	Assessing safety of new vaccines	CDC monitors new vaccines after their introduction using spontaneous reporting systems, and conducts population-based surveillance using electronic health data
CDC	Assessing vaccine safety in understudied populations	Special populations, such as pregnant women, immune deficient patients, and special ethnicities, have been historically excluded from vaccine clinical trials. CDC evaluates vaccine safety among these populations as well.
CDC	Continued research on statistical methods and study design	Because of the complexity of studying populations receiving vaccines, sophisticated statistical methods and study designs are being developed and refined for both active and passive surveillance. Continuing to refine near real-time surveillance techniques (e.g., rapid cycle analysis, RCA)
CDC	Communications Research	Research on knowledge, attitudes, beliefs, and behaviors related to vaccine safety and AEFI reporting, and continuously improving strategies for communicating risks
DoD and VA	Pandemic Vaccination Safety	Utilizes near real-time analysis to identify possible safety signals
DoD	Detecting AEFIs in special populations	Pregnancy registries are mined to assess maternal and fetal/infant outcomes after vaccination
VA	Seasonal flu active safety surveillance	Identify possible adverse outcomes in the VA healthcare system such as GBS, anaphylaxis, Bell's palsy, encephalitis, meningitis, idiopathic thrombocytopenia, optic neuritis, seizures and convulsions
VA	End of season analysis	Yearly assessment of influenza vaccine associated AEFIs in the VA healthcare system



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Improving the Reporting of Vaccine Safety Signals

The Vaccine Adverse Event Reporting System (VAERS), supported jointly by CDC and FDA, provides a method for reporting clinically significant adverse events occurring after administration of any vaccine licensed in the U.S. According to the CDC, there are approximately 30,000 VAERS reports each year.³³ Reports to VAERS act as potential signals that alert scientists of possible cause-and-effect relationships between a drug and an adverse event, which can then be investigated further through other vaccine safety monitoring initiatives.

To improve the quality and accessibility of AEFI reporting in this digital age, CDC designed and tested an updated version of the paper-based reporting form used since 1990. Changes are being made to both improve the quality and usefulness of the information and to improve user experience—creating a more efficient report form. With a modernized appearance, the form can be filled out and saved electronically—a frequent request from users. Additionally, new data reporting fields provide greater regulatory or public health value, exemplified by the addition of demographic and health status fields. The proposed new VAERS form (below, right) was posted to the Federal Register for a public comment period in late November 2014 and is anticipated to officially release in 2015.

The image shows the 'OLD' version of the VAERS form. It is a complex, multi-sectioned paper form with a blue header. The header includes the VAERS logo and website information. The form is divided into several numbered sections: 1. Patient Name, 2. Date of birth, 3. Sex, 4. Date and time of vaccination, 5. Date and time adverse event started, 6. Age at vaccination, 7. Report is about vaccine administered to a pregnant woman, 8. Prescriptions, 9. Allergies, 10. Other illness, 11. Chronic or long-standing health conditions, 12. Facility/clinic name, 13. Form completed by, 14. Best doctor/healthcare professional to contact, 15. Facility/clinic name, 16. Type of facility, 17. Medical tests and laboratory results, 18. Describe event(s), 19. Patient recovered, 20. Patient's race, 21. Result or outcome of event, 22. Any other vaccines received, 23. Has the patient ever had an adverse event, 24. Patient's ethnicity, 25. Status at time of vaccination, 26. Vaccinated at Military/DoD site. The form contains numerous checkboxes, text boxes, and tables for data entry.

The image shows the 'NEW (proposed)' version of the VAERS form. It features a modernized design with a blue header and a clear layout. The header includes the VAERS logo and website information, along with a note that items 2, 4, 5, 6, 17, 18, and 21 are essential. The form is divided into several numbered sections: 1. Patient name, 2. Date of birth, 3. Sex, 4. Date and time of vaccination, 5. Date and time adverse event started, 6. Age at vaccination, 7. Report is about vaccine administered to a pregnant woman, 8. Prescriptions, 9. Allergies, 10. Other illness, 11. Chronic or long-standing health conditions, 12. Facility/clinic name, 13. Form completed by, 14. Best doctor/healthcare professional to contact, 15. Facility/clinic name, 16. Type of facility, 17. Medical tests and laboratory results, 18. Describe event(s), 19. Patient recovered, 20. Patient's race, 21. Result or outcome of event, 22. Any other vaccines received, 23. Has the patient ever had an adverse event, 24. Patient's ethnicity, 25. Status at time of vaccination, 26. Vaccinated at Military/DoD site. The form contains numerous checkboxes, text boxes, and tables for data entry.

³³ www.cdc.gov/vaccinesafety/Activities/vaers.html

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Monitoring Adverse Events in a More Timely Manner

The most rapid monitoring for events following immunization is through VAERS (described above), in which data-mining is done regularly by FDA and CDC (e.g., daily to weekly during flu season) to look for signals, indicative of potential adverse events, that are disproportionately reported. In addition, the Vaccine Safety Data-link, supported by CDC, does Rapid Cycle Analysis for adverse events associated with flu vaccine every year. The RCA evaluates multiple health conditions that may occur after vaccination, including Guillain-Barré Syndrome (GBS).

Built on systems in place to monitor the pandemic H1N1 vaccine in 2009, FDA continues to advance safety monitoring for influenza with near real-time surveillance of GBS following influenza vaccine. Every year, since 2009, using weekly updated Medicare claims data, monitoring begins in mid-August and starts testing when a pre-specified number of vaccinations are observed in the system. Testing is done through use of an analytic tool (Updating Sequential Probability Ratio Test or US-PRT) that incorporates sequential testing and can make adjustments for both clinical delay and processing delay of claims. In the event of a signal, an early signal evaluation plan is instituted, and if necessary, a later evaluation plan with medical record review follows.

Because of the rapidity with which claims are entered into the system, near real-time surveillance within the Medicare population is an important national tool for influenza vaccine safety monitoring, as it represents one of the largest population groups receiving influenza vaccine. The system has successfully detected a signal in the 2010-11 influenza season and evaluated the signal using a refined signal evaluation plan. For the 2014-15 influenza season, the monitoring started on August 9, 2014. The primary analysis includes all influenza vaccines. The secondary analysis is designed to stratify by vaccine type, age group, and risk window definition. Despite these signals, GBS is quite rare. According to CDC data, each year, about 3,000 to 6,000 people in the U.S. develop GBS – so it is important to assess influenza vaccination in the context of this background rate in the population to determine whether GBS following vaccination may be causally related. Because both vaccination and influenza disease are seasonal and may be concurrent in a community, and the risk of developing GBS induced by influenza infection may be greater than the risk following immunization, is important to carry out these analyses

Monitoring Systems Supporting the Expansion of Maternal Immunization

As outlined in the previous chapter, maternal immunization is important. In essence, one vaccine potentially protects two—the mother and her developing child, and that child once s/he is born. This strong proof-of-principle has led to the recommendation of certain vaccinations during pregnancy—notably influenza and pertussis currently. With these recommendations comes the need to ensure that we have safety monitoring systems in place to assess this population.

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FDA continues to improve systems for vaccine safety in infant and maternal vaccination, with the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program. This program, through the use of large, linked databases for active surveillance and research, initiated two studies evaluating the safety of immunizations administered to pregnant women.

The first study seeks to evaluate the risk of cleft lip and cleft palate (orofacial birth defects), which are estimated to occur in over 4,500 babies each year. The second study seeks to evaluate the risk of spontaneous abortion (miscarriage), which is estimated to occur in 8-20% of pregnancies before week 20 of gestation, and of which 80% occur in the first 12 weeks of pregnancy.

Both studies were launched to further develop the infrastructure and methods to evaluate the safety of maternal immunization. Study results could provide the FDA with a complementary approach to current standards for safety monitoring: pregnancy registries and spontaneous reporting systems. Though influenza vaccines are the focus of both studies, the methods and infrastructure being developed will be applicable to other vaccines given to pregnant women.

Maternal immunization with Tdap vaccine has been the focus of other safety studies in 2014. Findings from a preliminary study, published in the May 7, 2014, issue of *Journal of the American Medical Association*, concluded that receiving the Tetanus Toxoid Reduced Diphtheria, Toxoid, and Acellular Pertussis Vaccine (Tdap) vaccine in the third trimester of pregnancy, between 30 and 32 weeks of gestation, did not increase the risk of severe adverse events for either the mother or infant.³⁴

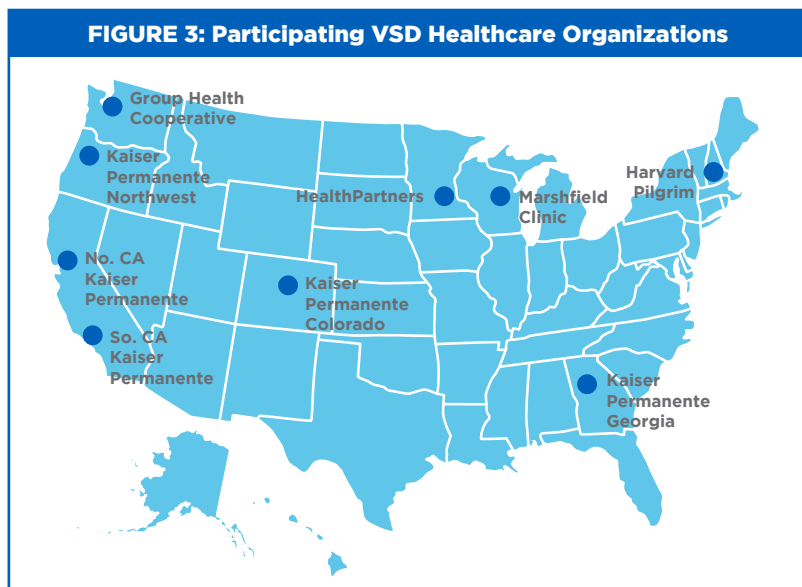
Sponsored by the CDC, the Clinical Immunization Safety Assessment (CISA) project, in collaboration with investigators of the aforementioned study, and funding from NVPO, began enrollment in the spring of 2014 for an observational study to further evaluate the safety of Tdap vaccine. Participants are pregnant women who are at 20 weeks or more of gestation and receiving Tdap as part of standard practice and non-pregnant women who are receiving initial Tdap. Injection-site (local) and systemic reaction data will be assessed on the vaccination day and during the 7 days post-vaccination using diaries.

Pregnant women in the study are monitored until delivery with comprehensive obstetric and neonatal outcomes obtained from review of the electronic medical record. Pregnancy outcomes among study participants will be compared with historical outcomes from summary data. In addition, follow-up will be conducted for infants born to mothers who received Tdap during pregnancy to assess health outcomes and growth parameters through 6 months of life.

³⁴ Munoz F, Bond N, Baker C, et al. Safety and immunogenicity of tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: a randomized clinical trial. *Jama* [serial online]. May 7, 2014;311(17):1760-1769 from: MEDLINE Complete, Ipswich, MA.

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CDC also supports the Vaccine Safety Datalink (VSD), a collaborative project between CDC's Immunization Safety Office and nine health care organizations, published over a dozen vaccine safety studies in 2014, many of which revolved around influenza vaccination during pregnancy. VSD studies are often based on questions or concerns raised from medical literature and reports to VAERS. VSD has established that vaccination of pregnant women has not been associated with adverse health events in the past, and work is ongoing to continue to monitor the safety of vaccines given to pregnant women. One current VSD study is evaluating two aspects of safety for Tdap vaccination in pregnant women: (1) the safety of Tdap in pregnant women exposed to tetanus-containing vaccines in the past and (2) the safety of Tdap in pregnant women co-administered with trivalent influenza vaccine (TIV), among pregnant women vaccinated during 2007-2012. Other studies are focusing on pregnant women receiving influenza vaccines.



These studies will help lay the groundwork for future vaccines to be recommended for pregnant women, such as vaccines for group B streptococcus and respiratory syncytial virus. Findings from this variety of safety studies will help researchers, practitioners and the public better understand the role maternal immunizations might play in protecting the vulnerable maternal and infant populations.

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Reviewing Safety Systems Data to Look at Influenza Vaccine and Narcolepsy

The vaccine safety system in the U.S. also stays in-sync with safety systems from other parts of the world, and the signals they are observing. For example, an increased risk of narcolepsy, a chronic neurological disorder caused by the brain's inability to normally regulate sleep-wake cycles, was found following vaccination with a monovalent 2009 H1N1 influenza vaccine that was used in several European countries during the H1N1 influenza pandemic. This risk was initially found in Finland, followed by additional European countries also detecting an association. Most recently, scientists at the United Kingdom's (U.K.) Health Protection Agency (HPA) have found evidence of an association between the vaccine (Pandemrix) and narcolepsy in children in England. The findings are consistent with studies from Finland and other countries.³⁵

³⁵ www.cdc.gov/vaccinesafety/Concerns/h1n1_narcolepsy_pandemrix.html

ADVANCING VACCINE SAFETY SYSTEMS

This particular vaccine was manufactured in Europe and specifically produced for pandemic 2009 H1N1 influenza. It was not used before 2009, and has not been used since the influenza pandemic season (2009-2010). It contains an oil-in-water emulsion adjuvant called ASO3. As mentioned under Goal 1 of this report, adjuvants are substances added to a vaccine to increase the body's immune response to that vaccine. Pandemrix was not licensed for use in the United States. In fact, no adjuvanted influenza vaccines were used in the United States during the H1N1 influenza pandemic or in any other influenza season. One licensed pandemic influenza vaccine, the H5N1 vaccine, contains an adjuvant called ASO3. This vaccine is included in the U.S. pandemic influenza vaccine stockpile, but it is not available to the general public.

In response to the events in Europe, the CDC evaluated data using U.S. vaccine safety monitoring systems. Data from the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD) were reviewed and no indication of any association between U.S.-licensed H1N1 or seasonal influenza vaccine and narcolepsy was found. In October of 2014, CDC published a study in *Neurology* on the association between 2009 H1N1 influenza vaccines, 2010/2011 seasonal influenza vaccines, and narcolepsy. The analysis included more than 650,000 people who received the pandemic flu vaccine in 2009 and over 870,000 people who received the seasonal flu vaccine in 2010/2011. The study found that vaccination was not associated with an increased risk for narcolepsy.³⁶

A three year international project assessing the risk of narcolepsy associated with ASO3- and MF59-adjuvanted H1N1 vaccines is also ongoing. CDC leads the study in collaboration with NVPO and BARDA, and in partnership with national, regional and local public health authorities and individual healthcare facilities. Funding this type of study is important, as findings may have an impact on US and international pandemic influenza programs, both in terms of product selection for stockpiles and for public confidence in vaccination programs and public health. Study results may be used to guide future work on adjuvanted pandemic influenza vaccination in selected age and risk groups.

³⁶ Duffy J, Weintraub E, Vellozzi C, DeStefano F. Narcolepsy and influenza A(H1N1) pandemic 2009 vaccination in the United States. *Neurology* [serial online]. November 11, 2014;83(20):1823-1830.

ADVANCING VACCINE SAFETY SYSTEMS**Piloting New Ways to Monitor Safety**

The VA developed a pilot surveillance program to monitor specific adverse events of interest for the influenza vaccine in 2010. The active surveillance program became fully operational during the 2012 influenza season, and now the program, VA MedSAFE, conducts a biweekly analysis to monitor specific AEFIs throughout the season. The VA also conducts an end-of-season analysis annually to further assess the AEFIs and evaluate potential signals. An active surveillance vaccine safety system began pilot testing for zoster vaccine in 2014, with pneumococcal and Tdap vaccines to be added in 2015.

Also specific to influenza vaccine event reporting, the VA's National Center for Health Promotion and Disease Prevention provides clinical guidance for providers on the reporting of adverse reactions to influenza vaccines in the VHA Seasonal Influenza Manual. They also advise on adverse reaction reporting for all vaccines via their Clinical Preventive Service Guidance Statements. These VA protocols for event reporting further illustrate the HHS commitment to uphold strict safety and reporting standards.

Additionally, CDC's CISA program, a national network of vaccine safety experts, recognized that text messaging offers a convenient and cost-efficient way to help monitor vaccine safety in pregnant women. CDC is now conducting a feasibility study to determine whether text messaging could be an effective adjunct to safety monitoring of inactivated influenza vaccine (IIV) in pregnant women. The study includes pregnant women at less than 20 weeks of gestation, who received an inactivated influenza vaccine (IIV). Study volunteers are periodically sent text messages throughout their pregnancy to track vaccination and experiences between and after. If results demonstrate value, then such a 'system' could be easily scalable to enhance future vaccine safety monitoring efforts in pregnant women and preparedness for an influenza pandemic or other public health emergency.

ADVANCING VACCINE SAFETY SYSTEMS**Assessing Causality for Adverse Events Following Immunization**

Project investigators from CISA completed a causality algorithm and published their findings in the August 24, 2014, issues of *Vaccine*. The algorithm was designed to assist health care professionals in evaluating individual patients who have developed an adverse event following immunization (AEFI).³⁷ The online tool was published for public use in 2014. Clinicians can also seek vaccine safety consultation from this group at no cost.³⁸

Investigating New Safety Signals

Vaccine safety monitoring systems are in place to detect early warning signals and generate hypotheses about possible new adverse events following immunization or changes in frequency of known events. Partners across the immunization system work to maintain and improve these systems.

For example, FDA conducted a large-scale assessment of febrile seizures involving multiple vaccines (trivalent influenza vaccines, 13-valent pneumococcal conjugate vaccine) in the PRISM system.³⁹ The febrile seizure safety study did not find evidence of a statistically significant elevated risk for febrile seizures in children 6-59 months of age following TIV, PCV13 or DTaP-containing vaccine during the 2010-2011 season.⁴⁰ Staff from FDA and CDC worked collaboratively to develop presentations with results for the FDA febrile seizure study and a similar CDC study for presentation at the Advisory Committee on Immunization Practices meeting in June 2014. The CDC study, which also examined rates of febrile seizure in infants 24-59 months of age, compared those who had received LAIV to those who received IIV, found no significant difference in fever rates on vaccination day or within two days post-vaccination with LAIV4 vs. IIV (IIV3 of IIV 4). There was also no significant difference detected in fever rates 3-10 days post-vaccination. The CDC febrile seizure study made use of text messaging as a surveillance mechanism for parents to report fever, post-vaccination.⁴¹

Also using the PRISM system, an increased risk of intussusception after vaccination with the second-generation rotavirus vaccines RotaTeq (RV5, a pentavalent vaccine) and Rotarix (RV1, a monovalent vaccine) was identified. This association was studied among infants in the United States 5.0 to 36.9 weeks of age and concluded that RV5 was associated with approximately 1.5 (95% CI, 0.2 to 3.2) excess cases of intussusception per 100,000 recipients of the first dose. The secondary analysis of RV1 suggested a potential risk, although the study of RV1 was underpowered. These risks must be considered in light of the demonstrated benefits of rotavirus vaccination.

³⁷ Halsey N, Edwards K, Vellozzi C, et al. Algorithm to assess causality after individual adverse events following immunizations. *Vaccine* [serial online]. August 24, 2012;30:5791-5798.

³⁸ www.cdc.gov/vaccinesafety/Activities/cisa/cisa_studies.html

³⁹ www.mini-sentinel.org/assessments/medical_events/details.aspx?ID=181

⁴⁰ Final Report on Febrile Seizures After 2010-2011 Trivalent Influenza Vaccines

www.mini-sentinel.org/work_products/PRISM/Mini-Sentinel_PRISM_Influenza-Vaccines-and-Febrile-Seizures-Report.pdf

⁴¹ Stockwell et al presentation from June 2014 ACIP meeting.

ADVANCING VACCINE SAFETY SYSTEMS**Using Safety Reports to Improve Healthcare Practices**

The January 31, 2014, issue of CDC's MMWR, "Rotavirus Vaccine Administration Errors" looked closely at reports submitted to the Vaccine Adverse Events Reporting System (VAERS) of administration of rotavirus vaccines by injection. An evaluation of VAERS found 39 reports of incorrect administration of rotavirus vaccines by injection and 27 reports of eye splashes between January 1, 2006 and August 1, 2013.⁴² The report served to remind vaccinators that rotavirus vaccines should not be injected into a child, and that proper administration instructions using the manufacturers' oral applicator devices (squirted gently and slowly into the child's cheek) should be followed.

Progressing Vaccine Safety Research

The safety and effectiveness of vaccines are under constant study. Safety testing, and the research studies documenting this work, often begins as soon as a new vaccine is contemplated, continues until it is evaluated by FDA to make an approved determination, and is monitored indefinitely after licensure. Research studies continue to find vaccines to be a safe and effective way to prevent serious disease. The sections below highlight some of the noteworthy vaccine safety research contributions made over the last year.

Studying Vaccine-Associated Fever and Febrile Seizure

CISA is also investigating the use of prophylactic antipyretics (using medicines that reduce fever), immediately after vaccination and within the following 24 hours post-vaccination, to assess the ability to reduce the rate of fever following vaccination. However, there is some evidence that taking medicines such as acetaminophen or ibuprofen to prevent fever after vaccination may blunt immune responses to some vaccines in some children. CISA is conducting a study to assess the effect of these medicines on the immune responses and rates of fever after inactivated influenza vaccine in healthy children 6 through 47 months of age, during the 2014-15 influenza season. Children in the study will be followed for the occurrence of fever, fussiness, changes in appetite and sleep patterns, and use of medical services on the day of and day following vaccination. Antibody to influenza antigens contained in the 2014-2015 vaccine will also be assessed at baseline and four weeks following vaccination. Information from this study will be used to better understand potential risks and benefits of using prophylactic antipyretics to prevent fever or febrile seizure after IIV and design future studies.

⁴² www.cdc.gov/mmwr/preview/mmwrhtml/mm6304a4.htm

ADVANCING VACCINE SAFETY SYSTEMS

Systematically Reviewing Vaccine Safety Studies

NVPO commissioned the Agency for Health Care Research and Quality (AHRQ) to conduct a comprehensive independent review of published literature on the safety of routine vaccines in the United States as an adjunct to IOM's Adverse Event Committee. The report, entitled: Safety of Vaccines Used for Routine Immunization in the United States, was used to inform the vaccine safety scientific agenda (above). Study results, which were featured in the July issue of *Pediatrics*, included key findings reaffirming that while serious adverse events can occur, they are rare.⁴³

Of the over twenty thousand studies first queried, 67 studies were deemed eligible for inclusion in the analysis. Results indicated that evidence was high for measles/mumps/rubella (MMR) vaccine and febrile seizures, and also detected an association between varicella vaccine and complications in immunodeficient individuals. There was strong evidence that MMR vaccine is not associated with autism, a matter of much public concern and media attention in recent years. Results also provided moderate evidence that rotavirus vaccines are associated with intussusception.

