THE NATIONAL VACCINE PROGRAM OFFICE

MID-COURSE REVIEW OF THE 2010 NATIONAL VACCINE PLAN

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NVPO
NATIONAL VACCINE PROGRAM OFFICE

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACRONYMS

Abbreviation	Definition
2-D	Two-Dimensional
ACIP	Advisory Committee on Immunization Practices
ACS	American Cancer Society
AEFI	Adverse Event Following Immunization
ASH	Assistant Secretary for Health
ASPR	Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
BIO	Biotechnology Innovation Organization
CDC	Centers for Disease Control and Prevention
CICP	Countermeasures Injury Compensation Program
CMS	Centers for Medicare & Medicaid Services
DOD	U.S. Department of Defense
DPT	Diphtheria, Pertussis, and Tetanus
EHR	Electronic Health Record
FDA	U.S. Food and Drug Administration
GID	Global Immunization Division
GPEI	Global Polio Elimination Effort
GVAP	Global Vaccine Action Plan
HHS	U.S. Department of Health and Human Services
HIPC	Human Immunology Project Consortium
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
HPV	Human Papillomavirus
HRSA	Health Resources and Services Administration
IHS	Indian Health Service
IIS	Immunization Information System
IT	Information Technology
MCM	Medical Countermeasure
NGO	Nongovernmental Organization
NIAID	National Institute of Allergy and Infectious Diseases

Abbreviation	Definition
NIH	National Institutes of Health
NVAC	National Vaccine Advisory Committee
NVP	National Vaccine Plan
NVPO	National Vaccine Program Office
OA	Opportunity Area
ONC	Office of the National Coordinator
PHEMCE	Public Health Emergency Medical Countermeasure Enterprise
PRISM	Postlicensure Rapid Immunization Safety Monitoring
R&D	Research and Development
RFI	Request for Information
RSV	Respiratory Syncytial Virus
SAGE	Strategic Advisory Group of Experts
SAHM	Society for Adolescent Health and Medicine
SMART	Strategic Multi-Attributable Ranking Tool
TB	Tuberculosis
Tdap	Tetanus, Diphtheria, and Acellular Pertussis
TIV	Trivalent Inactivated Influenza Vaccine
UNICEF	United Nations Children's Emergency Fund
U.S.C.	United States Code
USAID	U.S. Agency for International Development
USG	U.S. Government
VA	U.S. Department of Veterans Affairs
VAERS	Vaccine Adverse Event Reporting System
VFC	Vaccine for Children
VICP	National Vaccine Injury Compensation Program
VPD	Vaccine-Preventable Disease
VSD	Vaccine Safety Datalink
WHO	World Health Organization
WIR	Wisconsin Immunization Registry

EXECUTIVE SUMMARY

The U.S. Department of Health and Human Services National Vaccine Program Office (NVPO) developed the 2010 National Vaccine Plan (NVP) with input from federal partners and nonfederal stakeholders and guidance from the National Vaccine Advisory Committee to provide a strategic approach for preventing infectious diseases and improving the public's health through vaccination for 2010 to 2020.

Since the release of the NVP in 2010, the immunization landscape has changed. NVPO anticipated the need for the Mid-course Review to consider possible changes to the NVP that would ensure that the plan continued to be responsive to current environmental realities. The Mid-course Review is intended to reflect on the priorities and progress toward goals laid out in the NVP. The review addresses the following fundamental questions:

- Broadly speaking, is the NVP meeting its goals?
- Which key opportunities in the national vaccine and immunization enterprise are poised for significant progress between now and 2020?
- Is the vaccine and immunization enterprise moving in the direction needed based on the current environment?

The NVP Mid-course Review has three goals in addressing these three fundamental questions:

1. Identify the top achievements from the first five years (2010 to 2015).
2. Determine the three to five greatest opportunity areas for the timeframe 2016 to 2020, and define what success will look like (outcomes) in each area.
3. Develop indicators or metrics that can be used to track progress against each of the top three to five opportunity areas.

Findings of the report include 20 top achievements, as identified and validated by expert stakeholders across the entire immunization enterprise. In addition, findings include five opportunity areas that stakeholders felt are primed for major progress in the next five years. There was strong consensus that with appropriate support, the following areas could result in significant near-term achievements:

Opportunity Areas
Strengthen health information and surveillance systems to track, analyze, and visualize disease, immunization coverage, and safety data, both domestically and globally.
Foster and facilitate efforts to strengthen confidence in vaccines and the immunization system to increase coverage rates across the lifespan.
Eliminate financial and systems barriers for providers and consumers to facilitate access to routine, recommended vaccines.
Strengthen the science base for the development and licensure of vaccines.
Facilitate vaccine development.