Findings also refuted common misconceptions about the role of vaccines in a number of unrelated human health issues. For example, pneumonia and influenza vaccines do not increase the risk of cardiovascular or cerebrovascular events in the elderly. In contrast, by preventing serious infectious diseases that can have cardiovascular sequelae in the elderly, these vaccines are associated with a decreased risk of cardiovascular and pulmonary events. The review also confirmed that there is no link between childhood leukemia and childhood immunizations⁴⁴ – two events that may occur in a similar time period.

SUMMARY OF REPORT FINDINGS: SAFETY OF VACCINES USED FOR ROUTINE IMMUNIZATION IN THE UNITED STATES

There are some minor to moderate risks associated with some childhood vaccinations, but overall the evidence shows that vaccines are very safe.

MMR (measles, mumps, and rubella) vaccine is not associated with autism in children.

Several common vaccines for children—MMR, DTaP (diphtheria, tetanus, and acellular pertussis), Td (tetanus-diphtheria), Hib (Haemophilus influenzae type b), and hepatitis B—are not associated with childhood leukemia.

There is moderate quality evidence that vaccines against rotavirus, which causes diarrhea and dehydration in children, can increase the risk of a serious type of intestinal blockage called intussusception, but this event occurs in only 1 to 5 of 100,000 vaccinations, depending on vaccine manufacturer.

The study also supports earlier findings that the MMR vaccine, pneumococcal vaccine, and influenza vaccine (particularly when given along with pneumococcal vaccine) are associated with febrile seizures in children; actual occurrence is very rare.

⁴³ Safety of Vaccines Used for Routine Immunization in the United States. July 2014. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/research/findings/evidence-based-reports/vaccinestp.html>

⁴⁴ Maglione M, Das L, Gidengil C, et al. Safety of Vaccines Used for Routine Immunization of U.S. Children: A Systematic Review. *Pediatrics* [serial online]. August 2014;134(2):325-337.

ADVANCING VACCINE SAFETY SYSTEMS

Standardizing Vaccine Safety Case Definitions

To advance the science of immunization safety and “vaccinovigilance,” the Brighton Collaboration, an independent research network, led the development of globally acceptable vocabulary to characterize Adverse Events Following Immunization (AEFI). Adoption and common use of these case definitions for AEFIs will allow researchers to truly compare variables when reviewing data from multiple studies.

The methodology employed to determine these case definitions represents a model of global vaccine stakeholder collaboration. Participants included 500 experts from 57 developed and developing countries, with relevant experience in patient care, public health, clinical trials, safety surveillance and safety assessment. Case definition development follows the “Brighton Method,” which is based on systematic review of current evidence, consensus formation, structured peer review and scientific publication.

The development of the full set of key terms and definitions is in development. As consensus of case definitions is reached, ongoing work includes publication of the July 2014 Meeting Report, inclusive of interim key terms and concept definitions for immediate use. The process will culminate with the publication of Brighton guidelines to be used while assessing the safety of vaccines administered during pregnancy.

Final, published case definitions are expected to be endorsed by the World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS). They will also be recommended for use by the FDA, European Medicines Agency (EMA), CDC and the European Centre for Disease Prevention and Control (ECDC).

GOAL 3: SUPPORT COMMUNICATIONS TO ENHANCE INFORMED VACCINE DECISION-MAKING

INTRODUCTION

Thoughtful communications about the safety, efficacy and ultimate importance of vaccines for individual and population health, as well as systems approaches, are imperative in helping people make informed decisions about immunization for themselves and their families. Thus, Goal 3 is oriented toward the development of vaccine communications rooted in evidence-based approaches and timely, relevant messaging.

Multi-channel communications efforts are critical in reaching the U.S. public and achieving immunization coverage targets. Immunization activity in 2014 that focused on developing communications strategies implementing communication interventions and tools is detailed in this section. NVPO works to support the multiple federal and partner agencies that foster collaboration and facilitate accurate, transparent and audience-appropriate communication strategies about vaccines and vaccination.



FOSTERING COLLABORATION TO COMBAT HPV INFECTION

Human Papillomavirus (HPV) is a common sexually transmitted virus that is often asymptomatic but, in some cases, can lead to serious health consequences, including cancer. Approximately 79 million people in the United States are infected with HPV. HPV vaccine was introduced in the U.S. in 2006 and is now recommended for all 11-12-year-old girls and boys, yet vaccination coverage among adolescents is lower than that of any other recommended vaccine in this age group. More concerning is that efforts to improve uptake have stalled.⁴⁵ The Healthy People 2020 goal is to reach 80% HPV-vaccination coverage by 2020—which is far higher than the 38% of girls and 14% of boys aged 13-17 years who completed the three-dose HPV vaccine series in 2013,⁴⁶ according to data from the National Immunization Survey of teenagers. Moreover, using a dynamic model, a paper published in 2014 illustrated that increasing HPV vaccination coverage of young girls to 80% would avert over 50,000 lifetime cervical cancer cases.⁴⁷

President’s Cancer Panel Efforts to Combat HPV

In 2012-2013, the President’s Cancer Panel (PCP) evaluated the situation in the U.S. and recommended acceleration of HPV vaccination in their report entitled, “Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer.” The report suggests a multipronged strategy to improve vaccine uptake in the United States and globally. By recognizing HPV vaccination as an urgent national and global health priority, the U.S. National Cancer Program in concert with the nation’s immunization program has an unprecedented opportunity to contribute to primary prevention of millions of cases of preventable cancer. The report of the PCP features a number of overarching goals, each with specific objectives and designated stakeholders, working to improve uptake of HPV vaccine. Goals and objective examples follow:

TABLE 6: President’s Cancer Panel: Accelerating HPV Vaccine Uptake (examples)	
Goals and Example Objectives	Responsible Stakeholder(s)
Goal 1: Reduce missed clinical opportunities to recommend and administer HPV vaccines	
Objective 1.2: Providers should strongly encourage HPV vaccination of age-eligible males and females whenever other vaccines are administered.	Healthcare providers Health professionals organizations
Goal 2: Increase parents’, caregivers’ and adolescents’ acceptance of HPV vaccines	
Objective 2.1: CDC should develop, test, and collaborate with partner organizations to deploy integrated, comprehensive communication strategies directed at parents and other caregivers, and also at adolescents.	CDC
Goal 3: Maximize access to HPV vaccination services	
Objective 3.1: Promote and facilitate HPV vaccination in venues outside the medical home.	State and local health departments State legislatures American Pharmacists Association
Goal 4: Promote global HPV vaccine uptake	
Objective 4.1: The United States should continue its collaboration with and support of GAVI to facilitate HPV vaccine introduction and uptake in low-income countries.	The President Congress HHS (CDC, NCI, USAID)

⁴⁵ U.S. Centers for Disease Control and Prevention. (2013). HPV vaccine: Safe, effective, and grossly underutilized. Retrieved from www.cdc.gov/media/releases/2013/p0725-HPV-vaccine.html

⁴⁶ www.cdc.gov/mmwr/preview/mmwrhtml/mm6329a3.htm

⁴⁷ Chesson, Harrell W., Ekwueme, Donatus U, Saraiya, Mona, Dunne, Eileen F., Markowitz, Lauri E. The Estimated Impact of Human Papillomavirus Vaccine Coverage on the Lifetime Cervical Cancer Burden Among Girls Currently Aged 12 Years and Younger in the United States. (2014). Sexually transmitted diseases (0148-5717), 41 (11), 656. PMID: 25299411 DOI: 10.1097/OLQ.0000000000000199

FOSTERING COLLABORATION TO COMBAT HPV INFECTION

The PCP report includes several recommendations aimed to support utilization of alternative vaccination sites, such as pharmacies, as a promising strategy to increase vaccination access and coverage rates (see objective 3.1 above). NVPO has contractually partnered with the American Pharmacists Association (APhA) to help implement some of these recommendations. In March of 2015, NVPO will be conducting a survey to determine the current state of pharmacist-provided immunizations.

Learnings will inform future direction of pharmacists' involvement in HPV immunization activities. This partnership with APhA is designed to help NVPO implement several of the recommendations of the PCP report by understanding the barriers to pharmacy-based HPV vaccination and identifying and disseminating best practices.

Recommendations from NVAC

Concurrent to the HPV work of the PCP, and to address the currently low HPV vaccination coverage rates, the Assistant Secretary for Health (ASH) charged the NVAC with reviewing the current state of HPV immunization, to understand the root cause(s) for suboptimal vaccine uptake (both initiation and series completion), and to identify existing best practices, all with a goal of providing recommendations on how to increase use of this vaccine in young adolescents. The NVAC HPV Working Group identified additional recommendations that complement those found in the PCP report. The recommendations, developed after hearing from several external experts in the field, will incorporate the most recent data on strategies to increase HPV vaccination coverage. The final NVAC HPV Working Group report will be voted on by the NVAC in June 2015, and is expected to be publicly released soon thereafter.

Funding Cancer Centers and Collaborating to Prevent HPV

The National Cancer Institute at the National Institutes of Health (NIH) supported collaborations between NIH-funded cancer centers and state and local HPV vaccination programs and coalitions over the past year. During that time, strategies for increasing vaccine uptake, especially within the context of primary care, were created. And, in the fall of 2014 NCI announced that nearly \$2.5 million will be granted to 18 U.S. cancer centers to boost HPV vaccinations among boys and girls.

The National Foundation for Infectious Diseases (NFID) and Council of State and Territorial Epidemiologists (CSTE) are also taking a stance to prevent cancer through HPV vaccination. In May 2014, NFID and CSTE convened a roundtable of subject matter experts, with representation from professional medical associations, consumer health organizations and government agencies, to discuss the long-term health impact of HPV and the important role of increased HPV immunization. During this roundtable, an expert panel released a Call to Action for Healthcare Professionals (HCPs) to rally their support and action in vaccinating their patients

FOSTERING COLLABORATION TO COMBAT HPV INFECTION

against HPV. CSTE also shared information on qualitative discussions they held with 19 state epidemiologists in eight states regarding approaches to HPV vaccination.

Main Points of the Call to Action for Healthcare Professionals

- Recommend HPV vaccine with the same strength and conviction used to recommend other adolescent vaccines.
- Educate themselves about HPV and HPV vaccines.
- Inform their colleagues and staff so that everyone in the practice is delivering the same HPV messages.
- Communicate vaccination benefits to parents and adolescents at every opportunity.
- Make vaccination procedures routine and focus on ways to reduce missed opportunities.

The American Cancer Society, through a cooperative agreement with CDC's National Center for Immunization and Respiratory Diseases (NCIRD) awarded on September 30, 2014, is also working on two initiatives to combat HPV infection. The first organized the HPV Roundtable, to bring together a vast group of experts and other stakeholders with a vested interest in the prevention of HPV, from researchers to manufacturers to advocacy groups to head and neck surgeons.

A second CDC-ACS cooperative agreement focuses on increasing HPV vaccination rates at safety net clinics across the nation through improved provider awareness, education and system-wide processes. Federally Qualified Health Centers and Community Health Centers will implement practice-change demonstration projects to determine which intervention models facilitate the greatest increase in vaccination rates. Additionally, ACS will partner with state health departments and other state-based entities to facilitate systems changes and increase the availability and utilization of HPV vaccine.

HPV Communications Campaign Work

One strategy for communicating with HCPS and the public about the importance of HPV vaccination materialized in the form of the CDC-funded "You are the Key to Cancer Prevention" campaign, which launched in early 2014. Utilizing the tagline:

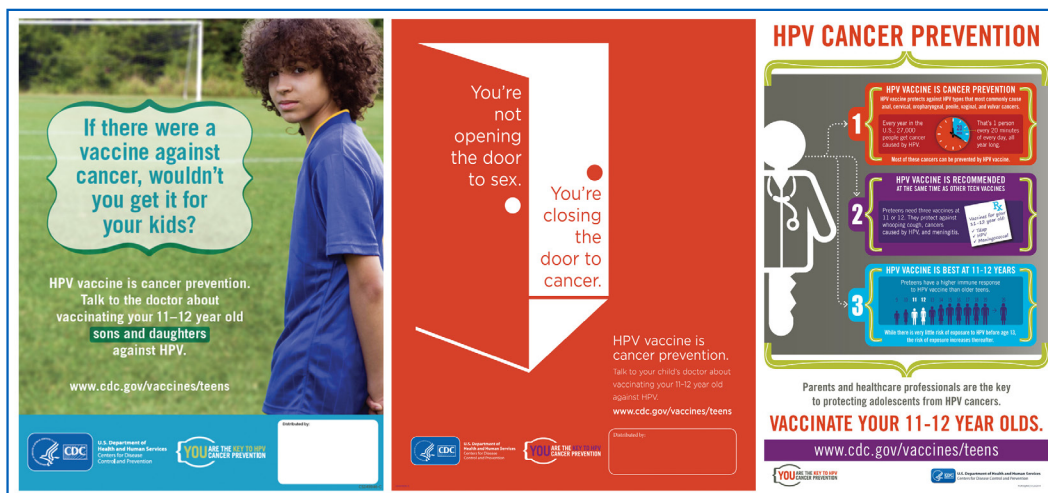
"You are the key to cancer prevention," this campaign targets health care providers, like pediatricians and adolescent health specialists, to underscore the importance of their role in HPV vaccination. The campaign emphasizes the ACIP recommendation for HPV vaccination: when girls and boys are 11-12 years old with "catch-up" doses for females up to age 26 and for males up to



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age 21 who were not vaccinated earlier in adolescence. Receiving the HPV vaccine at ages 11-12 offers earlier protection against infection, and immune response to the vaccine is often better in younger adolescents compared with older adolescents or young adults.

By targeting providers, the campaign attempts to prevent missed opportunities to vaccinate against HPV and provides messaging to strongly advise that the HPV vaccine be given at the same time as other recommended adolescent vaccines (Tdap, MCV13 and Influenza). The campaign provides videos, fact sheets, presentations on the burden of HPV infection, vaccine recommendations and talking points for providers, including advice on how to shift the HPV vaccine conversation from adolescent sexual activity to cancer prevention. The suite of campaign tools were designed to improve provider-parent and provider-patient communications surrounding HPV vaccine acceptance.



Beyond the campaign arm targeting providers, extensive formative research also indicated a need for a consumer-facing campaign to encourage HPV vaccination. This arm of the campaign targets parents through print ads, bus wraps, web banners and other media channels deemed popular with this audience. The public-facing campaign messages were designed to resonate with the parent as their child's ultimate protector and further drive the notion that they are not opening the door to sex, rather closing the door to cancer.

NVPO, in collaboration with Centers for Medicare and Medicaid Services (CMS), Office of Adolescent Health (OAH), and Office of Women's health (OWH), is working on the development of an HPV vaccination information hub on WebMD. The hub will be geared toward parents/guardians of adolescents and their vaccine needs and feature a variety of digital communications materials, like educational videos and articles about adolescent vaccines. Other communications pieces include: a quiz, an adolescent vaccine checklist, a branded page with widgets, fact sheets, and resource links. Content is scheduled to be live in the Spring of 2015.

FOSTERING COLLABORATION TO COMBAT HPV INFECTION

Addressing Issues of Vaccine Confidence

Achieving and maintaining high rates of immunity needed to sustain community-level protection against vaccine preventable disease, including HPV, requires high population confidence in vaccines and vaccinations. Vaccine confidence, as defined by the NVAC Vaccine Confidence Working Group (VCWG), refers to the trust that parents or health care providers have in:

- A. the recommended immunizations,
- B. the provider(s) who administers vaccines,
- C. the process that leads to vaccine licensure and the recommended vaccination schedule.

When confidence is high, people tend to support immunization recommendations and follow recommended schedules. When confidence is low or lacking, people may be more likely to hesitate, delay or forego recommended vaccinations. There is growing recognition for the need to better understand, monitor and measure vaccine confidence, its origins and its impact on immunization programs and on public health, as it appears to be a phenomenon in immunization programs in the U.S. and globally. For example, the WHO's Strategic Advisory Group of Experts (SAGE) on Immunization constituted a group on Vaccine Hesitancy which, in its report to SAGE, called for concerted action to stem hesitancy in certain parts of the world. Focused efforts of these expert working groups shows that vaccine confidence is an issue of many vaccine programs in many different locations, though may play out differently depending on the social/cultural context. Of note, the terms: "vaccine confidence" and "vaccine hesitancy" have been, at times, used interchangeably.

To better understand and address issues of vaccine confidence, the Assistant Secretary for Health (ASH) charged the National Vaccine Advisory Committee (NVAC) to report on how confidence in vaccines impacts the optimal use of recommended vaccines in the United States, including reaching HP2020 immunization coverage targets. This report, which was presented to the NVAC in 2015, recommends the need to identify and understand the determinants of vaccination acceptance among parents, underscoring what HHS and partners should be doing to improve parental confidence in vaccine recommendations and provides guidance on how to best measure confidence in vaccines and vaccination to inform and evaluate future interventions. The report includes recommendations from the NVAC VCWG on approaches for addressing vaccine confidence. These approaches include creating standardized definitions and measures for assessing vaccine confidence, improving provider education and patient counseling, and strengthening vaccine exemption policies. The final report, expected to officially release in the first half of 2015, will provide recommended strategies aimed at maintaining and improving immunization rates, especially among youth, to reach HP2020 goal levels.



COMMUNICATION SCIENCE APPROACHES TO IMPROVE DECISION-MAKING AND ACCEPTANCE

There are many ways of communicating the importance of vaccines to the public, but certain tactics have shown to be more effective with particular audiences. Selected examples of vaccine communication efforts are highlighted in the section below.

Infection: Don't Pass It On Campaign

Since 2005, the Veterans Health Administration (VHA) Public Health Strategic Healthcare Group (PHSHG) has led programs focused on improving veterans' health by promoting policies and practices for clinical public health issues. PHSHG is responsible for steering the VA-wide seasonal influenza vaccination campaign. PHSHG provides educational aspects of the seasonal flu program through the components of the Infection: Don't Pass It On (IDPIO) campaign. IDIO is an ongoing public health campaign targeting VA staff, veterans, their families and visitors to prevent the transmission of infection. Each year VA health care facility leadership work with designated flu teams to develop goals as a foundation for planning, executing, and evaluating the influenza vaccination campaign efforts. The goals of the influenza prevention campaign include measurable domains that reflect the nature, extent, and cultural specificity of the target populations.

SEASONAL INFLUENZA
Campaign Calendar

Use this as a planning guide for your seasonal influenza vaccination campaigns. It contains helpful activities within a timeline to assist you and your flu teams to plan, implement and evaluate your facility's campaign for vaccinating all health care personnel (HCP) and enrolled Veterans.

VA HEALTH CARE Defining **EXCELLENCE** in the 21st Century

- April: Evaluate & Review the Campaign (that just ended)
- May: Initiate the Planning Process
- June: Plan the Campaign
- July/Aug: Promote the Campaign
- September: Start the Campaign
- October/November: Conduct the Campaign
- December: Continue the Campaign
- January/February: Reinforce the Campaign
- March/April: Complete the Campaign

APRIL Evaluate & Review the Campaign (that just ended)

- Review current year vaccination rates among different services/departments and types of health care personnel and Veterans for opportunities to increase vaccination.
- Identify strengths and opportunities for improvement.
- Review various aspects of your flu vaccination program.

1

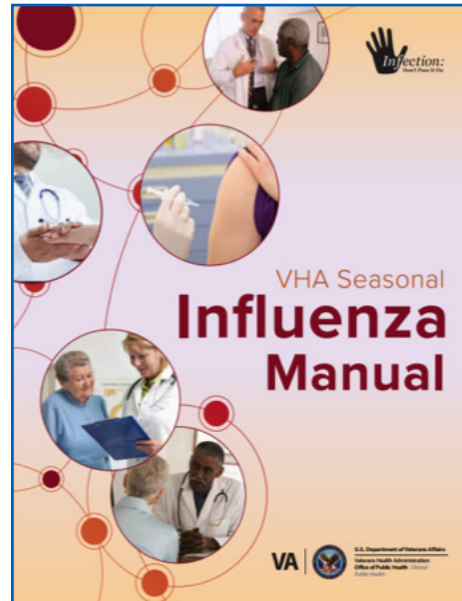
COMMUNICATION SCIENCE APPROACHES TO IMPROVE DECISION-MAKING AND ACCEPTANCE

The IDIO campaign develops and distributes education and communication resources for the VA community to promote:

- hand hygiene and respiratory etiquette
- annual seasonal influenza vaccination
- pandemic influenza preparedness and response
- correct and appropriate use of personal protective equipment
- basic public health measures to prevent transmission of infection

Embodying the above key messages, a variety of educational resources have been developed under the overarching Infection: Don't Pass It On campaign, such as posters, brochures, fact sheets, videos, a campaign calendar and timeline, and a seasonal flu manual. These materials are disseminated through mailings and [via download](#). During the season, staff in the field also receive updated influenza information through national phone conferences and a variety of written and electronic materials, including Flu Advisories, Flu Directives and Flu Tips.

The most recent *VHA Seasonal Influenza Manual*, now in the tenth edition, was released in July 2014 and was distributed to key VA contacts in early August. For the first time, the Manual was published with the intention of being used by VHA facilities for multiple years. Four influenza learning modules targeting different VHA audiences were also developed. The first, which was released in September, is titled *Clinical Perspectives on Influenza and Influenza Prevention* and, is intended for a clinical audience. The other modules include: *Perspectives on Influenza and Influenza Prevention*, meant for non-clinicians, *Influenza Campaign Planning, Executing, and Evaluating*, intended for use by flu coordinators and influenza teams, and *Hand Hygiene Monitoring and Evaluation*, meant for those in Infection Control.



GOALS OF THE VHA'S INFLUENZA PREVENTION CAMPAIGN

- Promote seasonal influenza vaccination to all Veteran patients. Note: This is based on the CDC recommendation of universal influenza vaccination of all people age 6 months and older.
- Reduce disparity of influenza vaccination rates by increasing the rate of vaccine among female patients and those patients under age 50.
- Promote consistent and proper documentation and tracking for all influenza vaccinations.
- Promote non-vaccine methods of preventing influenza, particularly hand hygiene and respiratory etiquette.
- Encourage the entire VA health care community to promote and support influenza

**COMMUNICATION SCIENCE APPROACHES TO
IMPROVE DECISION-MAKING AND ACCEPTANCE**

Each spring the VHA season influenza vaccine campaign's outputs are assessed and then used to inform the next year's campaign. As a part of PHS GH-led evaluation efforts, ten nationwide VHA site visits were conducted in 2014 to monitor and evaluate best practices in preventing the transmission of influenza infection. The VA reviewed health care provider influenza vaccination campaigns and hygiene monitoring and evaluation programs. They analyzed electronic health record data at the end of spring 2014 to find that approximately 2.69 million doses of influenza vaccine were ordered and approximately 1.94 million influenza vaccinations were administered during the 2013-2014 flu season. Figures from the 2013-2014 flu season illustrate that the VHA system is continuing to outperform national influenza vaccination averages. The 2013-2014 data showed that 76% of those ages 65 and older got vaccinated, and 59% of those 18-64 years of age got vaccinated.⁴⁸

The National Partnership Council (NPC), which promotes cooperative labor-management relationships in support of the VA's overall mission, began officially endorsing influenza vaccination in 2014 and released a promotional, VA-wide memo in July 2014. The memo captured NPC's position statement on influenza prevention by recognizing the importance of vaccination in protecting staff, patients and union members. The memo also underscored the role each VHA employee plays in promoting vaccination and disease mitigation strategies to strengthen a culture of safety and health within all VHA facilities. While vaccination is not currently mandated by VHA, community members who have no medical contraindications are encouraged to voluntarily get a free influenza vaccination at a VHA or external facility. For those getting vaccinated outside of a VHA location, they are asked to share that information with their designated employee health unit.

To help facilitate vaccine record keeping, information sharing, access and convenience, the VA Retail Immunization Care Coordination Program was created. This initiative partners pharmacy and retail clinics with the VA to expand access to flu shots for enrolled veteran patients. For example, a veteran can go to their local Walgreens pharmacy and get vaccinated without having to fill out cumbersome forms or carry around paper records. In a test program in Florida during the 2013-2014 influenza season, Walgreens successfully completed integration requirements for the Virtual Lifetime Electronic Record (VLER) to securely transfer health data, including flu shot status. VLERs are electronic health record programs that track the medical history of American soldiers through their entire service, from active duty to veteran status. As part of this secure health information sharing, immunization records are sent daily to the VHA and no user intervention is required. Over 1,800 veterans participated in this Florida Walgreens pilot.

⁴⁸ Knighton T. (September 12, 2014). Seasonal Influenza Program (presentation slides). U.S. Department of Veterans Affairs; Veterans Health Administration.

COMMUNICATION SCIENCE APPROACHES TO IMPROVE DECISION-MAKING AND ACCEPTANCE

Tools Encouraging Informed Decision-Making and Vaccine Uptake

While the ultimate goal is vaccine administration, communication tools driving socio-ecologic awareness of how vaccines protect the individual, their loved ones and even the broader community, help to drive uptake. This past year saw the introduction of new vaccine communication tools encouraging vaccination among different target populations, like long-term care (LTC) facility workers, veterans and women of reproductive age. Special populations may be more likely to change a health behavior or take action when messaging is tailored to, or addresses, their needs.

Influenza (Flu)

A Toolkit for Long-Term Care Employers

Increasing Influenza Vaccination among Healthcare Personnel in Long-term Care Settings

Recommend Tweet Share Language: English

Within this comprehensive toolkit are a number of resources intended to help long-term care facility, agency, or corporation owners and administrators provide access to influenza vaccination for their workforce and to help any employer of workers in long-term care understand the importance of influenza vaccination for their employees.

Antiviral Drug Shortage Call Center for Long-term Care Facilities

- In response to reports that long term care facilities are experiencing difficulty accessing antiviral supplies, CDC will coordinate with commercial partners to facilitate the rapid resolution of large orders of antiviral drugs for these institutional outbreak settings.
- Beginning on Monday, Jan. 12, the Division of Strategic National Stockpile (DSNS) is available from 7:00 a.m. to 7:00 p.m., EST Monday through Friday, to assist public health officials and health care facilities by coordinating with supply chain partners to rapidly redirect supply to the identified location.
- Contact DSNS at dsns-Request@cdc.gov for assistance with facility-specific unmet antiviral drug supply needs. For emergency needs overnight and on weekends, public health officials can contact the CDC Emergency Operations Center through established protocols.

The Why

Vaccinating Long-term Healthcare Personnel

Who is Considered Healthcare Personnel

The Importance of Influenza Vaccination

The Plan

Increasing Awareness, Emphasizing Prevention

Barriers and Strategies to Improving Influenza Vaccination among Healthcare Personnel

The Tools Available

Resources for Increasing Influenza Vaccination among Healthcare Personnel in Long-term Settings

Community Best Practices - Examples of Successful Influenza Vaccination

Flu, Prevention & Outbreak Response

Flu Basics

Prevention and Control of Seasonal Influenza with Vaccines

Influenza Toolkit for Long-Term Care Facility Staff

Health care personnel (HCP) work in environments where contact with patients, or infective material from patients, is routine. This puts HCP at risk for exposure to vaccine-preventable diseases and possible transmission to patients, their families, and other HCP.

COMMUNICATION SCIENCE APPROACHES TO IMPROVE DECISION-MAKING AND ACCEPTANCE

In a joint policy statement released in December of 2013, the Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS) called for universal immunization of health care personnel as recommended by CDC's Advisory Committee on Immunization Practices (ACIP). All paid and volunteer personnel working in health care settings should get vaccinated, unless there are medical contraindications.

The Healthy People 2020 goal is to achieve 90% influenza vaccination coverage annually among HCP in all health care settings. In recent years, there has been significant progress made toward this goal in all health care settings except long-term care environments. Vaccination of HCP in LTC settings is extremely important because people aged 65 years and older are at greater risk of serious complications from influenza. Influenza vaccine effectiveness is generally the lowest in the elderly, making vaccination of close contacts even more critical. According to CDC-analyzed results of an opt-in Internet panel survey of 1,882 HCP conducted in April 2014, 75.2% of HCP participants reported receiving an influenza vaccination during the 2013–2014 influenza season. Coverage was highest among HCP working in hospitals (89.6%) and lowest among HCP working in long-term care (LTC) settings (63.0%).⁴⁹

Studies have demonstrated the health benefits to patients when those caring for them have been vaccinated against seasonal flu. These benefits include the reduction of flu-related complications and reduction in the risk of death. NVPO, in partnership with CDC and support from the Office of Disease Prevention and Health Promotion (ODPHP), created a toolkit to specifically address the need for improved influenza vaccination rates among LTC. This web-based toolkit, [A Toolkit for Long-Term Care Employers: Increasing Influenza Vaccination Among Health Care Personnel in Long-term Care Settings](#), debuted during National Influenza Vaccination Week (NIVW) in December 2014, with the purpose of establishing and strengthening influenza immunization programs for HCP in long-term settings.

Toolkits for Routinizing Vaccination for Women

As a professional specialty organization and authority on women's health, the American Congress of Obstetricians and Gynecologists (ACOG) is dedicated to advancing women's health by building and sustaining the obstetric and gynecologic community. ACOG is also helping their members to improve communications about maternal and adolescent immunization. Recently, ACOG released three toolkits for Ob-Gyns to help routinize immunizations, especially maternal immunization during pregnancy, within their practices. The toolkits: [Influenza Immunization During Pregnancy](#), [Immunization Resources for Obstetrician-Gynecologists](#) and [Tdap Immunization](#) were disseminated to ACOG's 35,000 Fellows. With the promise of maternal immunization beginning to be understood, ACOG's stance on maternal immunization has the ability to frame vaccines as an important women's health issue.

⁴⁹ www.cdc.gov/mmwr/preview/mmwrhtml/mm6337a1.htm

OTHER SELECTED VACCINE COMMUNICATION EFFORTS

Further driving the momentum, ACOG launched a free immunization app for Apple and Android devices, providing immunization FAQs, alerts and resources. As of March of 2014, the app had over 14,500 downloads. Continuing to encourage vaccination to their patients, in August 2014 ACOG released an additional toolkit, called the Human Papillomavirus Vaccination toolkit. It includes a suite of materials, including the communication items developed as part of CDC's "You are the Key to Cancer Prevention" campaign, to help Ob-Gyns and their staff communicate with patients about the importance of getting vaccinated against HPV.

- In FY 2014-15, VA Preventive Medicine Services (10P4N) developed a section of their public website for Veterans Health Administration recommendations of specific vaccines. The information will include groups for whom each vaccine is recommended, and will also provide information about the benefits and potential harms of the vaccine.
- The Indian Health Service (IHS) partnered with CDC to develop influenza materials targeting American Indian and Alaska Native (AI/AN) communities. This included development and distribution of influenza posters tailored in design for AI/AN communities, the development of a radio PSA, and radio interviews on influenza to underscore the importance of influenza vaccination in AI/AN populations.
- In response to the increase in measles cases in 2014, CDC published a Morbidity and Mortality Weekly Report (MMWR) highlighting populations at risk for acquiring measles, and detailed MMR (Measles, Mumps, and Rubella) vaccine recommendations for routine use. CDC also released this information to the press, and held a media briefing to educate the public about the risk from measles and the recommended vaccinations to protect themselves.
- A 2014 NIH Health Information National Trends Survey Brief focused on awareness of the HPV vaccine to measure if it had increased from the previous year, when two-thirds of the general adult population had heard of HPV and the HPV vaccine. Prior to the vaccine's release, only one-third of women were familiar with HPV, and awareness among all adults was likely lower.
- In the Fall of 2014 CDC mobilized an Ebola Vaccine Team that collaborates with key partners in-country, including international organizations such as the World Health Organization, UNICEF, MSF (Doctors Without Borders), as well as each country's Ministry of Health, to address national, district- and community-level vaccine trial information and promotion needs. Health communication activities related to the vaccine clinical trials are in support of CDC's and others' efforts to assess the safety and effectiveness of candidate Ebola vaccines and reduce Ebola morbidity and mortality.

GOAL 4: ENSURE A STABLE SUPPLY OF, ACCESS TO, AND BETTER USE OF RECOMMENDED VACCINES IN THE UNITED STATES

INTRODUCTION

To maximize effectiveness and achieve positive public health outcomes, vaccines must first be available and accessible to the greatest number of people possible. Then assurances have to be in place to confirm that those vaccines will be used effectively to protect against vaccine-preventable diseases. As it stands, there are numerous barriers to success, including limited knowledge about recommended vaccines, lack of health care access and financial barriers.

HHS is working with numerous dedicated partners and public health allies to target these, and other, barriers. Effective and efficient vaccine delivery practices, reducing barriers to vaccine access, improving the exchange of data and utilization of immunization information systems, tracking vaccine supply, communicating the importance of vaccines to providers and the public, and monitoring vaccine coverage are all part of achieving Goal 4 of the National Vaccine Plan.



EXPANDING ACCESS TO VACCINES

Expanding vaccine access helps to lay the foundation for the U.S. to achieve national goals for immunization coverage, and people are more likely to get routinely recommended vaccines when they have easy access to those vaccines. HHS and its partners, dedicated to improving vaccine access across all socioeconomic strata, have continued to focus efforts on expanding the public's access to vaccinations. Information on the historic Affordable Care Act's impact on vaccine access, as well as efforts to enable health departments to bill for vaccine administration, is detailed below.

Affordable Care Act: Another Large Step in Improving Vaccine Access

Passage of the 2010 Affordable Care Act expanded access to health insurance for previously uninsured or underinsured Americans. The Affordable Care Act also expanded provision of clinical services, including vaccination. Beyond improving access to these services, the legislation gives states the authority to purchase adult vaccines with state funds from federally negotiated contracts and reauthorizes the Section 317 Immunization Grant Program. This program makes available federally purchased vaccines and grants to all 50 states, the District of Columbia, five large urban areas, and territories and protectorates to provide immunization services to priority populations. The Affordable Care Act also requires the General Accountability Office (GAO) to study and report to Congress about Medicare beneficiary access to recommended vaccines under the Medicare Part D benefit. This study was published in December 2011 and identified CMS administrative actions that were necessary to correct the limited access to vaccines.

The Affordable Care Act plays an important role in broadening the national vaccine infrastructure. While the Affordable Care Act eliminates some of the financial barriers to adult vaccination, some challenges remain. For example, Medicare patients may confront significant financial barriers when trying to receive a vaccine covered by Medicare Part D (e.g., herpes zoster). While most state Medicaid agencies cover at least some adult immunizations, not all may offer vaccines. Also, low-income individuals in states that do not elect to expand Medicaid to cover people with annual incomes of up to 138% of the federal poverty level may experience challenges.

EXPANDING ACCESS TO VACCINES

In 2014, NVPO, in collaboration with CMS, developed a CME/CE credit activity that summarized some of the changes to immunization coverage as a result of the Affordable Care Act. This e-learning module was made available through Medscape in September 2014. Highlights included:

TABLE 7: Examples of Immunization Coverage Changes Due to the Affordable Care Act	
Program	Impact Under the Affordable Care Act
Private Health Insurance	Under the Affordable Care Act, all non-grandfathered private health plans and healthcare Marketplace plans must provide coverage of routine immunizations recommended by the Advisory Committee on Immunization Practices (ACIP) and adopted by the CDC Director, without cost sharing.
Note: Grandfathered plans are those that were in existence on March 23, 2010 and haven't been changed in ways that substantially cut benefits, or increase costs for consumers.	
Medicaid	There is no cost sharing for adults to receive ACIP recommended vaccines through a Medicaid expansion plan. Vaccines are covered as an Essential Health Benefit (EHB) through "Preventive and Wellness Services and Chronic Disease Management.
Note: States continue to have the option to provide preventive benefits to adults enrolled in traditional Medicaid programs. However, these patients may have a co-pay depending on the state plan.	
Medicare	The Affordable Care Act did not make any changes to coverage of immunization under the Medicare program.
Note: Part B continues to provide coverage of influenza and pneumococcal vaccines, as well as Hepatitis b vaccine for people at increased risk and Tdap for wound management. These vaccines are all offered without cost sharing. Medicare Part D continues to provide coverage for other vaccinations necessary to prevent illness. Co-pays may vary by plan and patients receiving a vaccine under Part D should contact his or her plan to determine coverage.	
Vaccines for Children	The Affordable Care Act did not make any changes to the Vaccines for Children Program. The Affordable Care Act will enable better access to ACIP-recommended vaccines, but important challenges remain.

Expanding Vaccine Billing and Reimbursement Channels

In many cases, patients who receive free immunization services from health departments actually have health insurance that covers these services. The National Vaccine Advisory Committee (NVAC) recommended that states and localities develop mechanisms for billing insured patients served in the public sector and reinvest reimbursements in immunization programs.

The CDC-funded [Billables Project](#) launched in 2009 to address this need, to enable state and local health departments to bill insurance companies for immunization services provided to insured patients. Over the last 5 years, CDC has awarded \$27.5 million to 38 state and local health departments to support systems that bill and receive reimbursements for immunization services provided to insured patients, and to ensure that federally purchased vaccine is used for people who are uninsured or underinsured.⁵⁰

⁵⁰ www.cdc.gov/vaccines/programs/billables-project/index.html

EXPANDING ACCESS TO VACCINES

Each health department awardee develops a plan to implement billing processes through their immunization programs.

Goals for Health Departments

- Improve delivery of adult immunization services and increasing vaccination coverage in the community.
- Recover costs associated with community outreach programs, e.g., through non-traditional settings such as churches and senior centers, to deliver adult immunization and other preventive health services.
- Generate revenue to support adult and children immunization programs.
- Improve documentation of vaccines administered.

When health departments can be designated as “in-network providers,” they can bill health plans and other third payers for the immunization services they provide. In addition, health departments also establish and maintain immunization records in statewide immunization registries. Health department awardees can also access the Improving Reimbursement for Health Department Clinics Community of Practice (CoP), an online collaboration tool, to share expertise and experiences, success stories, tools, and ways of addressing barriers in planning and implementing billing projects.

In 2009, fewer than half of the 38 health departments participating in this project were billing Medicaid for immunization services. In 2014, 32 (84%) of these health departments bill and receive reimbursement from Medicare, Medicaid, and private health plans through a variety of methods.⁵¹ Money raised through these “alternative-provider” billing channels can be used to expand and improve state and local immunization services for both children and adults.

In the U.S., immunization coverage among children remains high, in part due to the success of the Vaccines for Children (VFC) program. Adolescent and adult vaccination coverage, however, remains low for most routinely recommended vaccines and well below Healthy People 2020 targets. Certain racial and ethnic disparities in relation to vaccination coverage also exist. Stakeholders across the national vaccine enterprise concur that there is a definite need for a plan to enable better uptake of recommended adult vaccines. The following two sections further explain work by HHS and partners to improve coverage among these populations.

Vaccinations are recommended across the lifespan, with specific vaccine recommendations for adults. Despite the availability of safe and effective vaccines, adult vaccination rates remain low in the United States, and racial and ethnic disparities exist. A strategic plan to improve adult immunization, coupled with updated adult

⁵¹ www.izsummitpartners.org/wp-content/uploads/2014/whatworks/Billables-Project.pdf

PRIORITIZING ADULT IMMUNIZATION

vaccination standards, highlights examples of work being done across the immunization system to improve rates of adult vaccination.

The National Adult Immunization Plan

In 2011 the NVAC recommended the development of a strategic adult immunization plan. Since then, much work has gone into the creation of a national plan for adult immunization and the National Vaccine Program Office plans to release the National Adult Immunization Plan (NAIP) in 2015. Developed with input from hundreds of stakeholders across every sector of the adult immunization landscape, the NAIP is a 5-year national plan channeling the collective efforts of all stakeholders (federal and nonfederal) and what can be achieved together.

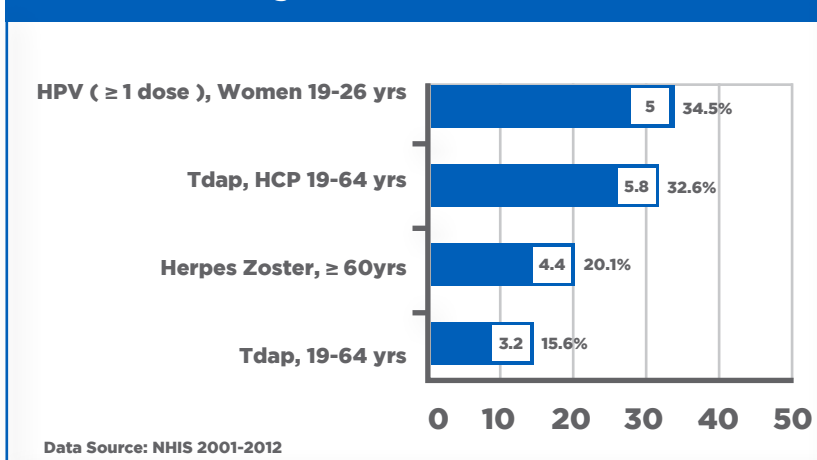
The ultimate vision of the NAIP is to protect public health and achieve optimal prevention of infectious diseases and their consequences through vaccination of all adults. The draft National Adult Immunization Plan was released for comment in February of 2015.

Adult Immunization Standards of Practice

In the March-April edition of Public Health Reports, the National Vaccine Advisory Committee released the new Adult Immunization Standards of Practice.⁵² The standards urge a wider range of immunizing and non-immunizing providers to proactively promote immunization to their patients, and emphasize that all health professionals play a role in vaccinating the public. This is increasingly important because patients receive vaccines in a variety of settings, such as pharmacies and workplace settings. The goal is to have all health care providers involved in the promotion of adult immunization.

The standards provide a protocol for assessing patients' vaccination status, strongly recommending needed immunizations, and either administering (including documenting), or referring patients to vaccinating providers. The standards aim to improve vaccination rates by guiding appropriate standards of practice across the healthcare system.

FIGURE 4: Non-Influenza Adult Vaccination Coverage with Increases 2011- 2012



⁵² www.publichealthreports.org/issueopen.cfm?articleID=3145



INTEGRATING IT SYSTEMS FOR IMPROVED INFORMATION SHARING

Maintaining and enhancing the capacity to monitor immunization coverage for both routine and non-routine vaccines requires complex data exchange across electronic data collection systems. Seamless integration of IIS and EHR systems is the ultimate goal, and HHS and its partners are helping to build systems and pilot programs to achieve this objective. Over the last year, partners across the national vaccine enterprise have made significant strides in improving the interoperability of vaccine data systems. The following section provides a snapshot of this progress.

Evaluating Immunization Information Systems

In an effort to improve immunization information sharing systems, CDC created an [Immunization Information Systems \(IIS\) Strategic Plan](#) to guide immunization investment decisions and strengthen the use of IIS and help CDC, awardees, providers, and stakeholders gain better insights into vaccine usage, coverage, trends, and needs nationwide.

To assist with prioritizing the strategic plan, NCIRD launched an intergovernmental IIS Executive Board of selected government-only stakeholders from state, local and federal levels, chosen to represent unique perspectives regarding the future of IIS.

The NCIRD IIS Strategic Plan currently presents short-, mid-, and long-term goals across five focus areas, with 11 underlying initiatives that have been prioritized within each focus area. The table below shows the current focus areas, long-term goals, and associated initiatives.

TABLE 8: NCIRD IIS Strategic Plan Highlights		
Focus Area	Long-term Goal	Associated IIS Strategic Initiatives
Nationwide Leadership	<ul style="list-style-type: none"> • There is a nationwide immunization and immunization information management program vision, strategy, policy and metrics. • There is an integrated immunization information management vision and strategy, standards, and policy with other public health disciplines (cancer registry, surveillance, etc.) 	<ul style="list-style-type: none"> • Planning for the Future State of IIS*
Sustainability	<ul style="list-style-type: none"> • Local, state and nationwide immunization information management programs have sufficient funding and resources such as informaticians, epidemiologists, economists, business analysts, contracts specialists, engineers, and information technologists. 	<ul style="list-style-type: none"> • Financial Sustainability and Cost Optimization* • IIS Workforce Development*
Service Delivery	<ul style="list-style-type: none"> • Immunization data sources, error checking and proposed revisions upon immunization event capture or transmission to IIS are clear and easy to understand for the user. 	<ul style="list-style-type: none"> • CDSi Adoption and Sustainability* • Immunization-centric EHR Certification*
Capacity & Infrastructure	<ul style="list-style-type: none"> • IIS produces timely and on-demand standardized immunization coverage analytics for all ages and publicly purchased vaccine management tools for the jurisdiction to support all immunization program functions and public health use. 	<ul style="list-style-type: none"> • Shared Services Access and Utilization* • Nationwide Adoption of IIS Interoperability Standards* • Data Analytics • IIS Certification*
Interoperability/ Data Management	<ul style="list-style-type: none"> • Data exchange among immunization information management systems is automatic and transparent regardless of location. 	<ul style="list-style-type: none"> • Nationwide Policy and Best Practice for IIS Interoperability* • Data Quality Services

INTEGRATING IT SYSTEMS FOR IMPROVED INFORMATION SHARING

In October 2014, CDC NCIRD convened an IIS Metrics Blue Ribbon Panel to work to determine what success means for IIS, and establish metrics and measures of success and critical paths for meeting IIS goals. Much of this work will focus on achieving higher levels of IIS performance and utility to meet widening uses of immunization information for a growing number of stakeholders. The initiative-specific metrics and measures developed by the IIS Executive Board, as well as work done internally at NCIRD, like the IIS Functional Standards 2013-2017, will be leveraged as input for the panel approach.