The Mid-course Review process identified 16 indicators that could provide a quantifiable way of tracking progress in the opportunity areas above, with at least one indicator focused on global progress for most opportunity areas. The suggested metrics this report presents will need to be finalized before inclusion in an update to the Implementation Plan. Finally, the considerations, opportunity areas, and indicators identified in this report provide a framework for the development of an updated Implementation Plan.

1 BACKGROUND

1.1 THE 2010 NATIONAL VACCINE PLAN

The U.S. Department of Health and Human Services (HHS) National Vaccine Program Office (NVPO) developed the 2010 National Vaccine Plan (NVP) with input from federal partners and nonfederal stakeholders and guidance from the National Vaccine Advisory Committee (NVAC) to provide a strategic approach for preventing infectious diseases and improving the public's health through vaccination for the coming decade.

The NVP provides a comprehensive strategy to enhance all aspects of the vaccine ecosystem, including research and development (R&D), supply, financing, distribution, safety, informed decision-making by consumers and health care providers, vaccine-preventable disease (VPD) surveillance, vaccine effectiveness and coverage monitoring, and global coordination. The NVP for 2010 to 2020 is organized around five goals:

- **Goal 1.** Develop new and improved vaccines.
- **Goal 2.** Enhance the vaccine safety system.
- **Goal 3.** Support communications to enhance 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.

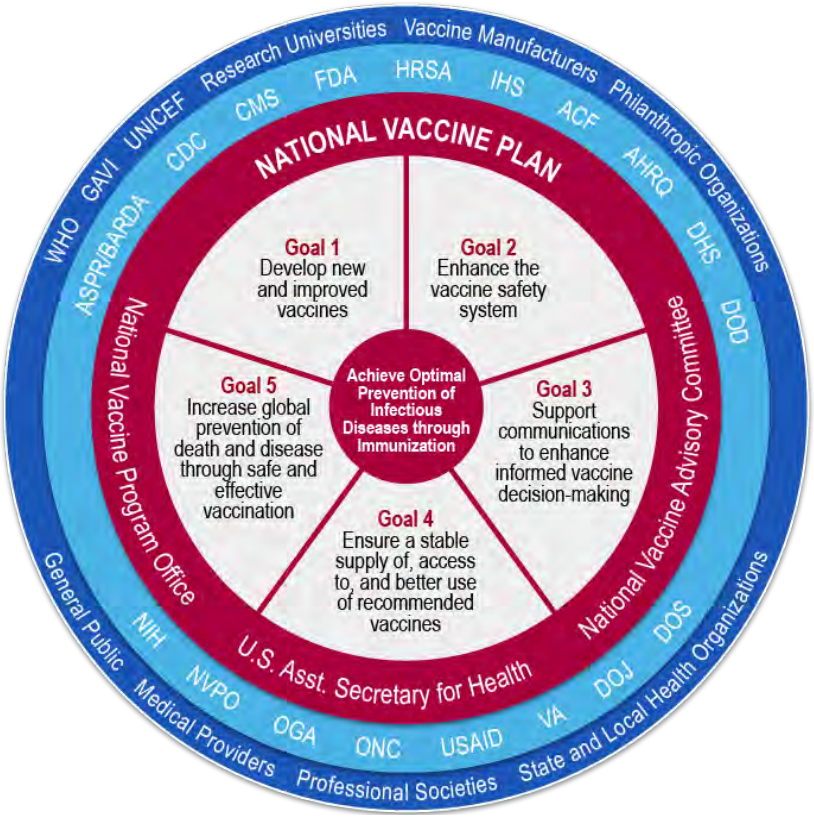
Each goal is supported by five to nine objectives and 22 to 45 strategies for a total of 34 supporting objectives and 147 supporting strategies. The objectives provide a framework for how each goal can be achieved, while the strategies provide a thorough series of activities that will help realize the objective and goal they support. In addition to the NVP, NVPO developed an Implementation Plan that describes 62 activities for the timeframe 2010 to 2015 and identifies the federal agencies that will lead and support each activity based on their respective missions.

1.2 VACCINE ECOSYSTEM

The goals and objectives described in the 2010 NVP require a coordinated, collaborative effort across the entire vaccine ecosystem, particularly among the federal stakeholders. The NVP identifies 17 federal agencies that have a role to play in the execution of the NVP, including departments both within and beyond HHS. In addition to the federal partners, the NVP highlights 10 nonfederal organizations and stakeholder groups that have a critical role in the execution of the NVP. Figure 1 provides an overview of how these entities come together to form the vaccine ecosystem. The 2010 NVP also provides an overview showing how stakeholders (federal and nonfederal) align to the goals and objectives. NVPO is responsible for ensuring stakeholder coordination and monitoring activities and achievements against the NVP on an ongoing basis.