The desired outcomes and success metrics are meant to both communicate the intended impact of the IIS strategic plan, and to enable measurement of progress along the way. The Blue Ribbon Panel has developed six overarching desired outcomes in response to their charge:

Blue Ribbon Panel Desired Outcomes

- Greater IIS support for relevant immunization program functions at the awardee level.
- Greater reliance on IIS data to meet federal immunization information needs (e.g., coverage assessments, Vaccines for Children (VFC) accountability).
- Increased nationwide harmonization of policies for data capture and use/sharing/exchange.
- More direct consumer access to their consolidated immunization history.
- Reduced performance disparities across IIS programs (“raise the floor” or “no IIS left behind”).
- More consistent and higher performing IIS through a nationwide validation program.

The results from the panel will ultimately be used to guide success for the IIS Strategy Initiative, as well as IIS as a whole. The next immediate step in operationalizing the IIS Strategic Plan is to determine how success will be defined for the IIS program, as a whole, and a clear direction for targets. Future activities may also include developing both communications and operational plans to support implementation of the strategic plan, and fuller development of the Blue Ribbon Panel’s proposed outcomes and metrics.

INTEGRATING IT SYSTEMS FOR IMPROVED INFORMATION SHARING

Partner Efforts to Integrate Information Systems

The Office of the National Coordinator's (ONC) meaningful use programs require the use of "Certified Electronic Health Record Technology" as defined by ONC through its standards and certification criteria. EHR technology certified to perform public health reporting functions require adherence and testing to nationally recognized standards and associated implementation guides. Toward that end, the immunization community has made significant progress toward systems that reduce variability and improve the quality of the data collected. ONC co-leads a regular Public Health-EHR Vendors Collaboration Initiative meeting. This meeting provides a forum where vendors and public health agencies identify solutions to issues and barriers to interoperability between EHRs and IIS.

Health Information Exchanges (HIEs), another ONC-supported effort in 2014, provide valuable data exchange and infrastructure supports to public health agencies to promote more seamless information exchange. HIEs can pool together data from many sources, such as hospitals, providers, laboratories, and pharmacies, which contribute to public health data collection. A few state health departments are requiring providers to submit public health data, including immunization data, through the state HIE which then sends the data to the state IIS. This allows EHRs to create one connection point for data reporting on public health.

ONC, with support from NVPO, has also made major strides in operationalizing The Hub Model, as it has come to be known. In late 2013, IIS staff from Oregon and Washington joined with ONC to pilot test this new model for interstate exchange of IIS data. This model leverages a central data hub to route query and update messages between and among IIS that have policies supportive of interstate data exchange. Oregon and Washington have had an existing data exchange agreement in place since 2006. However, from both a policy and operational perspective, the interstate exchange was in need of significant modernization. Funding for the Hub project allowed both states to accomplish three tasks:

Data Hub Project's Main Tasks

- Update their IIS data exchange module to comply with Release 1.5 of the HL7 2.5.1 Implementation Guide
- Develop functionality to query another IIS
- Modify their web service engine to connect with the Hub

One of the additional innovative components of the Hub project is that ONC, at the request of both Oregon and Washington, contracted directly with the respective registry vendors of the two participating states. This direct funding allowed the states to draft requirements and review design documents, while avoiding the cumbersome state contracting process. As of December 2014, both Oregon and

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Washington had established connectivity with the Hub and were testing messaging and querying functions. Following completion of testing, the updated interstate connection will go live, and Oregon and Washington will be able to share immunization registry data in real-time as well as lessons learned from their pilot. Evaluation activities surrounding data transactions and matching will also commence once the Hub is live. At the end of 2014, ONC was recruiting additional states for the next phase of the project and is in the process of finalizing contracts with registry vendors to connect immunization record data for Maryland and the District of Columbia. Current funding for the Data Hub project has focused on states without cross-jurisdictional data transmission and access policy issues. The Association of State and Territorial Health Organizations (ASTHO) is leading efforts to develop a community of practice for cross-jurisdiction immunization data sharing for states with strict data sharing policies to widen the meaningful use of immunization registry information in the U.S.

The Veterans Administration (VA) developed the VA Retail Immunization Care Coordination program to improve access and provide integrated immunization records with retail providers. The program will be available nationally for the 2014-2015 flu season at over 7,500 Walgreens locations with support for influenza, pneumococcal and shingles immunizations. The VA is working to expand to additional retail providers and to fund influenza immunizations regardless of coverage from third-party insurance or programs such as Medicare.

The program, as mentioned in Goal 3, was piloted in the VISN 8 Network of Florida for the 2013-2014 flu season. Enrolled veterans who chose to get a flu shot from Florida Walgreens locations had access to over 800 locations with extended hours, and were no longer required to remember to provide their immunization history to their local VA health care provider or fill out additional VA forms. Enrolled veterans continued to have the option to receive no-cost flu shots at 80 VA medical centers and clinics throughout the region. The program also received Honorable Mention from the VA Community Engagement Competition in May 2014 as an innovative solution to improve access and promote healthy lifestyles.

INTEGRATING IT SYSTEMS FOR IMPROVED INFORMATION SHARING

The Health Resources and Services Administration's (HRSA) Bureau of Primary Healthcare recently announced Health Center PCMH and Quality Awards to recognize health centers that have invested in or focused on practice transformation and quality improvement. Consistent with the Health Center Program's Quality Strategy and priority goals, BPHC intends to award supplemental funds to health centers that have been recognized as PCMHs and have improved performance on UDS clinical measures. Awards will be based on 2013 UDS data:

Quality Award Criteria

- EHR Reporters – health centers that report clinical measures on the full universe of patients using EHR as opposed to a sample of patient charts;
- Top Improvers – health centers that have demonstrated improvements in clinical measures;
- High Performers – health centers that have the highest performance compared to their health center peers using risk-adjusted quartile rankings; and
- Clinical Excellence – health centers that are the highest performers compared to national standards and benchmarks in key clinical areas.

In 2014, Indian Health Service (IHS) conducted a pilot project in one IHS region to develop a composite immunization measure to monitor adult vaccine coverage. This measure was then expanded nationally and included as a developmental performance measure for 2014. This is a first step in potentially including this as a required performance measure for IHS.

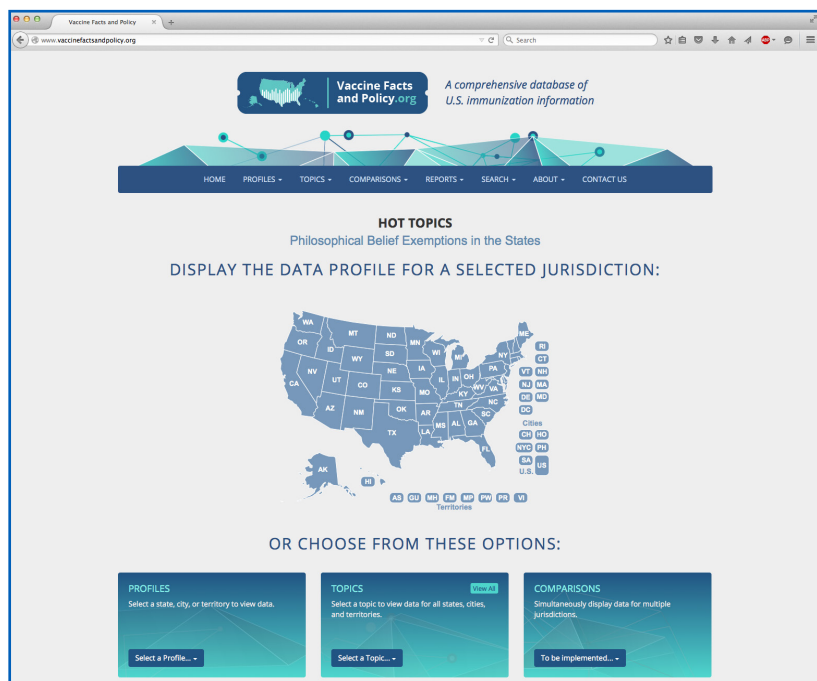
IHS also remains committed to health care reform and implementing provisions mandated by the Affordable Care Act requiring private insurers to cover all ACIP recommended vaccines at no cost. In 2014 IHS made provider reminders for all ACIP age-based vaccine recommendations mandatory. This includes reminders for HPV vaccine in adult females and males, and shingles vaccine for those 60 years and older. Initial work was completed toward the development of vaccine algorithms for patients with diabetes, chronic liver disease, immune suppression, and STI diagnoses. Work will continue in 2015 to develop immunization clinical decision support for vaccines recommended for these high-risk groups.

INTEGRATING IT SYSTEMS FOR IMPROVED INFORMATION SHARING

New Resource Looks at Immunization Infrastructure Data

In November 2014, the Association of Immunization Managers, in partnership with George Washington University and the Immunization Action Coalition, announced the launch of a new, interactive website. [Vaccine Facts and Policy website](http://www.vaccinefactsandpolicy.org) displays immunization infrastructure, environment and policy information for 64 states, cities and territories across the nation. The website, a major component of the Vaccine Facts and Policy (VFAP) project, seeks to provide relevant and accessible data in one place for immunization programs and stakeholders.

The site's comprehensive database includes a wealth of vaccine information. U.S. national, state, territory, and city immunization data and survey results from the Association of Immunization Managers are some of the featured available data. Site visitors can review immunization data at the program level, review aggregate survey responses by state, city and territory, identify immunization program components and activities, view data as a table or map format and save and print reports.



The data used in the project are primarily collected from national level sources including surveys and reports that have been completed by the nation's 64 immunization programs. All data are identified and linked to their original source. Website data currently comes from 14 sources, including the CDC Immunization Information Systems (IIS) Annual Report, AIM Partner data (e.g., AIRA, ASTHO), the National Immunization Survey, the National Health Interview Survey and the U.S. Census. "Having state level vaccine facts and policies consolidated in one easy-to-search location is a valuable tool for state immunization program managers who are looking at updating their own immunization policies. It is also a valuable tool for legislators and others interested in immunization laws, regulations and policies," commented Pejman Talebian, Chairman of AIM. The wide array of data available through the online database allows stakeholders to see a more complete view of the U.S. immunization landscape and infrastructure.

OTHER SELECTED ADVANCES IN VACCINE SUPPLY, ACCESS AND USE

- In 2013, NVPO, in partnership with the Center for Medicare and Medicaid Services (CMS), created an interactive map for researchers, providers, and health care workers to track influenza vaccination claims' rates of Medicare Fee-for-Service beneficiaries in real-time. The Interactive Mapping Tool provides information for every state, county and zip code in the United States, allowing users to search by demographic, age group and flu season. In 2014, the mapping tool was updated to include data for a time trend map permitting researchers, providers and health care workers to view flu vaccination claims' rates by week and compare those rates between locations, populations and flu seasons.
- CDC has been monitoring vaccine usage trends quarterly in order to refine targets for pediatric vaccine stockpiles. Incremental pediatric vaccine stockpile purchases and adjustments are made annually. CDC is continuing efforts to reach the goal of completing the stockpile for existing vaccines by the end of 2016.
- In 2014, FDA licensed a manufacturing facility which can produce cell-culture influenza vaccines. This is the first U.S. facility of its kind and is now approved for commercial production. The site, located in North Carolina, is slated to produce seasonal and pre-pandemic influenza vaccines, and will have the capacity to significantly ramp up production in the event of a pandemic.
- In 2014, HRSA's Countermeasures Injury Compensation Program (CICP) published in the Federal Register a Notice of Proposed Rulemaking (NPRM) to establish a Pandemic Influenza Countermeasures Injury Table. In 2015, the Program plans to publish a Final Rule in the Federal Register to make the Table proposed in the NPRM effective. The Table provides those making a request the presumption that their alleged injury was caused by a medical countermeasure if it meets the Table requirements and no other cause for the injury is found. This will likely increase the number of claims filed, because requesters who previously filed claims or allege to have injuries in the past will be given one year from the effective date of the Table to file claims for injuries on it.
- CDC's Influenza program continues to regularly update and add to vaccine-focused materials for clinicians on the CDC web site in 2014. CDC hosted or co-hosted at least ten influenza-vaccine-related webinars for clinicians through CDC's Clinician Outreach and Communication Activity (COCA); produced/co-produced numerous vaccine-related videos and web articles for clinicians through Medscape; developed an App for clinicians to download to their mobile devices that gives convenient access to ACIP recommendations and a decision-making algorithm; and answered clinician inquiries regarding influenza vaccination recommendations via the CDC-INFO inquiry system.

GOAL 5: INCREASE GLOBAL PREVENTION OF DEATH AND DISEASE THROUGH SAFE AND EFFECTIVE VACCINATION

INTRODUCTION

From the Internet in the palm of our hands to the ease of air travel, the world is more connected than ever before. With more channels for contact come more opportunities for the spread of infection and onset of disease. Globally, infectious diseases are the leading cause of death among children and contribute substantially to disease and disability affecting people of all ages.

Dedicated to protecting public health, HHS and partners recognize that the health of our nation is linked with the health of the global population. This dedication to global health is reflected in the objectives of Goal 5 of the National Vaccine Plan. Additionally, the National Vaccine Advisory Committee's recent global report and recommendations on global immunization will inform how HHS can best continue to contribute to global immunization efforts.



REDUCING THE GLOBAL IMPACT OF DISEASE

Immunization programs over the last few decades have been remarkably successful in preventing millions of childhood deaths, eradicating smallpox and eliminating the circulation of polio and measles from many countries around the world. In an era where new infectious diseases are being discovered and others are re-emerging, global vaccination programs are of critical importance. The information below provides a summary of U.S. efforts supporting a healthier world through immunization and disease prevention.

Supporting the Vaccine Alliance

In 2014, the U.S. Government expanded its strong commitment to fighting vaccine-preventable diseases, including through its longstanding and effective partnership with [Gavi, the Vaccine Alliance](#). Gavi's mission is to save children's lives and protect people's health by increasing access to immunization in poor countries, in which more than 85% of the world's unvaccinated children live.

In President Obama's 2013 State of the Union address he reaffirmed that ending preventable childhood deaths globally is a priority for the United States. In the time since, there has been record U.S. support for childhood immunization programs through Gavi. This was spotlighted in USAID's June 2014 [Acting on the Call plan](#), announcing the U.S. commitment to save the lives of 15 million children in developing countries; including through the use of high-impact interventions, such as vaccines.

As one of Gavi's six founding donors, the U.S. has galvanized global support for immunization, helping Gavi immunize nearly a half-billion children from 2000-2014 and preventing 6 million deaths. In 2011, at Gavi's inaugural Replenishment Conference, the U.S. made a 3-year, \$450 million funding pledge to Gavi, and committed \$513 million over the next three fiscal years, including \$200 million in the 2015 fiscal year budget. This brought USAID's total contribution, since Gavi's founding in 2000, to approximately \$1.4 billion. In total, donors will have committed \$8.4 billion toward Gavi's vaccine programs in developing countries from 2000-2017.⁵³

On January 27, 2015, at [Gavi's 2015 Replenishment Conference](#), hosted by the German government in Berlin, world leaders showed commitment and dedication to saving the lives of children in the poorest countries through immunization programs. The new pledges toward Gavi's 2016-2020 program cycle totaled \$7.5 billion. These funds will enable countries to immunize an additional 300 million children, averting 5 to 6 million deaths and yielding economic benefits of between \$80 and \$100 billion for developing countries through productivity gains and savings in treatment, transportation costs and caretaker wages.⁵⁴

⁵³ www.gavi.org/library/news/press-releases/2015/record-breaking-commitment-to-protect-poorest-children-with-vaccines/

⁵⁴ J. J. Stern (personal communication- review of USG and Gavi work 2014). January 12, 2015.

REDUCING THE GLOBAL IMPACT OF DISEASE

U.S. funding to Gavi supports vaccine purchases for the world's 73 poorest countries, including the 24 countries prioritized by USAID for ending preventable maternal and child deaths. Gavi provides support for several new and underused vaccines that are saving millions of lives. This includes vaccines against diseases considered to be some of the most fatal to children under age 5: pneumococcal disease and rotavirus. These vaccines are being introduced in an increasing number of developing countries. As of December 2014, Gavi had already reached 20 million children in USAID's priority countries with pneumococcal vaccine.

Gavi also supports immunization campaigns against diseases such as meningitis A, maternal and neonatal tetanus, and yellow fever. Its effort to make the benefits of vaccines in poor countries permanent for the next generation is part of an unprecedented acceleration of its programs, from 55 vaccine rollouts in 2011-2012 to more than 150 in 2014-2015. This is expected to expand further in Gavi's next program cycle, 2016-2020, which is focused on ensuring that the benefits of vaccines reach every child, even in the most remote areas – increasing to 50% from 5% the number of children who receive all 11 WHO-recommended vaccines. This is in line with the U.S.'s stated commitment to maternal and child health.

Gavi is also aiding countries in strengthening routine immunization programs by introducing at least one dose of inactivated polio vaccine (IPV) as a lead-up to the phased removal of oral polio vaccines (OPV). While OPV has successfully reduced polio cases by 99% worldwide, adding IPV to routine programs will improve immunity and help prevent new vaccine-associated outbreaks from emerging. In November 2013, Gavi's Board of Directors agreed to offer IPV for routine use and began providing it in 2014, with Nepal, another USAID priority country, the first to use Gavi support to introduce the vaccine.

In response to the ongoing Ebola epidemic in West Africa, Gavi plans to purchase millions of doses of an Ebola vaccine to support large-scale vaccination efforts. This commitment was announced in December of 2014, and indicates that the Alliance will be ready to act as soon as a safe, effective vaccine is recommended for use by the World Health Organization. Gavi's Board endorsed plans that could see up to \$300 million committed to procure the vaccines, to be used to immunize at-risk populations in affected countries. Up to an additional \$90 million could be used to support countries in introducing the vaccines and to rebuild devastated health systems and restore immunization services for all vaccines in Ebola-affected countries.

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Polio Eradication Efforts

As mentioned in the section above, polio incidence has dropped dramatically since the launch of global polio eradication efforts in 1988. This has been a major global health achievement that requires continued work and resources. [Polio Eradication Endgame Strategic Plan 2013-2018](#), a comprehensive, long-term strategy, addresses what is needed to deliver a polio-free world by 2018. The plan calls on countries to strengthen routine immunization programs and introduce at least one dose of IPV as a lead-up to the phased removal of OPV. While the oral polio vaccine has successfully reduced polio cases by 99% worldwide, adding IPV to routine programs will improve immunity and help prevent new vaccine-associated outbreaks from emerging.

The [Global Polio Eradication Initiative \(GPEI\)](#), in response to a directive from the World Health Assembly, required consultation with national health authorities, global health initiatives, scientific experts, donors and other stakeholders, to address the eradication of all polio disease, whether caused by wild poliovirus or circulating vaccine-derived poliovirus.

On March 27, 2014, the South East Asia Region was certified polio-free following India's achievement of remaining free of circulating endemic wild poliovirus for three consecutive years.⁵⁵ Of note, India was once considered the most complex challenge to achieving eradication, in large part due to low vaccine efficacy (VE) of trivalent oral polio vaccine (tOPV) against wild poliovirus types (WPV) 1 and 3 and



⁵⁵ Centers for Disease Control and Prevention (CDC). Polio-Free Certification and Lessons Learned — South-East Asia Region, March 2014. *MMWR Morb Mortal Wkly Rep.* October 24, 2014 / 63(42):941-946. www.cdc.gov/mmwr/preview/mmwrhtml/mm6342a2.htm

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high disease transmission rates in certain Indian states (Uttar Pradesh and Bihar) with dense infant populations. Now, four of the six regions of the World Health Organization have been certified polio-free: the Americas (1994), Western Pacific (2000), Europe (2002) and South East Asia (2014).⁵⁶

While no polio cases have been detected in India for more than three years, polio-virus transmission is ongoing in the three endemic countries: Afghanistan, Nigeria, and Pakistan. The GPEI's Independent Monitoring Board considers Nigeria and Pakistan to be the greatest challenges for eradicating polio. On May 5, 2014, after receiving advice from an Emergency Committee of independent experts and in order to protect progress toward eradication, WHO's Director-General declared the recent international spread of wild poliovirus a "public health emergency of international concern," and issued temporary recommendations under the International Health Regulations (2005) to prevent further spread of the disease.

Progress in Dengue Vaccine Development

Dengue infection is a threat to nearly half the world's population and is a pressing public health priority in many countries in Asia and Latin America, where epidemics occur. As many as 400 million people are infected with dengue each year, as a result of one of four related viruses transmitted by mosquitoes.⁵⁷ Although dengue rarely occurs in the continental United States, it is endemic in Puerto Rico and in many popular tourist destinations in Latin America, Southeast Asia and the Pacific islands. Currently, no dengue cure or treatment exists. As dengue cases rise, so does the urgent need for a preventive intervention, such as a dengue vaccine. A safe, effective and affordable dengue vaccine would represent a major advance for the prevention of this disease and alleviate its burden on low and middle-income countries where the disease tends to occur.

Results from the first of two Phase 3 clinical trials for Sanofi's dengue vaccine candidate were published in the *Lancet* on July 10, 2014. The study is a randomized, observer-blind, placebo-controlled multicenter trial involving 10,275 children aged 2 to 14 years in Indonesia, Malaysia, the Philippines, Thailand and Vietnam.⁵⁸

Data from this trial showed moderate efficacy (57%) against any confirmed dengue infection and moderate to good efficacy against particular serotypes (1 (50%), 3 (78%) and 4 (75%). Vaccine efficacy was statistically significant for all serotypes except serotype 2 (35%). The reason behind variable vaccine efficacy is still unknown, thus inviting further in-depth examination and analysis. The vaccine efficacy against dengue hemorrhagic fever was higher than 80% and the efficacy against hospitalized dengue was 67% in the 2-14 year olds studied in the five countries in Asia. These are both encouraging results.