As Figure 1 shows, ***collaboration across the entire vaccine ecosystem is critical*** for protecting individuals and communities against VPDs.

Figure 1: Overview of the Responsible Nonfederal and Federal Stakeholders that Comprise and Support the National Vaccine Program through Implementation of the National Vaccine Plan



An example of the need for coordinated collaboration is the nation's public health response to the 2014/15 Ebola outbreak. Rapid action was necessary and many federal, local, and international partners came together quickly to formulate and implement a range of actions. Considerable gaps in the scientific information about Ebola existed, no vaccines or treatment protocols were available, communication materials had to be created at home and abroad, and emergency plans had to be developed and put in place. Coordination across the U.S. government (USG) and other stakeholders, including vaccine manufacturers, on the prioritization and development of Ebola vaccine candidates resulted in an unprecedented vaccine development pace. Much of the coordination within the USG was done through the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), which is led by HHS's Assistant Secretary for Preparedness and Response (ASPR). The National Institutes of Health (NIH), collaborating with the Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), ASPR's Biomedical Advanced Research and Development Authority (BARDA), and the U.S. Department of Defense (DOD) — all PHEMCE partners — working side by side with vaccine manufacturers and international and multilateral partners, took the lead on vaccine development.

The need for an Ebola vaccine was recognized more than a decade before the 2014/15 Ebola outbreak, with HHS support of Ebola vaccine development starting in 2003. NIH conducted and supported research to strengthen the science base and understand all aspects of the Ebola virus and also supported development of multiple vaccine candidates that were available for further evaluation during the most recent outbreak. This work highlights the importance that advanced preparations play in enabling a rapid response to emerging infectious diseases. NIH, in collaboration with CDC and others, launched clinical trials in West Africa to evaluate the efficacy of two candidate vaccines. The DOD Defense Threat Reduction Agency contracted to produce more than 100,000 doses of cGMP vaccine for the clinical trials.

To further development efforts, CDC provided systems support in West Africa to develop the clinical and laboratory infrastructure necessary to run vaccine trials. More than 350 Sierra Leone trial staff were trained on good clinical practices and study protocol. Critical cold chain and

vaccine storage and handling needs were established so that the clinical sites could receive vaccine shipments, and vaccination and study site infrastructure were updated. FDA worked with its HHS partners to assure that study designs met regulatory expectations and that the data collected could support future regulatory action, expediting review of vaccine protocols and clinical trials data. FDA also collaborated internationally to reach regulatory convergence with the European Medicines Agency, World Health Organization (WHO), and African regulators to review regulatory submissions and determined multiple pathways to vaccine licensure for varying scenarios of Ebola disease. ASPR/BARDA funded commercial vaccine-development efforts for two of the most advanced Ebola vaccine candidates. Unprecedented and swift action by the U.S. Congress provided the economic coordination needed to address key barriers that inhibit commercial investment in vaccines for diseases like Ebola that do not have robust return-on-investment profiles.

1.3 Purpose of the Mid-course Review

Since the release of the NVP in 2010, the landscape has changed:

- Availability of new vaccines and vaccine technologies
- Consolidation of vaccine manufacturers
- Passage of the Patient Protection and Affordable Care Act
- Development of new communication strategies and tools to assess vaccine attitudes and beliefs
- Introduction of new or revised strategic plans (e.g., HHS agencies, Global Vaccine Action Plan [GVAP] from WHO).

NVPO anticipated the need for the Mid-course Review to consider possible changes to the NVP that would ensure that the plan continued to be responsive to current environmental realities. NVPO commissioned this review by an outside third party. The Mid-course Review is intended to reflect on the priorities and progress toward goals laid out in the NVP. The review is not intended to replace the NVP or evaluate organizations on their individual contributions to the NVP. Rather, the review addresses the following fundamental questions:

- Broadly speaking, is the NVP meeting its goals?
- Which key opportunities in the national vaccine and immunization enterprise are poised for significant progress between now and 2020?
- Is the vaccine and immunization enterprise moving in the direction needed based on the current environment?

1.3.1 Goals of the Mid-course Review

The NVP Mid-course Review has three primary goals in addressing these three fundamental questions:

1. Identify the top achievements from the first five years (2010 to 2015).
2. Determine the three to five greatest opportunity areas for the timeframe 2016 to 2020, and define what success will look like (outcomes) in each area.
3. Develop indicators or metrics that can be used to track progress against each of the top three to five opportunity areas.