⁵⁶ www.cdc.gov/polio/updates/

⁵⁷ www.who.int/mediacentre/factsheets/fs117/en

⁵⁸ Capeding M, Tran N, Bouckennooghe A, et al. Articles: Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial. *The Lancet*. October 11, 2014;384:1358-1365.



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This trial further established the safety of the vaccine in the first 12 months following the primary vaccine series, as results showed no signals of an increase in serious adverse events in the trial during the two years following the administration of vaccine. Study findings will help to shape further research in dengue vaccine development, and a fuller assessment of the efficacy of the vaccine will help to better understand the performance of this dengue vaccine candidate.

Additionally, the results of a dengue vaccine efficacy trial in Latin America were presented at the American Society of Tropical Medicine and Hygiene meeting in November 2014 and are expected to be published in early 2015. This Latin American study will help complement data from the Asian studies and provide a wider lens of analysis for a global vaccine.

In the meantime, other vaccine candidates continue to advance through the pipeline. A dengue vaccine developed by Takeda with early support from NIH/NIAID, and another developed by NIH/NIAID and the Butantan Institute in Brazil, are currently undergoing Phase 2 trials. The NIH/NIAID vaccine has been licensed to Panacea Biotec (India), Vabiotech (Vietnam), and Merck (USA). Recent studies concluded that TV005 is both safe and effective following a single subcutaneous injection, resulting in unprecedented levels of protection among vaccinated individuals. NIH/NIAID investigators will confirm these findings and participate in testing vaccine efficacy in regions where dengue virus transmission is endemic.

Preventing Influenza in Lower-Income Countries

Decades of experience show that influenza vaccine is the most cost-effective way to help prevent flu-related illness, hospitalization and death, missed school, and missed work. Despite the benefits of flu vaccination, establishing an effective vaccination program remains challenging for many lower-income countries. Partnership for Influenza Vaccine Introduction (PIVI) was established to work with low and lower-middle income countries to develop sustainable influenza vaccine programs to reduce the global burden of influenza. PIVI is a collaborative effort led by CDC in partnership with ministries of health (MoH), The Task Force for Global Health, the private sector, academic and NGO partners. These partners work together to procure and distribute influenza vaccine and evaluate the impact of vaccination in recipient countries.

Building on two successful years of a pilot Vaccine Donation Project, in 2014, PIVI expanded to include new donors to support influenza vaccination programs in additional eligible countries through in-kind and other funding. Contributions from donor partners catalyze a target country's ability to reduce the impact of influenza on the most vulnerable members of their population. Development of country influenza program sustainability plans, achievement of objective milestones and program evaluation are the benchmarks of PIVI success. PIVI's 2014 donors include returning partner bioCS who donated more than 750,000 doses of vaccine,

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Walgreens Company, and Amerisource Bergen, which together donated influenza vaccine and funds to purchase vaccine at reduced cost through the Pan-American Health Organization (PAHO) Revolving Fund. In addition, returning partner Becton Dickinson and Company (BD) donated ancillary supplies including sharps containers. PIVI's mission is also supported by a grant from the Bill & Melinda Gates Foundation awarded in 2013.

Laos and Nicaragua are two countries benefiting from PIVI oversight in the development and expansion of influenza vaccination programs. Laos is vaccinating against seasonal influenza for the third year running, and Nicaragua is vaccinating pregnant women against influenza for the second year in a row. This is made possible through guidance from the CDC and PIVI donations. Marked with an official launch in Luang Prabang, Laos, on April 30, 2014, the Laos Ministry of Health's National Immunization Program began administering influenza vaccine to pregnant women, health care workers, essential government employees, and people 50 years of age and older. The vaccines are distributed throughout the country in all 17 provinces and primarily through provincial and district hospitals. In Nicaragua, the donated influenza vaccine is supplementing other vaccine purchased by the Government of Nicaragua. Influenza vaccine is being distributed via Nicaragua's already-established network of influenza vaccination sites. PIVI plays a pivotal role by supplying donated influenza vaccine and supplies to countries that lack those resources but that are otherwise ready to establish or expand their influenza vaccination programs. Country-led program evaluation and sustainability planning are key components of the partnership's mission. PIVI's long term vision is for everyone around the world, and especially high-risk persons, to have equitable access to seasonal influenza vaccine. Collaborating with PIVI allows eligible countries to learn how to manage a seasonal influenza vaccination program, build their evidence base and attract additional resources. Ultimately, the sustainability plan for each program will vary from country to country, ranging from country-owned manufacturing capacity to negotiation of pricing between vaccine manufacturer and country.



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PIVI's mission is also bolstered by the different but complementary work of other key organizations, including the WHO Global Action Plan for Influenza Vaccines-II, the United States' pandemic influenza vaccine development program managed by HHS' Biomedical Advanced Research and Development Authority (BARDA), and the Global Alliance for Vaccines and Immunization (GAVI).

Enhance Sustainable Influenza Vaccine Production Capacity in Under-Resourced Countries

Objectives

- Protect people by reducing the global risk of influenza
- Develop and sustain influenza vaccine manufacturing capabilities and capacity for pandemic readiness
- Promote international investment, diplomacy and partnerships
- Achieve sustainable influenza vaccine production capacity worldwide by leveraging BARDA's unique resources

Approach

- Expanding global vaccine manufacturing capacity through technical support of manufacturers in developing countries
- Ensuring a skilled workforce that knows how to make good manufacturing practices (GMP) quality vaccine through training
- Providing in-country technical implementation assistance
- Making available technology for scalable manufacturing capacity

BARDA takes a multifaceted approach to building sustainable capacity for pandemic influenza vaccine production. The World Health Organization (WHO), Infectious Disease Research Institute (IDRI), the Biomanufacturing Training and Education Center (BTEC) at North Carolina State University and PATH all play critical roles in the BARDA- funded efforts to build and sustain global influenza vaccine capacity.

Building Global Influenza Vaccine Capacity

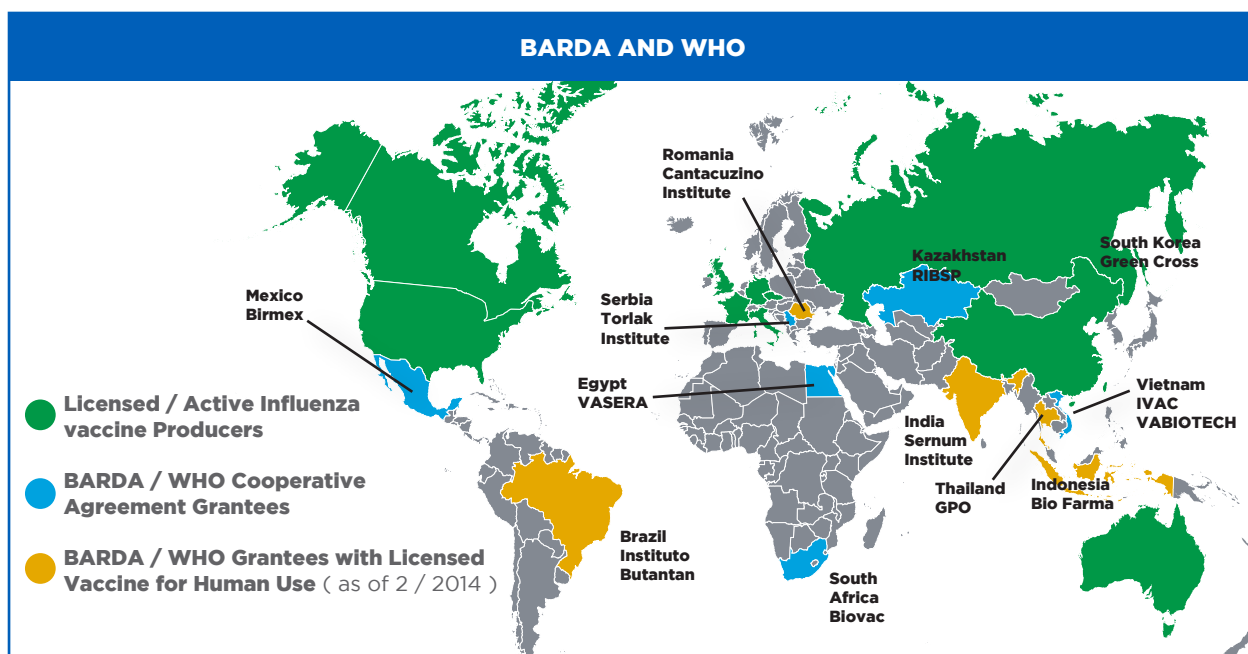
The Biomedical Advanced Research and Development Authority (BARDA) within HHS' Office of the Assistant Secretary for Preparedness and Response (ASPR) supports the development and availability of medical countermeasures (MCM) for chemical, biological, radioactive and nuclear (CBRN) threats, pandemic influenza, and emerging infectious diseases through advanced product development, stockpile acquisition/building, manufacturing infrastructure building, and product innovation.

The primary goal of BARDA's International Program Strategy is to enhance sustainable influenza vaccine production capacity in developing and under-resourced countries. This goal is driven by a variety of objectives, such as protecting people

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by reducing the global risk of influenza, which can be achieved through specific approaches, such as expanding global vaccine manufacturing capacity through technical support of manufacturers in developing countries.

This map displays the geographical distribution of influenza vaccine production. Licensed and active influenza vaccine providers are located in North America, Eastern Europe, Asia and Australia. If a pandemic threat arises, it is important to be able to reduce the production pressure on those facilities that produce vaccines for the entire world. Therefore, BARDA and WHO let several cooperative agreements and grant funding opportunities to support the capacity building of manufacturing sites in Central and South America, Africa, Central Europe, Asia and Asia Pacific. In the case of an emerging pandemic, these sites could provide vaccine in-country and in-region, thereby reducing potential bottlenecks in vaccine supply and ensuring greater access to influenza vaccines to more countries.



Over the last 9 years, global partners have contributed \$92.6 million toward international influenza vaccine capacity building programs, with \$15.4 million dollars granted in 2014 alone. For every dollar that BARDA and collaborators contribute to the program, seventeen dollars are invested locally to build influenza vaccine production capacity. Considerable progress has been made in the global drive to increase equitable access to influenza vaccines and improve international pandemic preparedness. In economic terms, this is a 99% return on investment. It was also reported in March 2014 that these efforts helped ramp up potential global seasonal vaccine production capacity, from around 500 million doses in 2006 to around 1.5 billion in 2013.⁵⁹

⁵⁹ Schafer J. October, 20, 2014 (presentation slides). Building Sustainable Influenza Vaccine Manufacturing Capacity Worldwide. U.S. Department of Health and Human Services; International Influenza Vaccine Manufacturing Capacity Building Program.

PROTECTING HEALTH AT HOME AND ABROAD

HHS and partners are committed to protecting the health of Americans and our neighbors abroad through effective intervention, like immunizations. The section below details two specific efforts used to guide efforts in securing a healthier world through vaccination.

The NVAC Global Immunization Report

Global immunization programs impact childhood morbidity and mortality rates and improve lives across our globe. In the Fall of 2014, Public Health Reports (PHR) published a special supplemental issue on Global Immunization, with a comprehensive report from the National Vaccine Advisory Committee (NVAC) on the U.S. Department of Health and Human Services (HHS) efforts toward achieving global immunization. The report began, however, in February 2012, when the U.S. Assistant Secretary for Health (ASH) charged NVAC with reviewing the role of HHS in global immunizations, the effect of global immunizations on global populations, and the effect of global immunizations on U.S. populations. The ASH asked for recommendations on how HHS can best continue to contribute, in ways consistent with its newly established Global Health Strategy and Goal 5 of the 2010 National Vaccine Plan. The NVAC was also asked to make recommendations on how to best communicate this information to decision-makers and the general public to ensure continued, sufficient resources for global vaccination efforts.

The resulting NVAC report provides expert recommendations and highlights priority areas for HHS to enhance the overall U.S. efforts toward preventing vaccine-preventable diseases worldwide, including completing global eradication goals for polio and elimination goals for measles, strengthening routine immunization programs and disease surveillance, enhancing capacity for monitoring vaccine safety, supporting vaccine research and development efforts to meet unmet public health needs, enhancing country decisions to introduce new and underutilized vaccines, and strengthening coordination of HHS efforts to support global immunization and global health goals.

This PHR supplement was funded by the National Vaccine Program Office (NVPO) and also features expert commentaries from leaders in global public health, including the HHS Office of Global Affairs, the U.S. Agency for International Development, the World Health Organization, and the Bill & Melinda Gates Foundation. The commentaries further underscore how our nation's health is inextricably linked to the health of the global population, and that the success of global vaccine programs depend on collaboration among global partners working toward the shared vision of the Decade of Vaccines: a world in which all individuals and communities enjoy lives free from vaccine-preventable diseases.

PROTECTING HEALTH AT HOME AND ABROAD

The Global Health Security Agenda

The Global Health Security Agenda (GHSA) advances a world safe and secure from infectious disease threats, brings together nations across the globe to make new, concrete commitments, and elevates global health security as a national leaders-level priority. In the U.S. context, the inputs from many are required to have the desired impact: the federal departments and agencies involved include the Departments of Health and Human Services, Agriculture, State, Defense, and the U.S. Agency for International Development. The GHSA is guided by nine specific goals, many of which include vaccines and immunizations explicitly or implicitly with the focus on preventing outbreaks, detecting threats and being prepared for rapid, effective responses to such threats.

In June of 2014 the G7 endorsed the GHSA, and Finland and Indonesia hosted commitment development meetings to spur action in May and August. In 2014, eleven lines of effort were developed in support of the GHSA, known as action packages. The action packages outline tangible, measurable steps required to prevent outbreaks, detect threats in real time, and rapidly respond to infectious disease threats, whether naturally occurring, the result of laboratory accidents, or an act of bioterrorism. The action packages include specific targets and indicators that can be used as a basis to measure how national, regional, and global capacities are developed and maintained over the long-term. Since February, involved countries made over 100 new commitments to implement the eleven action packages. For its part, the U.S. has committed to assist at least 30 countries over five years to achieve the objectives of the GHSA. The priority actions include combating antibiotic resistant bacteria, improving biosafety and biosecurity on a global basis and preventing bioterrorism.

NINE OBJECTIVES OF GLOBAL HEALTH SECURITY AGENDA

PREVENT

1. Prevent the emergence and spread of antimicrobial drug-resistant organisms and emerging zoonotic diseases, and strengthen international regulatory frameworks governing food safety.
2. Promote national biosafety and biosecurity systems.
3. Reduce the number and magnitude of infectious disease outbreaks.

DETECT

4. Launch, strengthen and link global networks for real-time biosurveillance.
5. Strengthen the global norm of rapid, transparent reporting and sample sharing.
6. Develop and deploy novel diagnostics and strengthen laboratory systems.
7. Train and deploy an effective disease surveillance workforce.

RESPOND

8. Develop an interconnected global network of Emergency Operations Centers and multi-sectoral response to biological incidents
9. Improve global access to medical and non-medical countermeasures during health emergencies.

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Moving forward, ten countries have agreed to serve as part of the GHSA Steering Group, which will be chaired by Finland starting in 2015, with representation from countries around the world, including: Canada, Chile, Finland, India, Indonesia, Italy, Kenya, the Kingdom of Saudi Arabia, the Republic of Korea, and the United States.

The Steering Group is charged with tracking progress, identifying challenges, and overseeing implementation for achieving the objectives of the GHSA in support of international standards set by the World Health Organization for Animal Health, the Food and Agriculture Organization of the United Nations, and the World Organization for Animal Health. This includes the implementation of internationally agreed standards for core capacities, such as the World Health Organization International



Health Regulations, the World Organization for Animal Health Performance of Veterinary Services Pathway, and other global health security frameworks. To provide accountability and drive progress toward GHSA goals, an independent, objective and transparent assessment process will be needed. Independent evaluation, conducted over the five-year course of the GHSA, will help highlight gaps and needed course corrections to ensure that the GHSA targets are reached.

The ongoing Ebola epidemic in West Africa serves as a tangible example highlighting the urgency for immediate action to establish global capacity to prevent, detect and rapidly respond to biological threats. Beginning in his 2011 speech at the United Nations General Assembly, President Obama called upon all countries to work together to prevent, detect, and respond to outbreaks before they become epidemics. As indicated by the G7 endorsement of the GHSA, all nations hold a shared responsibility to provide our world with health security and to accelerate action

LIST OF PARTICIPATING COUNTRIES

Australia	France	Japan	Pakistan	Spain	United Arab Emirates
Azerbaijan	Georgia	Jordan	Peru	Sweden	United Kingdom
Canada	Germany	Kenya	Portugal	Switzerland	United States
Chile	Guinea	Liberia	Republic of Korea	Thailand	Vietnam
China	India	Malaysia	Saudi Arabia	Turkey	Yemen
Denmark	Indonesia	Mexico	Sierra Leone	Uganda	
Ethiopia	Israel	Netherlands	Singapore	Ukraine	
Finland	Italy	Norway	South Africa		

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toward making our world safe and secure from all biologic threats. The section that follows takes a closer look at advancing specific preparedness efforts that represent major equities in U.S. vaccines and security.

The information below provides an overview of work, lead by BARDA, to advance preparedness efforts against biothreats: smallpox and anthrax.

Biothreat: Smallpox

In the event of a smallpox incident, BARDA supports the Public Health Emergency Countermeasures Enterprise (PHEMCE) strategy of having: enough smallpox vaccine for the general population, a smallpox vaccine for “at-risk” individuals (potentially contraindicated for a live replicating vaccine), two smallpox antivirals with different mechanisms of action to treat individuals symptomatic with disease, and vaccinia immune globulin to treat adverse events associated with vaccination. The combination of medical countermeasures will allow the PHEMCE to appropriately respond to a smallpox incident. BARDA’s strategy has been to support the development of a smallpox vaccine for “at-risk” individuals to augment the vaccine for the general population that was developed under a Centers for Disease Control and Prevention (CDC) contract. Since the current licensed smallpox vaccine (ACAM2000) carries a black box warning and is not recommended for use in immunocompromised individuals, the smallpox vaccine program is supporting the development of a third

generation smallpox vaccine, IMVAMUNE, which represents an alternative vaccine that will address the needs of special populations during a smallpox incident. BARDA’s strategic goals for this vaccine candidate have focused on supporting late stage development activities in support of potential licensure of IMVAMUNE, and deliveries to the Strategic National Stockpile (SNS) and maintaining that inventory. The product has the potential to be administered under Emergency Use Authorization (EUA) during a declared emergency to individuals with HIV+ or atopic dermatitis, in all age ranges and including pregnant women or nursing mothers. Additionally, BARDA is supporting the development of a lyophilized formulation of IMVAMUNE that will help maintain a sustainable and cost-effective stockpile capability for IMVAMUNE. BARDA and the PHEMCE will transition to the novel formulation as current inventory begins to expire, replacing expiring product with the lyophilized formulation. BARDA anticipates this transition to begin in 2017.

PROTECTING HEALTH AT HOME AND ABROAD***Biothreat: Anthrax***

BARDA supports the Public Health Emergency Countermeasure Enterprise (PHEMCE) strategy of having vaccines and antibiotics for post-exposure prophylaxis and anthrax antitoxins for the treatment of individuals who are symptomatic with anthrax disease in combination with antibiotics. The complement of antibiotics, vaccines, and antitoxins allow the USG to appropriately respond to an anthrax attack, saving lives. BARDA is working towards improving our nation's preparedness against an anthrax attack by investing in the development of vaccines to prevent disease caused by *Bacillus anthracis* or to treat individuals suspected of exposure in combination with antibiotics. BARDA's near-term strategy for anthrax vaccines utilizes funding to support improvements in the utility and capability of the existing licensed anthrax vaccine, BioThrax. Specifically, BARDA is funding projects to expand the vaccine's label indication

for post-exposure prophylaxis, increase the current US manufacturing production capacity, and support the development of an enhanced BioThrax formulation (NuThrax) that produces a faster immune response with fewer doses. BARDA's long-term anthrax vaccine strategy supports the advanced development of next-generation anthrax vaccines that may further reduce the number of doses required for protection, improve response concept of operations (CONOPS), and lower overall costs of stockpiling an anthrax vaccine within the Strategic National Stockpile (SNS). Currently, three next-generation vaccine candidates remain in the anthrax portfolio and will soon be evaluated in clinical trials to determine their potential as long-term replacement vaccines for the SNS. BARDA will continue to coordinate with our PHEMCE partners to develop and deliver safe and effective anthrax vaccines.

OTHER SELECTED ADVANCES IN GLOBAL IMMUNIZATION

- NIH/NIAID, WHO and BMGF co-hosted the Global Vaccine and Immunization Research Forum (GVIRF) to assess progress in research and development for vaccines to prevent diseases that pose substantial threats to global public health and identify challenges and opportunities in vaccine and immunization research and development. The NIAID Director presented a keynote address on “Vaccine Research and Development: Challenges and Opportunities” at the March 2014 meeting. The GVIRF is part of the Decade of Vaccines Collaboration and was developed to discuss the research and development component of the Global Vaccine Action Plan.
- The first rotavirus vaccine developed entirely in India, called ROTAVAC, was created by an NIH partnership with the Indian government and a biotechnology company, as well as by the Program for Appropriate Technology in Health and others. Results from a Phase 3 clinical trial showed ROTAVAC to be safe and effective. In early 2014, ROTAVAC obtained licensure in India, and in July 2014, the Indian Prime Minister announced the introduction of the vaccine into the country’s national immunization program.
- NIH/NIAID scientists have developed a trachoma vaccine that has been shown successful in a non-human primate model and is slated to start human clinical trials in summer/fall 2015. Blinding trachoma is an ancient neglected tropical disease caused by *Chlamydia trachomatis* for which a vaccine is needed. Epidemiological models of trachoma control indicate that a vaccine with the degree of efficacy shown by the NIH/NIAID candidate would significantly reduce the prevalence of infection and rates of reinfection, known risk factors which drive blinding disease. According to CDC, it is currently estimated that 84 million people have trachoma infection.