In addition to these primary goals, the Mid-course Review sought to obtain feedback from federal agencies on the objectives and activities that they led in the 2010 NVP and Implementation Plan, respectively. Just as the vaccine landscape has shifted, it is likely that the priorities and activities supported by the federal partners have adjusted accordingly. Updating the alignment of the objectives and activities described in the NVP or Implementation Plan to better reflect federal stakeholder roles and activities will facilitate the coordination and collaboration needed to execute the NVP.

1.3.2 How the Findings Will Be Used

The overriding goal of the NVP is to guide and facilitate national coordination and planning for vaccines and immunizations. Experts across the vaccination ecosystem have identified key areas that, with the right resources, are poised for significant advancement. Although all components of the 2010 NVP are important, these opportunity areas have the potential to make critical advancements in the vaccine and immunization enterprise. The five areas of greatest opportunity identified through the Mid-course Review will guide efforts and evaluation through the remaining Plan horizon. This document is also intended to educate funding officials and the broader immunization community about the future needs of the immunization enterprise, including the new administration that will come into office in January 2017. The findings and considerations laid out in this report establish a framework to help policymakers understand how they can best support the immunization community in preventing morbidity and mortality from VPDs.

Coordination is at the heart of the NVP's purpose. Effectiveness in achieving the goals of the NVP requires agreement on a shared purpose and vision among relevant government entities and coordination of a complex network of actors and activities. Accordingly, the findings of the Mid-course Review will also be used to identify those unmet needs and areas that could benefit the most from optimized coordination.

1.4 National Vaccine Program Office's Role in the National Vaccine Plan

NVPO is charged with organizing the execution of the NVP and communicating its priorities to decision-makers and the public. The NVP delineates the key federal and nonfederal stakeholders that have a role in the NVP's implementation as well as the goals and objectives each stakeholder supports.

NVPO roles include:

- Providing broad oversight of the NVP.
- Coordinating and facilitating activities.
- Identifying and addressing unmet needs.
- Convening federal and nonfederal stakeholders to advise on activities that support the NVP's goals.
- Filling gaps when activities needed do not fall under the purview of a specific agency, including facilitating broad, cross-cutting activities that affect many parts of the vaccine ecosystem.

Examples of NVPO activities include:

- Support of the Institute of Medicine's development of the Strategic Multi-Attribute Ranking Tool (SMART) Vaccines tool to provide the vaccine community with a decision-support framework to prioritize vaccines for R&D.
- Coordination of the Federal Immunization Safety Task Force to bring together federal partners involved in vaccine safety surveillance and science activities across U.S. populations.
- Collaboration with CDC to develop the Long-Term Care Facility Healthcare Provider Toolkit to improve influenza vaccination uptake among health care providers in long-term care facilities.
- Development of the National Adult Immunization Plan to provide a path forward for addressing the barriers to adult vaccination.

1.4.1 Role of the National Vaccine Advisory Committee

The NVAC was established to advise the ASH on the immunization system. NVPO, on behalf of the ASH, turns to the NVAC for advice and guidance on executing the NVP. The NVAC participated in the development of the NVP in 2010 and since then has provided guidance to the ASH on particular topics. Examples of NVAC guidance can be found in the following reports:

- Assessing the State of Vaccine Confidence in the United States: Recommendations from the National Vaccine Advisory Committee (NVAC, 2015c)
- NVAC Statement of Support Regarding Efforts to Better Implement IIS-to-IIS Data Exchange Across Jurisdictions (NVAC, 2015b)
- The National Vaccine Advisory Committee: Reducing Patient and Provider Barriers to Maternal Immunizations (NVAC, 2015a)
- Enhancing the Work of the Department of Health and Human Services National Vaccine Program in Global Immunization: Recommendations of the National Vaccine Advisory Committee (NVAC, 2014b)
- Recommendations from the National Vaccine Advisory Committee: Standards for Adult Immunization Practice (NVAC, 2014a)
- Protecting the Public's Health: Critical Functions of the Section 317 Immunization Program — A Report of the National Vaccine Advisory Committee (NVAC, 2013)
- A Pathway to Leadership for Adult Immunization: Recommendations of the National Vaccine Advisory Committee (NVAC, 2012)

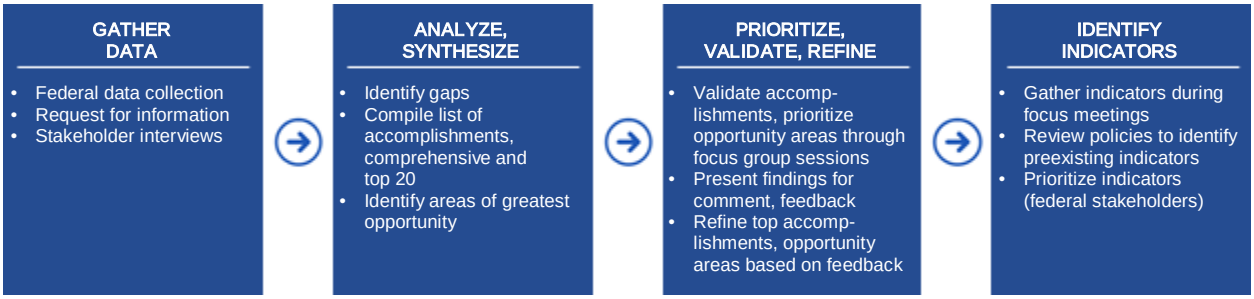
The NVAC also included discussions of the findings presented in the Mid-course Review during public committee meetings held in February and June of 2016. NVAC's independent assessment of these findings will be presented at their September 2016 meeting.

2 METHODOLOGY

A four-step process was used to create the Mid-course Review (Figure 2). During the first step, *Gather Data*, a broad range of input was obtained from the stakeholder community on the top achievements between 2010 and 2015, unmet needs or gaps, and the greatest opportunities for the next five years (2016 to 2020). The three activities used to obtain input included gathering

reports from federal agencies, a request for information (RFI) to nonfederal stakeholders (80 FR 61214), and stakeholder interviews[1]. In the second step, the information collected during the data-gathering effort was *analyzed and synthesized* into a list of the top achievements and greatest areas of opportunity. The third step in the process was to present identified achievements and opportunity areas to stakeholders for *validation, prioritization, and refinement,* as needed. Finally, in the fourth step, *identify indicators*, indicators that could be used to monitor progress against each prioritized opportunity area were identified. The following sections describe the methods used for each of the steps in Figure 2 in more detail.

Figure 2: Overview of the Mid-course Review Methodology



2.1 Data Gathering

To obtain broad input from the stakeholder community, three activities were used to capture input about progress achieved against the NVP from 2010 through 2015: (1) a review of data submitted by federal stakeholders, (2) an RFI from nonfederal stakeholders, and (3) stakeholder interviews with nonfederal experts in the field of immunization. Through these three mechanisms, information was gathered about the gaps and the direction needed for the next five years to ensure significant progress by 2020. The primary and secondary sources of data were qualitative. The data gathering took place between September and December 2015. Additional information is available in Appendix A: Data-Gathering Methods. Information collected through the posted RFI to nonfederal stakeholders was not subject to Chapter 35 of Title 44, United States Code (U.S.C.) — the Paperwork Reduction Act — as indicated in 42 U.S.C. 300aa-1 note (section 321 of Public Law 99-660).

2.2 Synthesis of Achievements and Opportunity Areas

The inputs from the federal agency reports, RFI, and stakeholder interviews were synthesized into a comprehensive list of achievements and opportunities, making note of those achievements or opportunity areas mentioned more than once or from more than one source. The comprehensive list of achievements and opportunities was further prioritized as described in Appendix B: Synthesis of Achievements and Opportunity Area Methods.

[1] While numerous stakeholders contributed to the Mid-course Review process, it is important to note that this work is the product of HHS.

2.3 Validation and Prioritization of Findings

Having synthesized the draft list of top 20 achievements as defined by stakeholders (federal and nonfederal) as the most noteworthy, and a comprehensive list of 10 opportunity areas, the next step was to validate the achievements and opportunity areas, and then prioritize them using stakeholder input. Appendix C: Validation and Prioritization of Findings Methods, describes how stakeholders were engaged to help validate and prioritize the achievements and opportunity areas initially identified. The criteria and methodology used to select the five opportunity areas are also included in Appendix C: Validation and Prioritization of Findings Methods.

2.4 Identify Indicators

An important feature of the Mid-course Review is the designation of indicators or metrics that can be used to monitor progress against the prioritized opportunity areas. During focus group sessions, participants were asked to identify potential metrics that could be used to monitor progress against opportunity areas. After the focus group session, a scan of applicable policies and strategic frameworks was conducted to identify potentially relevant metrics and added to the list of potential metrics that focus group participants identified. From these two sources, a list of 59 potential metrics was synthesized.