APPENDICES

APPENDIX 1: UPDATE ON THE NATIONAL VACCINE ADVISORY COMMITTEE

Background

Established in 1987, the National Vaccine Advisory Committee (NVAC) is an external federal advisory committee that advises the ASH, who serves as the Director of the National Vaccine Program, by making recommendations on matters related to the goals of the National Vaccine Program. The NVAC also monitors and provides feedback on updating and implementing the National Vaccine Plan.

NVAC brings together nonfederal subject matter experts from all areas of the field of immunization, including physician scientists, public health officials, nonprofit organizations, and industry leaders. NVAC meets in person three times a year in Washington, DC, to hear and comment on timely information relating to vaccines and immunization in need of attention. NVAC membership includes representatives from public and private organizations, including vaccine manufacturers, insurance providers, physicians, state and local health agencies, nonprofit organizations and the public.

The NVAC consists of 17 voting members: 15 public members, including the Chair, and two representative members. Public members are individuals who are appointed to the NVAC to exercise their own independent best judgment on behalf of the government. Representative members are individuals who are appointed to the NVAC to provide viewpoints of the vaccine manufacturing industry or groups engaged in vaccine research. To ensure that all members are truly qualified to serve on NVAC, the legislation establishing the committee requires the IOM to be consulted on the appointment of NVAC members. In addition, to ensure optimal coordination of the National Vaccine Program, representatives from governmental agencies that contribute to the National Vaccine Program serve as ex-officio members on the committee.

NVAC's current roster of members can be found on the NVPO website.⁶⁰

⁶⁰U.S. Department of Health and Human Services: National Vaccine Program Office. (2013). NVAC membership/roster. Retrieved from www.hhs.gov/nvpo/nvac/roster/index.html

UPDATE ON THE NATIONAL VACCINE ADVISORY COMMITTEE

By bringing together stakeholders that represent all areas of immunization, NVAC is able to provide advice and insights into the full range of vaccine- and immunization-related activities in the United States. Through monitoring and feedback into the immunization system, the role of the NVAC and the ASH's considerations of its recommendations ensures that the work of HHS, the U.S. government, and its many stakeholders is being directed appropriately to achieve the goals of the National Vaccine Program as outlined in the Public Health Service Act.⁶¹

- Vaccine research.
- Vaccine development.
- Safety and efficacy testing of vaccines.
- Licensing of vaccine manufacturers and vaccines.
- Production and procurement of vaccines.
- Distribution and use of vaccines.
- Evaluating the need for, the effectiveness of, and adverse effects of vaccines and immunization activities.
- Coordinating governmental and nongovernmental activities.
- Funding of federal agencies.

Historical Impact

Over the course of its nearly three decades of leadership, NVAC has addressed concerns in all parts of the immunization system. Through its review of issues in vaccine research and development, vaccine safety, vaccine communications, vaccine delivery, and through HHS's global immunization work, NVAC has provided key recommendations to improve immunization coverage in the U.S.

The NVAC is interested in strengthening the national immunization program at the systems level. This includes vaccination across the lifespan, and NVAC has contributed recommendations that address childhood, adolescent, and adult immunizations. NVAC has also considered immunization issues related to special populations such as health care workers and pregnant women. Past NVAC recommendations have had significant impact on the work of HHS and its partners. In 2011, NVAC released recommendations on how to move toward the removal of barriers to adult immunization. These recommendations included:

- Improving leadership on adult immunization at HHS.
- Allocating appropriate resources for adult immunization.
- Creating a national strategic plan for adult immunization.

⁶¹ Public Health Service Act, 42 U.S.C. § 300aa1. Retrieved from www.hhs.gov/nvpo/about/legislation.pdf

UPDATE ON THE NATIONAL VACCINE ADVISORY COMMITTEE

Following the release of aforementioned NVAC recommendations, the Adult Immunization Task Force (AITF) was formed within HHS to better coordinate adult immunization work across agencies and offices. The AITF forms the federal component of the National Adult and Influenza Immunization Summit (NAIIS), a partnership of more than 140 organizational stakeholders in adult and influenza vaccine research, production, distribution, administration, and advocacy, committed to achieving the Healthy People 2020 goals for adult and influenza vaccination. Both the AITF and the NAIS are working continuously to identify and carry out solutions to barriers to adult immunization.

In 2012 the NVAC made a series of recommendations that aimed to address gaps in health care personnel (HCP) influenza immunization.⁶² By getting vaccinated, HCP are both protecting themselves from contracting influenza and preventing the transmission of influenza to vulnerable patients. In summary, NVAC recommended that:

- Health care personnel employers establish a comprehensive influenza infection prevention program, including educating health care personnel on the benefits of influenza vaccination both to them and their patients.
- Health care personnel employers integrate influenza vaccination programs into their existing infection prevention programs.
- CDC and CMS should continue efforts to standardize the methodology used to measure health care personnel influenza vaccination rates across settings.
- Health care personnel employers strongly consider employer requirement policies for influenza vaccination of health care personnel in facilities that have implemented the above strategies yet continue to fail to reach target vaccination coverage goals.

In response to continually low influenza vaccination rates in health care personnel in long-term care facilities, NVPO and CDC, with support from the HHS Office of Disease Prevention and Health Promotion, launched a comprehensive toolkit. Released for public use in advance of the annual National Influenza Vaccination Week (NIVW) (December 2014), the LTC influenza toolkit provides resources, information, and best-practices for employers and administrators looking for ways to improve influenza vaccination among health care personnel in their long-term care facilities. While the toolkit was developed with long-term care facilities in mind, the information in the toolkit is applicable in any health care facility looking to improve vaccination coverage among their health care personnel.

⁶² National Vaccine Advisory Committee. (2012). Recommendations on strategies to achieve the Healthy People 2020 annual influenza coverage goal for health care personnel. Retrieved from http://www.hhs.gov/nvpo/nvac/influenza_subgroup_final_report.pdf

UPDATE ON THE NATIONAL VACCINE ADVISORY COMMITTEE

Historically, the NVAC has also placed importance on issues related to financing the U.S.'s immunization infrastructure, including focus on Section 317 Immunization Programs. Such programs, administered by the CDC, support high vaccination coverage levels and ensure low incidence of vaccine preventable diseases. NVAC's recommendations on this topic, which were published in 2013, are as follows:⁶³

- Confirmed the importance of maintaining the Section 317 Immunization Program.
- Called for innovative and efficient solutions from federal, state, tribal, and local public health officials that would help move vaccine coverage rates toward Healthy People 2020 goals through efficient means.

In a similar vein, the NVAC has been paying close attention to the implementation of the Affordable Care Act; legislation which has important implications for preventive health services, including vaccine access, administration and financing. While the full impact of the Affordable Care Act is not yet known, many concerns previously raised by the NVAC regarding vaccine financing should be resolved through its full implementation.

Working Groups

The NVAC does the majority of their work through working groups, which meet regularly. NVAC working groups are developed to explore specific vaccine-related issues in-depth, bring their findings back to NVAC for discussion, and develop recommendations for the full committee to consider. If recommendations are accepted by the full committee, they are submitted to the ASH for his or her consideration to guide HHS' work in these areas. Both NVAC members and nonmember experts participate on these working groups. Working group recommendations lay out possible strategies for HHS and its partners that will remove barriers to achieving national goals for immunization, as identified by Healthy People 2020 and the National Vaccine Plan.

In 2014, NVAC had three active working groups considering available evidence and developing recommendations on HPV vaccination coverage, maternal immunization, and vaccine confidence and its impact on childhood immunization coverage, which were identified as important areas by the ASH, and align with Healthy People 2020 goals for immunization and infectious disease. A fourth working group was convened late in 2014 that will focus on reviewing the progress of the National Vaccine Plan (2010-2020), as the plan has reached its midcourse mark.

⁶³ National Vaccine Advisory Committee. (2013). Protecting the public's health: Critical functions of the Section 317 Immunization Program- A report of the National Vaccine Advisory Committee. Public Health Reports, 128, 78-95. Retrieved from www.publichealthreports.org/issueopen.cfm?articleID=2949

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HPV Vaccination Working Group

Since 1998, NVAC has drawn attention to the issue of low adolescent vaccination rates through resolutions, recommendations, and oversight. Following a resolution on adolescent vaccine coverage in 1998, NVAC included adolescents in the Standards for Immunization Practice in 2003. In 2008, the NVAC working group on adolescent immunization released recommendations on how to increase routine adolescent immunization coverage, with their major recommendations focusing on strategies to reduce the number of missed opportunities to immunize adolescents.⁶⁴

Despite this, uptake of the HPV vaccine has been low among adolescents and has remained stagnant in recent years. The NVAC working group on HPV vaccination is conducting a review of the current state of HPV immunization to understand the root causes for the observed relatively low vaccine uptake of HPV vaccine (both initiation and series completion), and to identify existing best practices, all with a goal of providing recommendations on how to increase use of this vaccine in young adolescents.

The NVAC hosted a number of sessions on HPV during their committee meetings, including a discussion in February 2014 of the President's Cancer Panel (PCP) report and a full session in June 2014 on Planned Actions to Address HPV by a number of stakeholder groups. In addition to endorsing the recommendations of the PCP on HPV vaccination, the NVAC HPV Vaccination working group has come up with additional recommendations to be presented to and considered by the full Committee. These recommendations involve implementation strategies to drive HPV vaccination uptake, including the exploration of a simplified administration schedule. The working group's recommendations will be presented during the February 2015 NVAC meeting and a Committee vote is anticipated for the June 2015 NVAC meeting.

Maternal Immunization Working Group

NVAC continues to work on the issue of maternal immunization—immunizing pregnant women to prevent VPDs in both the mother and her infant. When certain vaccines are given to pregnant women, the vaccine can potentially prevent serious illness in both the mother and the baby following birth. Currently, two vaccines are recommended for pregnant women: the seasonal influenza vaccine and Tdap. Data are suggestive that maternal transfer of immunity through immunization may provide infants with protection against severe complications from these diseases before they are old enough to receive their own vaccinations. However sub-optimal uptake of these vaccines continues to leave very young infants at risk.

In 2012, the Maternal Immunization Working Group (MIWG) was formed to examine the existing best practices related to maternal immunization, and to provide

⁶⁴ National Vaccine Advisory Committee. (2008). Adolescent vaccination: Recommendations from the National Vaccine Advisory Committee Adolescent Working Group. Retrieved from www.hhs.gov/nvpo/nvac/adolescentvaccinationrecommend.pdf

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recommendations that will contribute to the formation of a maternal immunization platform for seasonal influenza vaccine, Tdap, and other vaccines in development, such as respiratory syncytial virus and Group B strep. The MIWG report with recommendations was voted on and approved by the NVAC in June of 2014 and was featured in the January/February 2015 issue of Public Health Reports. In this report, five major areas of opportunity to strengthen maternal immunization programs and to increase uptake of recommended vaccines among pregnant women are identified and listed below. The NVAC report describes, in depth, barriers to maternal immunization and the resulting recommendations are intended to offer evidence-based solutions for strengthening maternal immunization efforts:

- Enhancing communication to address the safety and effectiveness of all currently recommended immunizations during pregnancy
- Maximizing obstetric provider recommendation and administration of recommended maternal immunizations
- Focusing efforts to improve financing for immunization services during pregnancy and postpartum
- Supporting efforts to increase the use of electronic health records (EHRs) and immunization
- Recognizing and addressing current vaccine liability law barriers to optimize investigations and uptake of recommended and future vaccines during pregnancy

Vaccine Confidence Working Group

With the use of recommended childhood vaccines, the rates of vaccine-preventable diseases in children are at historically low levels. Although vaccines, like any drug or medical treatment, have their risks, research has shown childhood immunizations and the childhood vaccine schedule to be very safe. However, a small subset of parents in the United States is refraining from vaccinating their children, or choosing to follow alternative vaccination schedules. To better understand why this is happening and create strategies to prevent the small number of children who have not been fully vaccinated from growing, an NVAC working group is examining the issue of vaccine confidence among parents of children aged 0–6 years.

Continuing work which commenced in 2012, the Vaccine Confidence Working Group (VCWG) has reviewed the available evidence and literature concerning how confidence in vaccines and in our immunization program and services impacts the optimal use of recommended childhood vaccines in the United States. After considering the available information on this topic, the working group will issue rec-

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ommendations to the ASH on how to best measure confidence in our vaccines and vaccination recommendations, as well as our immunization programs and types of interventions that may be needed to ensure that parental confidence does not become an impediment to optimal use of vaccines in the prevention of serious childhood infections and their consequences. Presentation of the VCWG recommendations for NVAC consideration is scheduled for the February 2015 NVAC meeting and a Committee vote is anticipated for the June 2015 NVAC meeting.

Looking Forward

The health care landscape is continuing to shift. Millions of adults now have access to preventive health services with no cost-sharing, including immunizations, as a result of the passage of the Affordable Care Act. NVAC continues to monitor the impact this historic legislation has on immunization access.

NVAC work on adult immunization continues to come to fruition through efforts being made by HHS and other partners. These initiatives to create a strong adult immunization system in the United States will help to support the increased demand for immunization that may be brought about by the Affordable Care Act. While this new adult immunization system takes shape, NVAC will play a pivotal role in advising in its creation.

The NVAC continues to play a significant role in enhancing the nation's immunization efforts, as exemplified through the policy recommendations presented by the NVAC working groups. As NVAC persistently improves the approach of its work and focuses its attention on issues of national importance, their impact and effectiveness will continue to be recognized for their success in helping improve the nation's vaccine enterprise.

APPENDIX 2: PROGRESS ON THE IMPLEMENTATION OF THE NATIONAL VACCINE PLAN

The action steps listed below constitute the National Vaccine Plan Implementation, 2010–2015,⁶⁵ and were chosen to ensure a robust immunization program for the United States. These action steps were or are currently being carried out by HHS and its federal partners, the VA and the DoD. Updates on the progress toward achieving these action steps are listed in the table.

TABLE 9: Goal 1: Develop New and Improved Vaccines
Priority A: Develop a catalogue of priority vaccine targets of domestic and global health importance.

Lead agency	Action step	Progress report	Status
NVPO	A1. NVPO will support the development of a framework to prioritize preventive vaccines and convene a workshop to obtain input from key partners on this framework through a contract with the IOM.	Framework has been developed by the IOM. A stakeholder meeting was held in November 2012 to obtain stakeholder input on the tool.	Completed
NVPO	A2. NVPO will support the development of a methodology for identifying priority vaccine targets for domestic and global health priorities through a contract with the IOM.	IOM developed a software tool called SMART Vaccines that helps inform prioritization of needed vaccines. The software was made available to the public for download and use on September 30, 2013.	Completed
NVPO	A3. NVPO will support the production of a catalogue of priority vaccine targets of domestic and international importance through a contract with the IOM.	Development of the SMART Vaccines tool was completed and presented at the February, 2014 meeting of the National Advisory Committee. NVPO has entered into a new funding agreement with the Institutes of Medicine to create curated databases for prospective users of the tool.	Projected completion date: Early 2015

TABLE 10: Priority B: Strengthen the science base for the development and licensure of new vaccines.

Lead agency	Action step	Progress report	Status
NIH	B1. NIH will fund a broad range of basic and clinical research studies on topics including mechanisms of host-pathogen interaction, host immune response, new vaccine targets, and vaccines against bacterial, viral, and parasitic microbes. Information about these projects will be included on publicly available websites, such as NIH RePORT (Research Portfolio Online Reporting Tools) and ClinicalTrials.gov, as well as in scientific publications.	Per NIH's RePORT, NIH spent ~ \$1.65 billion on vaccine-related research in fiscal year (FY) 2014. The budget figure includes extramural and intramural projects. Each NIH Institute/Center's contribution to vaccine related research can be accessed publicly through the NIH RePORT database by querying "Vaccine Related" http://report.nih.gov/categorical_spending.aspx	Ongoing through the end of 2015
ASPR	B2. ASPR/BARDA will support the advanced development of next-generation cell-based and recombinant influenza vaccines with the goal of making more influenza vaccine available faster during influenza pandemics.	In 2009, ASPR/BARDA entered into a public-private partnership with Novartis to build the first facility in the United States capable of manufacturing cell-based influenza vaccine. In 2012, ASPR/BARDA expanded that partnership and established a Center for Innovation in Advanced Development and Manufacturing at this facility, with a future goal of manufacturing this new cell-based influenza vaccine at this new facility. In November of 2012, the FDA approved Flucelvax®, a cell-based influenza vaccine. The vaccine was developed through a public-private partnership between ASPR/BARDA and Novartis. In June 2014, The Novartis Holly Springs facility was licensed by FDA to manufacture Flucelvax cell-based influenza vaccine, a realization of the goal to dramatically increase the pandemic influenza vaccine manufacturing capacity in the United States. In January of 2013, the FDA approved Flublok®, the first trivalent influenza vaccine made using an insect virus (baculovirus) expression system and recombinant DNA technology. ASPR/BARDA has also supported the advanced development of recombinant virus like particle (VLP) vaccine candidate being developed by Novavax. In response to the emergence of the novel avian H7N9 influenza virus in China in 2013, Novavax used their recombinant VLP technology to produce an H7N9 vaccine candidate and was the first manufacturer to publish clinical data from an H7N9 vaccine clinical trial. This rapid response capability strongly supports the rationale for continued development of recombinant based influenza vaccines.	Ongoing through 2015

⁶⁵ U.S. Department of Health and Human Services. (2011). National vaccine plan implementation: Protecting the nation's health through immunization. Retrieved from www.hhs.gov/nvpo/vacc_plan/2010%20Plan/nationalvaccineplan.pdf

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Lead agency	Action step	Progress report	Status
ASPR	B3. ASPR/BARDA will coordinate and support efforts to optimize production and testing of influenza vaccines with the goal of decreasing the time needed to make vaccine available in an influenza pandemic.	The Influenza Vaccine Manufacturing Initiative is an interagency program with participation from ASPR/BARDA, CDC, FDA and NIH. As a result of efforts to optimize vaccine production, high yielding H7N9 production viruses were successfully tested in human clinical trials. Head-to-head vaccine yield comparison of improved candidate vaccine viruses are planned in Fall 2014 followed by commercial demonstration batches. A new mass spectrometry method to speed the calibration of vaccine potency assay reagents was successfully developed. The WHO essential regulatory laboratories in the US and UK will transition to the new method following several seasons of side by side comparison with the traditional method. Multiple alternative potency assays were shown to be feasible replacements for the current potency assay. The participation of global commercial and regulatory stakeholders was enlisted to evaluate and select the most appropriate alternative assay(s). Preparations for comparison studies are in progress. A newly developed rapid sterility system that reduces the time for sterility testing from 14 days to 5 days has moved from development into manufacturing with product launch announced to begin in 4Q14.	Ongoing through 2015
FDA	B4. FDA will develop and implement a research agenda that focuses on expanding the development of applied research with the goal of enhancing the safety and effectiveness of vaccines and facilitate product development.	For information on relevant FDA research, see http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/ucm234680.htm and http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/default.htm , which are links to scientific publications and select summaries on current FDA research relevant to enhancing the safety and effectiveness of vaccines and facilitating product development.	Ongoing through 2015
ASPR	B5. ASPR/BARDA will fund cooperative agreements with U.S.-based universities to support Advanced Bio-manufacturing Training Programs for scientists from manufacturers in developing countries.	As of June 2014, over 300 scientists from developing countries have attended these and other ASPR/BARDA-supported trainings. In 2013, the courses were expanded, in collaboration with the FDA and WHO, to include participants from National Regulatory Authorities in developing countries. In 2014, influenza biomanufacturing training lecture and practical materials were translated in collaboration with respective manufacturers in developing countries.	Ongoing through 2015
ASPR	B6. ASPR/BARDA will fund development of clinical trial and laboratory infrastructure in developing countries for the evaluation of candidate influenza vaccines in preclinical research.	To date, eight ASPR/BARDA-funded vaccine manufacturers in developing countries have conducted clinical trials with their own influenza vaccine. Seven of these manufacturers have now licensed influenza vaccines, and one vaccine has achieved WHO prequalification status.	Ongoing through 2015
NIH	B7. NIH will fund product development research on 15 vaccines for infectious diseases and related conditions.	The NIH/NIAID Partnership program stimulates collaborative efforts and multidisciplinary approaches to rapidly advance promising infectious disease vaccine candidates and platform technologies through the product development pathway. This program has uniquely fostered many new research collaborations between experts from different disciplines of academia and industry. In FY 2013, NIH/NIAID supported multiple projects through the Partnerships for Development of Vaccine Technologies initiative, which focuses on preclinical development of candidate technologies (including adjuvants) that would improve vaccine effectiveness and/or simplify vaccine delivery to patient populations during a natural outbreak of an infectious disease or following the intentional release of an infectious agent.	Projected completion date: End of 2015
NIH	B8. NIH will evaluate five new formulations/technologies with potential to improve vaccine immunogenicity, safety, delivery, and/or dosing.	NIH supports research on new and improved vaccine formulations/technologies, including products that may be easier to store, ship, and deliver in resource-limited settings and during public health emergencies. FY 2014 examples include efforts to develop a micro-needle influenza vaccine patch, and vaccine delivery via electroporation devices, and research into the use of micro-needles to deliver inactivated rotavirus, MMR, and polio vaccine.	Projected completion date: End of 2015

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Lead agency	Action step	Progress report	Status
NIH	B9. NIH will fund preclinical services for investigators to develop and evaluate five candidate vaccines.	NIH/NIAID provides vaccine development services for use in the investigation, control, prevention, and treatment of a wide range of infectious agents. These services support the following products: vaccines, vaccine components including adjuvants, vaccine delivery systems, other biologics, and Biosafety Level (BSL)-2, BSL-3, and BSL-4 challenge material. Vaccine testing services include assay development for non-clinical and clinical samples; nonclinical immunogenicity and efficacy studies; clinical and nonclinical sample testing; and safety and toxicity testing. Vaccine manufacturing services include feasibility, gap analysis, and product development plan support; process development; product release assay development including potency assays; pilot and cGMP manufacture; audits; and regulatory activities and documentation.	Projected completion date: End of 2015
NIH	B10. NIH will fund multifunctional clinical research sites to expand the range of studies conducted among diverse populations in the United States and international settings.	NIH/NIAID re-competed the Vaccine and Treatment Evaluation Units. Awards, which were made in late FY 2013. The sites will carry out clinical studies and trials spanning a wide spectrum of infectious diseases and will have the ability to conduct studies in international populations, including in resource-poor settings. Studies may include healthy volunteers from birth to mature adults, pregnant women, and subjects with diseases that are endemic to the specific location. Recent studies included a phase IIb trial to determine the optimal dosage, safety, and immune response produced by two different doses of pneumococcal vaccine in older adults and a safety and immunogenicity clinical trial of a prime-boost mix of injected and spray flu vaccines.	Projected completion date: End of 2015

**TABLE 11: Goal 2: Enhance the Vaccine Safety System
Priority B: Strengthen the science base for the development and licensure of new vaccines.**

Lead agency	Action step	Progress report	Status
FDA	B11. FDA will develop and implement a research agenda focusing on enhancement of vaccine safety evaluation; including laboratory research, bioinformatics for exchanging information, overseeing the safety of vaccine products, and new epidemiological methods.	For information on relevant FDA research, see http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/ucm276981.htm , http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/ucm234680.htm , and http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/default.htm , which are links to scientific publications and select summaries on current relevant FDA research.	Ongoing through 2015
NIH	B12. NIH will fund preclinical and clinical research related to the development of safe and effective vaccines, including studies among healthy adults as well as specific populations such as infants and children, the elderly, and people with weakened immune systems.	NIH/NIAID supports preclinical and clinical vaccine research, including studies among special populations. Examples include developing and improving neutralizing antibodies that prevent HIV infection in high-risk adult and pediatric populations, pertussis vaccine in healthy pregnant women, safety and immunogenicity of sequential rotavirus vaccine schedules, staged phase I/II hepatitis C prophylactic vaccine, a phase IIb, open-label, dose-ranging study of 13-valent pneumococcal conjugate vaccine in adults 55 through 74 years of age previously vaccinated with 23-valent pneumococcal polysaccharide vaccine, and H7N9 vaccine clinical trials.	Projected completion date: End of 2015

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TABLE 11: Priority C: Enhance timely detection and verification of vaccine safety signals and develop a vaccine safety scientific agenda.