During the federal stakeholder interviews, participants were asked to review the list of potential metrics identified and comment on which metrics, if any, they thought would work well as indicators of the opportunity areas identified in the Mid-course Review. The goal was to identify two or three indicators against each of the top five opportunity areas for a total of 10 to 15 indicators. Developing new indicators is resource intensive and creates the potential for duplication of effort. For these reasons, the focus was on identifying preexisting metrics, where possible, that could be used to monitor progress against the opportunity areas identified by the Mid-course Review. Federal stakeholder feedback was tracked and used to develop the final list of 16 metrics.

3 Findings

The three overarching goals of the Mid-course Review were to identify:

- Top achievements in the timeframe 2010 to 2015 against the NVP.
- Areas of greatest opportunity in the next five years (2016 to 2020).
- Preexisting indicators that can be used to monitor the overall health of the vaccine ecosystem as well as progress against each priority opportunity area identified in the next five years (2016 to 2020).

This section describes the findings in each of these three areas.

Two cross-cutting themes emerged across all areas of emphasis: collaboration and capitalizing on technology. ***Collaboration was essential for many of the successes achieved in the past five years.*** Examples of productive collaborations included everything from interagency collaboration at the federal level, to collaborations among federal and nonfederal stakeholders, and partnerships among nonfederal groups. Collaborations contributed to the major achievements across all five goals, and many of the successes highlighted in the achievement

section were the product of a joint effort between two or more stakeholders. Collaborations will continue to play an increasingly important role in the vaccine ecosystem as the complexity of the challenges continues to rise, particularly in the health information technology (IT) arena.

Capitalizing on advances in technology was also an important theme*,* both in terms of the progress that has occurred in the past five years and the types of activities that will be needed to make significant advances in the next five years. Over the past five years, technological advancements contributed to the progress toward nearly every goal in the NVP. One particularly exciting area underway is focused on new platforms with the potential to accelerate the development of vaccines to prevent new and emerging diseases. The trend toward the increased uptake and use of technology extends beyond the vaccine ecosystem to the entire health care enterprise both domestically and globally. For this reason, many stakeholders thought that the next five years would be particularly fruitful in terms of addressing some of the policy issues that often accompany technological advances, such as the legal ramifications of data sharing.

3.1 ACHIEVEMENTS

A synthesis of the top achievements, with input from a broad range of stakeholders across the vaccine ecosystem, emphasized where the major successes have occurred as well as areas where progress is needed (Appendix B). Table 1 provides an overview of game-changing achievements that have had a significant impact on the vaccine ecosystem since the current NVP was originally created in 2010. Additional background, discussion, and analysis of the achievements in each goal area is provided after Table 1.

Table 1: Top Achievements, 2010 to 2015

Goal	Achievements
Goal 1 — Develop New and Improved Vaccines	• New vaccines coming to market and new indications for existing vaccines (e.g., human papillomavirus [HPV], MenB, pneumococcal disease) • Improvements in the influenza vaccine, including the use of cell-based technologies, adjuvants, recombinant DNA, quadrivalent vaccines, and high-dose vaccines, and new delivery technologies (e.g., Jet Injector and ID injection) • Basic research to improve our understanding of the host immune response, especially as it relates to vaccination • Vaccines resulting from strong public-private development partnerships, such as MenAfriVac®, ROTAVAC®, and Ebola vaccines
Goal 2 — Enhance the Vaccine Safety System	• U.S. safety systems (Postlicensure Rapid Immunization Safety Monitoring [PRISM], Vaccine Safety Datalink [VSD], and Vaccine Adverse Event Reporting System [VAERS]) are robust and effective, with good collaboration at the federal, state, and local levels • Global leadership from the USG on the use of new technologies to produce safer, more effective vaccines (i.e., FDA's role in developing WHO Guidelines on the Nonclinical Evaluation of Vaccine Adjuvants and Adjuvanted Vaccines) • Ability to rapidly acquire and analyze safety data during an emergency (e.g., WHO data sharing in the context of public health emergencies)

Goal	Achievements
Goal 3 — Support Communications to Enhance Vaccine Decision-Making	• Implementing collaborative, comprehensive approaches to promote vaccine uptake (e.g., HPV vaccination among adolescents) • Engagement and collaboration on efforts to better understand and increase parent, health care provider, and public confidence in recommended vaccines and immunizations • Broad federal and nonfederal collaboration to help foster recognition of the value of vaccines and the importance of immunization recommendations among policymakers and public health advocates
Goal 4 — Ensure a Stable Supply of, Access to, and Better Use of Recommended Vaccines in the United States	• Reducing financial barriers: near-universal coverage for children and first-dollar coverage under the Affordable Care Act • National Vaccine Injury Compensation Program (VICP) and Countermeasures Injury Compensation Program (CICP) compensation programs addressed critical safety and liability factors; both programs are working well • Continued high vaccine coverage rates for pediatric vaccines and increased coverage rates observed across the lifespan and in special populations, including pregnant women • Development and Promotion of NVAC's Standards for Adult Immunization Practices and the release of HHS' National Adult Immunization Plan to help improve coverage rates among adults and foster vaccine and vaccine-related innovation • Updated preparedness and response framework for influenza pandemics including development of CDC's Influenza Risk Assessment Tool • Improving access to and acceptance of vaccination providers in nontraditional health care settings (e.g., pharmacists, public health departments) • Advances in the use of health IT, including pilot projects to demonstrate the utility of two-dimensional bard codes and development of Immunization Information System (IIS) query/response standards
Goal 5 — Increase Global Prevention of Death and Disease Through Safe and Effective Vaccination	• Progress against global elimination goals, including polio, measles, and rubella • Endorsement of the GVAP from 194 countries at the 65th World Health Assembly to set a united, global vision for a world free of VPDs • Introduction of new vaccines into Gavi-eligible countries

3.1.1 Achievements Toward Goal 1: Develop New and Improved Vaccines

This section highlights top achievements in the 2010 through 2015 timeframe against Goal 1, Develop New and Improved Vaccines.

Since 2010, several new vaccines have come to market:

- In February 2010, FDA licensed a new pneumococcal conjugate vaccine that increased coverage from seven to 13 pneumococcal serotypes for infants and young children.
- Since 2010, FDA has licensed six new quadrivalent influenza vaccines for infants, children, and adults.
- In 2014, FDA licensed the first vaccines to prevent meningococcal type B disease. Also in 2014, FDA approved an HPV vaccine that expanded protection from certain cancers from four to nine viral strains.

- In 2013, FDA licensed the first adjuvanted influenza vaccine for use during a pandemic. In 2015, FDA licensed the first seasonal influenza vaccine to contain an adjuvant for use in the elderly.

Public-private partnerships also played a noteworthy role in developing and bringing several important new vaccines to market, predominantly for use in the developing world, including:

- MenAfriVac, released in 2010, which has played a critical role in breaking the cycle of meningitis A epidemics in Africa. MenAfriVac is the result of a partnership among WHO, PATH, FDA, the U.S. Agency for International Development (USAID), the Bill & Melinda Gates Foundation, the Michael & Susan Dell Foundation, Gavi, the United Nations International Children's Emergency Fund (UNICEF), and others
- ROTAVAC, a new rotavirus vaccine licensed in 2014 that was developed through a public-private partnership among NIH, PATH, and Bharat Biotech, a private Indian biotechnology company, for manufacturing, licensure, and use in India
- Ebola vaccine candidates (2) entered phase 2 clinical trials in West Africa in 2015 through clinical research partnerships with NIH and CDC.

In 2015, FDA licensed BioThrax®, a vaccine to protect against anthrax, for a new indication. Initially developed and licensed for pre-exposure prophylaxis, FDA approved a supplemental Biologics License Application for the prevention of disease following suspected or confirmed exposure to Bacillus anthracis *for people 18 through 65 years of age in conjunction with recommended antibiotic treatment. ASPR/BARDA led and supported the research needed for this expanded indication.*

In addition to new vaccines, stakeholders noted that there have been significant improvements to existing vaccines, particularly for influenza. Improvements to the influenza vaccine include the approval and use of quadrivalent formulations as well as vaccines produced using new cell-based and recombinant DNA production platforms. In 2012 and 2013, FDA licensed six new vaccines, including four quadrivalent vaccines, to prevent seasonal influenza: Flucelvax®, Flublok®, Fluarix Quadrivalent, FluLaval Quadrivalent, FluMist Quadrivalent, and Fluzone Quadrivalent. NIH, ASPR/BARDA, FDA, and vaccine manufacturers played critical roles in the development of these vaccines. NIH also supported the development of Fluzone Intradermal, which is administered intradermally and uses less antigen than the influenza vaccine injected intramuscularly.

Although the vision of a universal influenza vaccine has yet to be realized, NIH-supported activities have helped achieve significant progress toward this goal. NIH has helped characterize novel biomarkers and correlates of protection for influenza vaccines, including the role of broadly neutralizing antibodies and molecular determinants of cross-reactive antibodies, to inform the rational design of universal influenza vaccines. NIH researchers are assessing nanoparticle vaccine platforms to improve the potency and breadth of influenza virus immunity. NIH is also collaborating with academic researchers and biotechnology companies to develop promising clinical candidates using a variety of immunizing proteins and adjuvants to stimulate a vigorous response.