Lead agency	Action step	Progress report	Status
NVPO	C1. NVPO will fund a literature review of vaccine safety to inform development of a vaccine safety scientific agenda.	The NVPO/AHRQ developed literature review of vaccine safety was released July 1st, 2014, along with a summary publication in the journal Pediatrics: http://www.ahrq.gov/news/newsroom/press-releases/2014/com-monvaccines.html . The report found scientific evidence that addresses several common concerns about a variety of vaccines. For example, the report found strong scientific evidence that: There is not a link between measles, mumps and rubella (MMR) vaccines and autism. There is not a link between pneumonia and influenza vaccines and cardiovascular or cerebrovascular events in the elderly. There is not a link between MMR; diphtheria, tetanus, and pertussis (DTaP); tetanus and diphtheria (Td); Haemophilus influenzae type b (Hib); and Hepatitis B vaccines and childhood leukemia. In addition, the report found that there is moderately strong scientific evidence that: There is not a link between human papillomavirus (HPV) vaccines and appendicitis, stroke, seizures, venous thromboembolism, onset of juvenile arthritis or onset of type 1 diabetes. There is not a link between inactivated influenza vaccines and adverse pregnancy outcomes (such as miscarriage, low birth weight, and premature birth) for women who receive the vaccine while pregnant.	Completed
Federal Immunization Safety Task Force (ISTF): CDC, FDA, VA, IHS, and DoD	C2. The ISTF will increase the number of infants, children, adolescents, and adults enrolled in active surveillance systems for adverse events following immunizations [e.g., VA, IHS, DoD] in the United States to 90 million.	As of November 2012, 107 million individuals were enrolled.	Completed
FDA	C3. FDA will contract with private health care data systems to access claims-based information for vaccine safety surveillance in the PRISM program under FDA's Mini-Sentinel initiative. This will allow FDA to assess whether vaccine exposure might be associated with health outcomes of interest.	Under the PRISM program of FDA's Mini-Sentinel Initiative, the first protocol-based safety assessment of over 1 million doses of rotavirus vaccines is complete, and the results were publicly posted in June 2013. These results led to the first safety labeling change stemming from a Mini-Sentinel protocol-based safety assessment.	Completed
FDA and CMS	C4. FDA and CMS will monitor the safety of seasonal influenza vaccines in Medicare beneficiaries using Medicare databases.	In the 2012/13 season, actively monitored for GBS with no observable signal to date among over 16.1 million influenza vaccinations in the Medicare System. Actively working to expand methodologies to conduct surveillance for other adverse events such as anaphylaxis.	Ongoing through 2015
ISTF	C5. The ISTF will use the information from the NVPO-funded literature review of vaccine safety and develop a vaccine safety scientific agenda.	The NVPO/AHRQ-developed literature review of vaccine safety was released July 1st, 2014, along with a summary publication in the journal Pediatrics: http://www.ahrq.gov/news/newsroom/press-releases/2014/com-monvaccines.html . The review provides the most comprehensive review to date of published studies on the safety of routine vaccines. NVPO has subsequently compiled and disseminated a draft safety agenda to federal partners for input and feedback.	Completed
ISTF	C6. The ISTF will increase the number of infants, children, adolescents, and adults enrolled in active surveillance systems for adverse events following immunizations [e.g., VA, IHS, DoD] in the United States to 100 million.	As of February 2013, 111.5 million individuals were enrolled.	Completed
CDC	C7. CDC will redesign the online electronic reporting form for VAERS to include new fields that capture additional demographic information and implement web-based features to expedite complete and accurate online reporting.	Much progress has been made on VAERS form redesign to date: discussion with stakeholder groups including physicians, immunization program managers, immunization partners; addition of needed data fields and removal of unused fields; form reorganization; development of a savable form; usability testing with layperson volunteers; pilot testing of electronic interface; and reduction in availability of non-electronic reporting modalities.	Projected completion date: End of 2014

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Lead agency	Action step	Progress report	Status
FDA and CDC	C8. FDA and CDC will enhance reporting by improving the ability to submit reports to VAERS electronically, to facilitate efficient, complete, and accurate reporting of adverse events following immunization.	A redesigned VAERS form has undergone cognitive testing with medical professional and layperson volunteers and "smart-form" development and deployment is scheduled for completion by the end of 2015.	Projected completion date: End of 2015
CDC	C9. CDC will conduct research and development for technologies to facilitate reporting to VAERS from handheld devices such as application software and to incorporate technologies into EHRs to facilitate VAERS reporting, such as provider prompts.	Under a phase 1 SBIR, a feasibility project has developed a prototype app. CDC has supported an ongoing study to implement provider prompts for possible vaccine safety concerns in EHRs. The updated VAERS form will have a more user-friendly web interface. The VAERS app development is complete and phase II SBIR is underway to enable interface of the app with the online VAERS site. The EHR prompts project is complete and dissemination is under consideration.	Projected completion date: End of 2015
FDA	C10. FDA will take steps toward providing patients, providers, and manufacturers with a single reporting portal for adverse events by recommending VAERS data structure modifications to allow compatibility with adverse event reporting systems used for other medical products.	Consumer and health care providers can report vaccine adverse events to VAERS online on the VAERS website. While this reporting is still a separate portal from that used for other regulated medical products, FDA and CDC are working to align vaccine adverse event data elements with those used for drugs and other products. The eVAERS initiative, a joint FDA and CDC project, is restructuring the VAERS database to allow it to accept electronic adverse event reports from vaccine manufacturers, in the same way that FDA currently accepts electronic reports for drugs and other products.	Projected completion date: End of 2015
CDC	C11. CDC will ensure that health plans with the capacity to rapidly and regularly provide complete medical records and chart review data for immunization participate in vaccine safety surveillance through the VSD.	CDC announced and work has begun under a new IDIQ contract with health plans. In competing this new contract, CDC invited any health plan with the capacity to provide this level of health data to apply; the IDIQ includes all successful applicants.	Projected completion date: End of 2015
CDC	C12. CDC will support VSD contractors in rapid assessments of all vaccine safety signals of significance.	VSD conducted rapid cycle analysis for influenza vaccine safety (2012-2013) and will implement active monitoring for adverse events for influenza vaccine for the 2013-2014 season. Through the VSD Indefinite Deliverable Indefinite Quantity contract, the VSD detected a signal of increased risk of intussusception following RV1 vaccine through continuous monitoring. In FY 2014, rapid cycle analysis will be conducted for HPV vaccine administered to males. VSD continued to conduct rapid cycle analysis for influenza vaccine safety (2013-2014) and will implement active monitoring for adverse events for influenza vaccine for the 2014-2015 season. 2013-2014 VSD analysis identified an increased risk for febrile seizures when infants were administered influenza, pneumococcal, and tetanus/diphtheria/pertussis vaccines in a single visit. VSD has conducted an initial safety analysis of Tdap vaccination of pregnant women and there are plans to enhance that analysis. DVD staff collaborated with ISO and VSD sites to communicate updated findings on the risk of intussusception following rotavirus vaccines and CDC staff conducted a re-assessment of rotavirus vaccines risks and benefits. These data were presented to the ACIP and the VIS was revised to reflect confirmed low risk of intussusception following rotavirus vaccines. The rotavirus vaccine risk versus benefit analysis for the US was also published in a peer review journal.	Projected completion date: End of 2015
FDA and CDC	C13. FDA and CDC will receive manufacturer reports of vaccine adverse events electronically in accordance with International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) E2B(R3) standards.	The eVAERS initiative, a joint FDA and CDC project, is re-structuring the VAERS database to allow it to accept electronic adverse event reports from Vaccine Manufacturers in compliance with the ICH E2B (R3) standards for electronic adverse event reporting. The ICH E2B (R3) standards are international standards for the format and content of electronic adverse event submissions from manufacturers. The Agencies have made significant progress in defining the technical requirements and structure for eVAERS. The pilot testing with manufacturers commenced in late 2013/ early 2014 and CDC has worked with FDA to facilitate the implementation of electronic reporting to VAERS by manufacturers.	Projected completion date: End of 2015

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**TABLE 12: Goal 3: Support communications to enhance informed vaccine decision-making
Priority D: Increase awareness of vaccines, vaccine preventable diseases, and the benefits/risks of immunization among the public, providers, and other stakeholders.**

Lead agency	Action step	Progress report	Status
FDA	D1. FDA will enhance communication to stakeholders by utilizing social media (including Twitter) to distribute FDA-specific news and content about vaccines (e.g., new approvals, safety issues, etc.).	During Calendar Year 2013, FDA developed vaccine-related content for consumers, health care providers and regulated industry on an array of topics including but not limited to safety information on rotavirus vaccine; global vaccine safety surveillance; research on influenza vaccine development; research findings on residual formaldehyde in infant vaccines; a guide for parents on childhood vaccines, etc. FDA/CBER averaged 3–4 vaccine-specific postings per month during this time period.	Ongoing through 2015
NVPO	D2. NVPO will launch a comprehensive government website on vaccines and immunization.	Vaccines.gov was launched in March 2011	Completed
ONC	D3. ONC will promote consumer engagement projects to allow parents access to vaccination history data from IIS, including clinical decision support tools.	ONC, in partnership with pilot states, is working to provide consumers with access to IIS through a secure, easy-to-use online portal. These portals also provide Blue Button® compliant download capabilities. Consumer access to immunization records through the pilot is underway in seven states and one large metropolitan area also currently offering consumer access to their IIS. This project is funded by CDC and NVPO.	Ongoing through 2015
NVPO	D4. NVPO will launch a Spanish language comprehensive government website on vaccines and immunization.	The Spanish translation of vaccines.gov launched in February of 2012.	Completed
FDA	D5. FDA will use specified metrics to evaluate use of Twitter as a means to communicate with stakeholders.	Metrics have been identified, and tracking has begun.	Completed
CDC	D6. CDC will assess the accessibility and usability of Vaccine Information Statements (VIS) for different target audiences. CDC will use this information to revise VIS as needed.	All updated VISs are being produced in a simplified and standardized format, and these changes underwent ad hoc testing associated with Education, Information and Partnership Branch training courses. VIS website has been updated, and includes all VISs in html format, which will be easily accessible using smart phone. VIS pages will now be syndicated, so VISs will be automatically updated for people who link to them. All VISs have also been made assessable in rtf format, at request of some providers, to be compatible with their electronic systems. Barcodes are added to all updated VISs to facilitate recording of VIS name and edition date. In conjunction with National Center for Immunization and Respiratory Diseases, CDC's Influenza program conducted formative research in 2011 and 2013 to test the acceptability and clarity of specific flu-related messages with the general public, at-risk populations, and health care providers. Results from focus group testing directly informed the revision of key communication materials for those audiences. CDC's Influenza program also reviewed data on how CDC-INFO inquiries on flu and flu vaccine were being routed through the agency for response. Review of the data indicated there were new opportunities to respond to inquiries more efficiently, so Influenza program worked with offices across the agency to install a more efficient triage process. CDC's Influenza program also worked with web developers in CDC's Office of the Director to conduct two proactive reviews of the CDC Influenza web site. These reviews yielded actionable steps that Influenza program then took to improve visitors' experience in finding the site easily with search engines, navigating through the site, and accessing content.	Projected completion date: End of 2015

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TABLE 13: Goal 4: Ensure a stable supply of, access to, and better use of recommended vaccines in the United States
Priority E: Use evidence-based science to enhance vaccine preventable diseases surveillance, measurements of vaccine coverage, and measurement of vaccine effectiveness

Lead agency	Action step	Progress report	Status
CDC	E1. CDC will increase the number of virus specimens received and characterized annually from global National Influenza Centers for use in determining vaccine strain selection (Target: 11,000 virus specimens characterized).	11,358 virus specimens were characterized in FY 2013	Completed
CDC	E2. CDC will continue to monitor the number of indigenous cases of paralytic polio, rubella, congenital rubella syndrome (CRS), measles, Hib, diphtheria, tetanus, mumps, pertussis (in persons <7 years), and varicella (in persons <18 years) to evaluate the impact of vaccine policy and programs.	CDC continues to support the National Notifiable Disease Surveillance System (NNDSS) which is the source of U.S. national surveillance data for these pathogens. For certain pathogens, data is received from specialized surveillance systems to address specific surveillance requirements to monitor the number of cases and to evaluate program/policy impact. These data are analyzed and results are routinely shared with local, state, national, and international public health partners. In response to the surge in measles cases during 2014, weekly updates were instituted on the CDC website of reported measles cases to CDC. To enhance laboratory capacity for confirmation of bacterial and viral vaccine preventable diseases, Domestic Laboratory Reference Centers (4) were established and perform CDC developed molecular methods for rRT-PCR, sequencing and genotyping.	Ongoing through 2015
CDC	E3. Within one year of a disease becoming newly vaccine preventable CDC will implement a plan for documenting and reporting vaccine impact.	Made critical investments to enhance influenza Vaccine Effectiveness surveillance network so that more providers and patients are enrolled allowing for rapid and more comprehensive VE data gathering. Continued evaluations of vaccine effectiveness of pneumococcal conjugate vaccine (PCV13, recommended for young children in 2010) and meningococcal conjugate vaccine for adolescents; published study showing impact of PCV7 vaccination of infants in reducing pneumonia in all age groups. Published studies of diphtheria-tetanus-pertussis vaccine (DTaP) effectiveness in 5-10 y.o. children, showing waning immunity within 5 years after 5th DTaP dose, and completed study showing waning immunity within 2 years after Tdap booster dose in adolescents. CDC has published data showing that rotavirus vaccines are highly effective in preventing severe rotavirus disease and that vaccine effectiveness does not wane over time in U.S. children. CDC monitors the impact of rotavirus vaccine in the United States through the National Respiratory and Enteric Viruses Surveillance System and the New Vaccine Surveillance Network. CDC's Division of Viral Diseases conducted a varicella vaccine effectiveness study to monitor the effectiveness of the 2-dose varicella vaccine policy that was adopted in 2007. The results indicate that 2-dose varicella vaccination is highly effective and confers higher protection than a 1-dose regimen. High 2-dose varicella vaccination coverage should maximize the benefits of the varicella vaccination program and further reduce varicella disease burden in the US. DVD demonstrated the substantial impact of rotavirus vaccines on diarrheal hospitalizations domestically and hospitalizations and mortality globally. DVD research showed that both rotavirus vaccines are >85% effective in preventing severe rotavirus disease in U.S. children with the effectiveness sustained over time In postlicensure evaluations, DVD confirmed ~50% post-licensure zoster vaccine effectiveness among adults 60 years and older, consistent with pre-clinical trial estimates. Additionally, the evaluation provided the first estimates of effectiveness of zoster vaccine to prevent herpes zoster ophthalmicus and herpes zoster hospitalizations CDC monitors the impact of rotavirus vaccine in the United States through the National Respiratory and Enteric Viruses Surveillance System and the New Vaccine Surveillance Network. In 2013, CDC published a number of studies on the effectiveness and impact of rotavirus vaccines. These included studies on the effectiveness of monovalent and pentavalent rotavirus vaccine, the impact of the pentavalent rotavirus vaccine in preventing rotavirus hospitalizations and emergency department visits and the indirect impact of vaccine on gastroenteritis hospitalizations in older children and adults. CDC also published a paper on trends in national rotavirus activity before and after introduction of rotavirus vaccine in the US, 2000 to 2012.	Ongoing through 2015

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Lead agency	Action step	Progress report	Status
CMS	E4. CMS will track and publicly report the percentage of nursing home residents that are assessed and appropriately given influenza vaccine.	No update	Projected completion date: End of 2015
CDC	E5. CDC will increase the number of public health laboratories monitoring influenza virus resistance to antiviral agents to 15.	18 public health laboratories are monitoring influenza virus resistance to antiviral agents.	Completed
CDC	E6. CDC will increase the percentage of Pandemic Influenza Collaborative Agreement grantees (CoAg) (state, local, territorial, and tribal project areas) that meet the standard for surveillance and laboratory capability criteria.	42.5 percent of CoAg grantees met the standard for surveillance and laboratory capability criteria for 2012.	Completed

TABLE 13: Priority F: Eliminate financial barriers for providers and consumers to facilitate access to routinely recommended vaccines.

Lead agency	Action step	Progress report	Status
NVPO	F1. NVPO will provide an annual update to NVAC on progress toward strengthening and improving the vaccine financing system in the United States to facilitate access to routinely recommended vaccines.	In September 2009 and September 2012, NVPO gave updates on the implementation of NVAC recommendations for vaccine financing. In September of 2011, NVAC heard information on vaccine financing coordination. In February 2010, June 2010, and June 2011, NVAC was given vaccine financing updates. In February and September, 2013, NVAC was given a series of presentations on the Affordable Care Act and potential impact on vaccine financing issues; and in June, 2014 NVAC heard information on the current state of section 317 funding.	Ongoing through 2015
HRSA	F2. HRSA will measure the percentage of children seen at HRSA-funded health centers who receive all-age appropriate routinely recommended vaccines by their third birthday.	Relevant HRSA programs measure the percentage of children who receive recommended vaccines. In addition, HRSA continues dialogue with stakeholders toward aligning childhood immunizations to increase immunization rates and reduce preventable infectious diseases.	Ongoing through 2015
CDC	F3. CDC will support 28 immunization grantees to develop plans and 14 immunization grantees to implement plans to enable billing for vaccine services provided by public health clinics.	Of the original 14 grantees, 11 are implementing third party billing. Currently, 38 of 64 immunization grantees have received funds for planning or are implementing plans for billing, or both. The National Association of County and City Health Officials developed a national toolkit on third-party billing.	Completed
CDC	F4. CDC will provide guidance to immunization grantees to not use Section 317 vaccines for routine vaccination of fully insured patients. Section 317 is a discretionary federal program distributed to the states to provide money for vaccine purchase and to develop vaccine infrastructure.	Immunization grantees received guidance on the use of Section 317 vaccines for routine vaccination of fully insured patients in July 2012. Beginning October 1, 2012 all grantees indicated compliance with the policy in their vaccine-purchasing plans.	Completed

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TABLE 13: Priority G: Create an adequate and stable supply of routinely recommended vaccines and vaccines for public health preparedness.			
Lead agency	Action step	Progress report	Status
CDC	G1. CDC will continue to track the status of vaccine supplied in the United States and maintain a strategic national stockpile of vaccines that are available to state and local health departments during public health emergencies and when local supplies are depleted or unavailable.	All FY 2014 pediatric stockpile purchases have been submitted.	Ongoing through 2015
ASPR	G2. ASPR/BARDA will continue to support, through public-private partnerships, the development of domestic influenza vaccine manufacturing capacity to address seasonal and pandemic influenza vaccine needs.	Through ASPR/BARDA, HHS awarded three-year contracts to five U.S.-licensed influenza vaccine manufacturers to produce master vaccine seed stocks, clinical investigational lots, and prepandemic vaccine stockpiles for viruses with pandemic potential before a pandemic occurs. The contracts also allow HHS to purchase live-attenuated and cell-based vaccines in addition to conventional egg-based vaccine in a pandemic.	Ongoing through 2015
FDA	G3. FDA will convene/cosponsor three scientific meetings to facilitate the development of an effective vaccine against a number of preventable infectious diseases for which there is not a vaccine currently available.	In 2012, FDA convened or cosponsored three scientific meetings. January 2012: FDA, in partnership with NIH, CDC and NVPO convened a public workshop to identify and discuss key issues related to the development and evaluation of human cytomegalovirus vaccines. June 2012: FDA cosponsored the Universal Influenza Vaccines Meeting with NIH/NIAID. September 2012: FDA's Vaccines and Related Biological Products Advisory Committee met to examine the role of emerging technologies for detecting adventitious agents in assessing whether novel human tumor-derived cell-line substrates are suitable for vaccine production.	Completed

TABLE 13: Priority H: Increase and improve the use of interoperable health information technology and EHRs.			
Lead agency	Action step	Progress report	Status
ONC	H1. ONC will certify national standards for EHRs to ensure that eligible professionals and hospitals may be assured that the systems they adopt are capable of performing the required functions.	In February 2014, ONC released the Voluntary 2015 Edition EHR Standards and Certification Criteria NPRM that proposed "bug fixes" to the 2014 Edition criteria, promotes interoperability, and allows for flexibility. ONC anticipates the final rule for the NPRM will be published by the end of 2014.	Ongoing through 2015
ONC	H2. ONC will collect information on barriers to implementing meaningful use requirements for immunization through the CRM (Sales Force) tool. The CRM (Sales Force) is a milestone management tool that tracks the progress of Regional Extension Centers (RECs) towards meeting their goals of enrolling providers and getting providers to achieve meaningful use.	ONC has continued to address issues and barriers to implementation through technical assistance during years two and three of Stage 1 and Stage 2 of Meaningful Use. FAQs and other resources to address these issues have been developed and will be placed on healthIT.gov. ONC co-leads with CDC a Stage 2 MU PH Reporting Requirements Task Force that led to the development of guidance and recommendations for public health agencies. ONC and CDC also co-lead a Public Health/EHR Vendor Collaboration meeting that provides a forum to discuss and address issues and opportunities for interoperability between EHRs and IIS.	Ongoing through 2015
ONC	H3. ONC will perform surveys of select providers enrolled to receive services from RECs to determine issues/barriers with IIS and compatibility with EHRs.	ONC has continued to address issues and barriers to implementation through technical assistance during years two and three of Stage 1 and Stage 2 of Meaningful Use. FAQs and other resources to address these issues have been developed and will be placed on healthIT.gov. ONC co-leads with CDC a Stage 2 MU PH Reporting Requirements Task Force that provides a forum to discuss and address interoperability between EHRs and IIS. IIS testing of standard messages uncovered variability between states. ONC convened and facilitated state workgroups to reduce this variability and promote interoperability.	Ongoing through 2015
ONC	H4. ONC will register 100,000 primary care providers to receive services from RECs and ensure that 60 percent of those have adopted the use of EHRs.	Well over 100,000 primary care providers have registered with RECs as of 12/31/2012.	Completed

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TABLE 14: Goal 5: Increase global prevention of death and disease through safe and effective vaccination. Priority I: Improve global surveillance for vaccine preventable diseases and strengthen global health information systems to monitor vaccine coverage, effectiveness, and safety.

Lead agency	Action step	Progress report	Status
CDC	I1. CDC will continue to serve as a global reference lab for polio, measles, and rubella.	Provided basic and advanced diagnostic support, including genomic sequencing, to polio-endemic and outbreak-affected countries, to identify virus reservoirs and sources of outbreaks. Molecular methods for confirming measles and rubella infections were introduced in all 6 WHO Regions in the Regional Reference Labs (some national). A system for QA/QC is actively being pursued to standardize and validate the methods. CDC is helping to develop global sequence databases for measles and rubella to facilitate more efficient tracking of transmission pathways. MMRHLB has provided advanced training to WHO network laboratories to strengthen capacity for molecular testing. MMRHLB has developed a global proficiency panel for molecular testing in WHO laboratories. CDC also supports global polio surveillance and the Global Polio Laboratory Network through reference diagnostics, training and provision of reagents to GPLN laboratories, coordination of the QA/QC program for CDC developed molecular assays to characterize poliovirus isolates. Since 2010, the number of GPLN laboratories using CDC-developed and supported molecular assays has increased by over 40%; nearly 60% of the 146 GPLN laboratories, including those supporting all endemic and outbreak countries, are using the CDC assays.	Ongoing through 2015
CDC	I2. CDC will provide surveillance and laboratory capacity to monitor progress in reaching global polio eradication, guide programmatic response, and implement the polio eradication end-game strategy.	CDC has contributed significantly to the more than 99 percent decline in global polio cases from more than 350,000 cases reported annually in 1988 to 407 cases reported in 2013. India, one of the four remaining endemic countries (Nigeria, Afghanistan, and Pakistan) in 2010, has not had a case of polio transmission since January 2011. November of 2013 marked one year's passage without a recorded case of wild poliovirus type 3, one of the two remaining polio types. CDC and the GPEI partners are aligned behind a joint strategy, which is articulated in the Polio Eradication and Endgame Strategic Plan (2013–2018), which has four major pillars: 1) Poliovirus Detection and Interruption; 2) Routine Immunization Strengthening and OPV (oral polio vaccine) Withdrawal; 3) Containment and Certification; and 4) Legacy Planning. CDC has continued to work with WHO to ensure accreditation of polio, measles, and rubella laboratories in key endemic and outbreak-affected countries and increased global lab capacity to support sensitive VPD surveillance by transfer of CDC-developed polio, measles, and rubella virus detection and characterization technologies. CDC has continued to work with WHO to ensure accreditation of polio laboratories in key endemic and outbreak-affected countries and increased global lab capacity to support sensitive polio surveillance by transfer of CDC-developed poliovirus detection and characterization technologies. Co-lead investigator on SURVAC, a multi-country project centered in Africa and supporting integrated disease surveillance for vaccine preventable diseases. Provided training and financial support to approximately 400 individuals annually who are subsequently deployed by WHO to strengthen surveillance for polio, measles and rubella at country level (STOP). Conducted polio, measles and rubella outbreak investigations in multiple high priority countries (e.g., Federated States of Micronesia; Jordan; Democratic Republic of Congo; Ethiopia). Provided critical financial and technical support to WHO-based global laboratory networks for polio, measles and rubella and for new vaccine surveillance.	Ongoing through 2015
CDC	I3. CDC will provide a descriptive report of progress on immunization activities in the FETP.	Working with ministries of health and other partners, FETP residents conduct investigations and share scientific data to improve health outcomes. Recently, CDC trained FETP residents in Ethiopia, Uganda, and Sudan to recognize the signs and symptoms of polio as a mechanism to strengthen the surveillance capabilities in those countries (as the FETP residents conduct field investigations).	Ongoing through 2015

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TABLE 14: Priority J: Support global introduction and availability of new and under-utilized vaccines to prevent diseases of public health importance.

Lead agency	Action step	Progress report	Status
CDC	<p>J1. CDC will continue to provide surveillance, laboratory, and vaccine program implementation capacity to support national decision-making on new vaccine introduction, and to enable introduction of new vaccines including pneumococcal vaccine, rotavirus vaccine, meningococcal vaccine, and HPV vaccine in GAVI eligible countries.</p>	<p>CDC's Division of Bacterial Diseases is providing support for accelerating introduction of pneumococcal conjugate vaccines, as part of GAVI's Accelerated Vaccine initiative-Technical Assistance Consortium and work closely with other strategic countries in various regions. As part of this we support PCV effectiveness studies in South Africa, Kenya, Brazil, and Uruguay and initiated a study with Bangladesh and Pakistan. We have supported evaluation of the impact of meningococcal conjugate vaccines surveillance in Burkina Faso, Niger, Mali, Nigeria and Ghana, and planning to initiate similar studies in 6 additional countries in the meningitis African belt. As the Global reference laboratory for the WHO invasive Bacterial Surveillance network, we provide assistance to all WHO regions to strengthen laboratory and epidemiologic capacity for bacterial disease surveillance, in order to provide countries with evidence to help them introduce bacterial vaccines (pneumococcal, Hib, meningococcal conjugate vaccines) or evaluate their impact post introduction to sustain the immunizations program long term. Over 50 countries are currently part of the surveillance network, mainly located in the African region. For HPV, CDC has a qualitative study in Kenya regarding communication issues for HPV vaccine introduction as well as ongoing consultations by CDC HPV laboratory with the Pan American Health Organization (PAHO) and Argentina's Ministry of Health regarding laboratory preparations for HPV prevalence monitoring in the Americas. CDC participates in several key international meetings, including a WHO Regional Consultation on Cervical Cancer Prevention and Control; a WHO Scoping Meeting on development of second generation HPV vaccines; a PAHO TAG meeting during which CDC presented data on alternative HPV vaccination schedules; and the President's Cancer Panel on Challenges of Global HPV Vaccination Introduction. To date, 47 countries around the world have introduced rotavirus vaccines through their national immunization programs, including 15 GAVI-eligible countries. CDC provided assistance to WHO and GAVI Alliance in supporting these introductions. CDC, Division of Viral Diseases provides technical assistance to WHO and member countries for disease surveillance and for monitoring rotavirus vaccine impact, effectiveness, and safety after the vaccine is introduced. The CDC Rotavirus Program has worked collaboratively with WHO HQ and each of the regional offices to document rotavirus disease burden by providing epidemiologic and laboratory support to the rotavirus surveillance networks in each of the WHO regions. The data generated from these surveillance networks have been used by countries to advocate the need for and cost effectiveness of rotavirus vaccine introduction and to monitor the impact, effectiveness, and safety of the vaccine post-introduction. These data have also been used to reaffirm WHO's recommendation for the use of rotavirus vaccines in all countries and particularly in those countries with high child mortality due to diarrheal disease. Since 2010, rotavirus vaccine has been introduced in 27 GAVI eligible countries. In many of those countries, CDC provided hands-on assistance with the evaluation of vaccine effectiveness and safety.</p>	Ongoing through 2015
ASPR	<p>J2. ASPR/BARDA will provide financial and technical support for the WHO GAP, including capacity building for vaccine production at developing country manufacturers, royalty-free adjuvant production, specialized training in advanced biomanufacturing skills and clinical/laboratory infrastructure building.</p>	<p>Fourteen manufacturers in thirteen developing countries have received technical and financial support from ASPR/BARDA to establish influenza vaccine manufacturing capacity. Seven influenza vaccines have been licensed for use in the manufacturers' respective countries, increasing the manufacturing capacity for pandemic vaccines to over 280 million doses, toward a 2016 goal of 500 million pandemic doses. ASPR/BARDA provides targeted clinical trial and manufacturing technical support for these developing country vaccine manufacturers to enable advanced development of new influenza vaccines and plans to establish an adjuvant hub to allow for faster development of adjuvanted influenza vaccines.</p>	Ongoing through 2015

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Lead agency	Action step	Progress report	Status
FDA	J3. FDA will develop and implement a research agenda to facilitate the development of vaccines against tropical and neglected diseases.	FDA is working to develop an assay to identify the serotype of the infecting dengue virus in subjects whose illness meets the diagnostic criteria for dengue, during clinical trials of dengue vaccines in endemic areas. FDA has demonstrated that a monoclonal antibody that recognizes all four serotypes of NS1 (a glycoprotein secreted from dengue-infected cells) is able to bind to the infected cells and give a positive result in the ELISA. Further, FDA research has shown that two monoclonal antibodies, one against dengue serotype 2 and one against dengue serotype 1 do recognize the respective NS1 proteins in a specific manner. Research efforts are underway at FDA to contribute to the development of novel vaccines for the prevention of tropical and neglected diseases, including but not limited to, tuberculosis, polio and dengue. http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/BiologicsResearchAreas/ucm124378.htm Recent examples include the development of in vitro assays to characterize new tuberculosis vaccine preparations. FDA is participating in an international collaborative effort to develop in vitro assays to screen new candidate vaccines, assess the potency of new vaccine formulations, and evaluate the immunogenicity of new vaccines in humans. FDA's studies in mice have demonstrated the validity of the in vitro approach because in vitro vaccine activity results correlated significantly with in vivo vaccine effectiveness data. In addition, FDA is examining alternative methods for administration of tuberculosis vaccines.	Ongoing through 2015
FDA	J4. FDA will participate in international collaborative studies to establish and maintain international reference materials and standards for biologics.	Efforts in this area for various vaccines are underway. This reference standard continues to be used and is provided to the global community by FDA. In addition, FDA routinely participates in international collaborative studies to produce, calibrate, and supply reference reagents for inactivated influenza vaccines. The current assay used to measure potency of inactivated influenza vaccines is a single-radial immunodiffusion (SRID) assay that utilizes a strain-specific antibody to measure the content of virus hemagglutinin (HA) in the vaccine in comparison to a homologous HA reference antigen. Due to the yearly updating of the influenza vaccine, new reagents (reference antigen and corresponding antiserum) for measuring vaccine potency are needed for every new strain incorporated into the vaccine. Since influenza vaccine standardization is a global effort, WHO's Essential Reference Laboratories (FDA/CBER is one of the four WHO ERLs) collaborate to produce and calibrate these reagents. In the past year, FDA has produced one new reference antigen for the seasonal vaccine and was the lead agency in its calibration. Also, FDA participated with the other ERLs in calibrating several new reference reagents needed to maintain a sufficient supply of reagents for manufacturers. In addition, FDA collaborates with the other WHO ERLs to produce similar potency reagent sets for pandemic influenza vaccines that are under evaluation. In the past year, new reagents were needed for vaccines being developed for the emerging H7N9 viruses in China. FDA was the lead agency in production and calibration of the first H7 reference reagent and to date; FDA is the only regulatory agency that has been able to produce an H7-specific antiserum that works with the H7N9 candidate vaccines. To produce this potency antiserum FDA utilized a novel method of immunization with H7 Virus-like particles that was developed a few years ago as an alternative technique should such an emergency arise. The FDA was also a member of the Working Group for a Guideline on Quality, Safety and Efficacy of Typhoid Vi Capsular Polysaccharide Conjugate Vaccine, chosen as the major author of the non-clinical section and major contributor to the manufacturing and quality control section. In October 2013, WHO's Expert Committee on Biological Standardization adopted the Guidelines on the Quality, Safety and Efficacy of Typhoid Conjugate Vaccines http://www.who.int/biologicals/areas/vaccines/TYPHOID_BS2215_doc_v1.14_WEB_VERSION.pdf?ua=1 FDA is also a part of the U.S. Pharmacopeial Convention Working Group on Glycoconjugates Vaccines. In October 2012, the group completed a final draft the U.S. Pharmacopeial Convention chapter outlining recommendations for the manufacture of polysaccharide and glycoconjugate vaccines for human use.	Ongoing through 2015

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Lead agency	Action step	Progress report	Status
FDA	J5. FDA will build regulatory capacity in developing countries, which may include training, participation in WHO assessments, and other international activities.	FDA has participated in approximately 18 WHO-sponsored meetings to strengthen regulatory capacity building and providing advice to developing countries' National Regulatory Authorities on vaccine development and evaluation. In addition, FDA was a participant with other National Regulatory Authorities in developing the WHO Guidelines on the Nonclinical Evaluation of Vaccine Adjuvants and Adjuvanted Vaccines, which was adopted by WHO Expert Committee on Biological Standardization in October 2013. http://www.who.int/biologicals/areas/vaccines/ADJUVANTS_Post_ECBS_edited_clean_Guidelines_NCE_Adjuvant_Final_17122013_WEB.pdf	Ongoing through 2015
ASPR	J6. ASPR/BARDA will provide technical support in vaccine manufacturing, including training on vaccine production, analytical evaluation, laboratory techniques, and clinical evaluation, to developing country manufacturers for the WHO GAP. This training may take place on-site in developing countries and at established educational institutions in the United States.	As of June 2014, over 300 scientists from developing countries have attended these and other ASPR/BARDA-supported trainings. In 2013, the courses were expanded, in collaboration with the FDA and WHO, to include participants from National Regulatory Authorities in developing countries. In 2014, influenza biomanufacturing training lecture and practical materials were translated in collaboration with respective manufacturers in developing countries.	Projected completion date: End of 2015
OGA	J7. OGA will provide policy and diplomatic support for the WHO GAP by co-organizing and facilitating workshops to bring together supporting infrastructures in influenza vaccine development in developing countries, including ministers of health, ministers of finance, vaccine manufacturers, nongovernmental organizations, regulatory authorities, and policy makers.	OGA has cohosted 7 workshops with WHO since 2010. The most recent workshop was in June 2013 in Atlanta, Georgia, and was titled Workshop on Enhancing Communication around Influenza Vaccination. The workshop welcomed 93 participants from 31 countries. The outputs from the breakout sessions and discussions directly informed a framework to strengthen national and regional communication systems around vaccination.	Projected completion date: End of 2015
OGA	J8. OGA will facilitate development of new partnerships across HHS, across the U.S. government, and with other international partners not previously engaged for support of the WHO Action Plan to Increase Pandemic Influenza Vaccines.	Through workshops cosponsored with WHO (see Action Step J7) OGA facilitated the development of new partnerships that support Pandemic Influenza Vaccines. The AVMI is a notable new partnership formed through the workshop series in 2011. AVMI brings together 12 vaccine manufacturers in Africa, for Africa. This major initiative was formally announced by the President of Benin at the Africa Union meeting in January 2013.	Projected completion date: End of 2015

APPENDIX 3: HEALTHY PEOPLE 2020 BACKGROUND OF IMMUNIZATION AND INFECTIOUS DISEASE GOALS

For more than three decades, Healthy People has provided science-based, 10-year national health promotion and disease prevention goals and objectives for improving the health of all Americans. Launched in December 2010 by the Office of Disease Prevention and Health Promotion within HHS, Healthy People 2020 establishes benchmarks, sets targets, and monitors progress over time in order to

1. Encourage collaborations across communities and sectors.
2. Empower individuals toward making informed health decisions.
3. Measure the impact of prevention activities.

The objectives in the Immunization and Infectious Diseases Topic Area focus on increasing immunization rates for people of all ages, which will reduce the incidence of vaccine-preventable infectious diseases. The National Vaccine Plan was developed with Healthy People 2020 immunization objectives in mind. The plan reinforces the work of HHS and its partners to achieve the Healthy People 2020 vaccination coverage goals.

Vaccines are among the most cost-effective clinical preventive services and are a core component of any preventive services package. Childhood immunization programs provide a very high return on investment. For example, each birth cohort vaccinated with the routine immunization schedule (this includes DTaP, Td, Hib, polio, MMR, hepatitis B, and varicella vaccines) saves 33,000 lives, prevents 14 million cases of disease, reduces direct health care costs by \$9.9 billion, and saves \$33.4 billion in indirect costs. Despite the progress made to date, approximately 42,000 adults and 300 children in the United States die each year from vaccine-preventable diseases.⁶⁶ Communities with pockets of unvaccinated and under-vaccinated populations are at increased risk for outbreaks of vaccine-preventable diseases.

Healthy People 2020 data show that, as of 2011, the majority of childhood and toddler vaccination coverage rates are at or are higher than their Healthy People 2020 targets. Our challenge is to maintain these high coverage rates. In addition, more work needs to be done to improve adolescent and adult vaccination coverage rates. The National Vaccine Plan provides a roadmap on how to protect all Americans from vaccine-preventable diseases. For specific information on HP2020 immunization and infectious disease objectives and status updates, please visit the [Healthy People 2020 website](http://www.healthypeople.gov/2020).

⁶⁶ <http://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases>

APPENDIX 4: STAKEHOLDER WEBSITE GUIDE

Administration for Children and Families (ACF) - www.acf.hhs.gov

Agency for Healthcare Research and Quality (AHRQ) - www.ahrq.gov

Assistant Secretary for Health (ASH) - www.hhs.gov/ash

Assistant Secretary for Preparedness and Response (ASPR) - www.phe.gov/about/aspr

Bill and Melinda Gates Foundation - www.gatesfoundation.org

Biomedical Advanced Research and Development Authority (BARDA)
- www.phe.gov/about/barda

Center for Biologics Evaluation and Research (CBER)
- www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber

Centers for Disease Control and Prevention (CDC) - www.cdc.gov

Centers for Medicare and Medicaid Services (CMS) - www.cms.gov

Decade of Vaccines Collaboration - www.dovcollaboration.org

Food and Drug Administration (FDA) - www.fda.gov

(The) GAVI Alliance (GAVI) - www.gavialliance.org

Health Resources and Services Administration (HRSA) - www.hrsa.gov

Healthy People Initiative - www.healthypeople.gov

Indian Health Service (IHS) - www.ihs.gov

Institute of Medicine (IOM) - www.iom.edu

Immunization Action Coalition - www.immunize.org

National Center for Immunization and Respiratory Diseases (NCIRD)
- www.cdc.gov/ncird

National Institute of Allergy and Infectious Diseases (NIAID) - www.niaid.nih.gov

National Institutes of Health (NIH) - www.nih.gov

National Vaccine Program Office (NVPO) - www.hhs.gov/nvpo

STAKEHOLDER WEBSITE GUIDE

NIH Research Portfolio Online Reporting Tools (RePORT) - report.nih.gov

Office of Global Affairs (OGA) - www.globalhealth.gov

Office of Global Health Diplomacy - www.state.gov/s/ghd

Office of the National Coordinator for Health Information Technology (ONC)
- www.healthit.gov

United Nations Children’s Fund (UNICEF) - www.unicef.org

U.S. Agency for International Development (USAID) - www.usaid.gov

U.S. Department of Defense (DoD) - www.defense.gov

U.S. Department of Health and Human Services (HHS) - www.hhs.gov

U.S. Department of Homeland Security (DHS) - www.dhs.gov

U.S. Department of Justice (DoJ) - www.justice.gov

U.S. Department of State - www.state.gov

U.S. Department of Veterans Affairs - www.va.gov

World Health Organization (WHO) - www.who.int

APPENDIX 5: INFORMATION AND RESOURCES FOR THE PUBLIC

www.vaccines.gov and espanol.vaccines.gov

Vaccines.gov, available in English and Spanish, is the federal gateway to information on vaccines and immunization for infants, children, teenagers, adults, and seniors. Vaccines.gov provides resources from federal agencies for the general public and their communities about vaccines across the lifespan.

www.flu.gov

Flu.gov provides one-stop access to U.S. government seasonal, H1N1 (swine), H5N1 (bird), H3N2, and pandemic flu information for the general public, health professionals, policy makers, and community leaders.

www.cdc.gov/vaccines

Vaccine and immunization information from CDC. Individuals can also contact CDC with questions about vaccines and immunizations at 1-800-CDC-INFO (1-800-232-4636).

<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/default.htm>

Information about how the FDA evaluates the safety and effectiveness of vaccines before they are licensed (approved) for use in the United States, how they monitor safety and quality after licensure, and how FDA uses available tools to report adverse events following vaccination. It also includes information on FDA-approved labeling for vaccines.

www.niaid.nih.gov/topics/vaccines

Details NIAID's role in vaccine research and highlights particular research projects.

www.vaccineinformation.org

The Immunization Action Coalition provides a wide variety of educational resources for health professionals and the public on vaccines and the diseases they prevent.

vaccine.healthmap.org

The HealthMap Vaccine Finder is a free, online service where users can search for locations that offer vaccines, including pharmacies, health clinics, and health departments.

vaers.hhs.gov

VAERS is a national vaccine safety surveillance program that collects information about adverse events that occur after the administration of vaccines. Individuals can report a reaction following vaccination to VAERS online, by fax, or by mail. More information on how to report adverse events following vaccination can be found on the VAERS website.

INFORMATION AND RESOURCES FOR THE PUBLIC

www.hrsa.gov/vaccinecompensation

The Vaccine Injury Compensation Program provides a way to resolve vaccine injury claims and compensate those found injured as a result of vaccines. This site provides information about how to file a claim, a review of adverse events related to vaccines, and answers to frequently asked questions.

www.healthit.gov/patients-families

Learn about how health information technology, such as electronic health records, can improve health care for you, your family, and your community.

www.healthypeople.gov/

Healthy People provides science-based, 10-year national objectives for improving the health of all Americans. Healthy People has established benchmarks and monitored progress over time in order to: encourage collaborations across communities and sectors, empower individuals toward making informed health decisions and measure the impact of prevention activities.