FDA is also conducting research on influenza vaccines, developing new and improved methods for characterizing vaccines, measuring the protective immune response elicited by vaccination,

and improving vaccine manufacturing. Examples include efforts to expedite reagent preparation, develop improved candidate vaccine viruses, and develop and evaluate improved assays for measuring vaccine potency. Other studies at FDA focus on identifying correlates of protection for seasonal and pandemic influenza vaccines, developing better methods of measuring the immune response to novel vaccine platforms, and evaluating the safety and potential benefit of adjuvants to improve vaccine effectiveness. FDA, as one of four WHO Essential Regulatory Laboratories, collaborates with other WHO Essential Regulatory Laboratories and WHO Collaborating Centers in studies to determine the vaccine composition of seasonal influenza vaccines and develop candidate vaccine viruses for strains of influenza with pandemic potential.

The elderly are at high risk for influenza complications. In December 2009, FDA licensed a high-dose trivalent inactivated influenza vaccine (TIV) for adults aged 65 years and older. FDA researchers collaborated with other federal partners to measure the effectiveness of this high-dose influenza vaccine compared to standard-dose TIV in Medicare beneficiaries aged 65 years or older by obtaining outcomes from Medicare claims for primary care and hospital services. This work, published in Lancet Infectious Disease *(Izurieta et al., 2015), is the first assessment of effectiveness of the high-dose vaccine in preventing influenza-related hospitalizations. In this large population-based study of the U.S. elderly, the high-dose vaccine was 20 percent more effective than standard-dose vaccine.*

Basic research underpins all vaccine successes. Stakeholders highlighted the significant improvement basic research has made over the past five years in our understanding of the host immune system. For example, advances in molecular imaging techniques have made it possible to investigate the mechanism by which RNA viruses like respiratory syncytial virus (RSV) evade the innate immune system. Application of virtual modeling techniques enabled researchers to develop a three-dimensional computer model of a lymph node so that scientists could study T-cell trafficking, activation, dynamics, and efficiency of priming and clonal expansion under different conditions. Basic research initiatives such as the NIH B Cell Epitope Discovery Program have also helped identify and characterize neutralizing antibodies against such infectious agents as influenza, smallpox, hepatitis C, dengue, chikungunya, and Lassa fever. The findings from basic research will help pave the way for more effective vaccine design.

In addition to advancing basic research, NIH supports a variety of mechanisms to translate these discoveries into candidate products. Through its Partnerships Program, NIH encourages new research collaborations among experts from different disciplines of academia and industry and ensures that basic research findings and technologies are translated into new product-development approaches. In addition, the National Institute of Allergy and Infectious Diseases (NIAID) offers a suite of preclinical services to the infectious diseases research community that provide access to microorganisms, research reagents, and developmental services that can fill knowledge gaps critical to scientific research and moving products along the development pathway. These services also act to lower the risk to potential commercial partners. Furthermore, the work being done at the Vaccine Research Center at NIH was noted for the important role it plays in bridging the gap between basic research and product development. ASPR/BARDA also plays a critical role in product development and technology modernization as well as providing the resources and expertise for development of emerging disease vaccines — for example, influenza H5N1, Ebola, chikungunya, and Zika. ASPR/BARDA

continues to invest in novel vaccine production methods that would enable faster manufacturing in the event of an emergency. For example, they are supporting continuous manufacturing, a manufacturing method that integrates the production process steps into a single production stream. ASPR/BARDA, in collaboration with manufacturers, also continues to address the issue of seasonal influenza vaccines that sometimes may not be an optimal match for circulating strains. In conjunction with CDC, FDA, and NIH, ASPR/BARDA is supporting efforts to address the emergence of a significantly drifted influenza virus later in the vaccine development and production cycle and to incorporate better matched strains into the vaccine composition.

3.1.2 Achievements Toward Goal 2: Enhance the Vaccine Safety System

Stakeholders engaged during the Mid-course Review, including safety experts, consistently said that the U.S. safety system is robust and working well. Of all the goals, this one consistently received feedback that progress was being made.

Through the Defense Health Agency, DOD collaborates with FDA on postlicensure studies of vaccines that protect service members but are not routinely administered to the public, including 21st-century smallpox, anthrax, adenovirus, and Japanese encephalitis virus vaccines.

Among the adverse event reporting databases, both VSD and PRISM were noted as being particularly active and producing high-quality, useful data. Many stakeholders also indicated that our ability to rapidly acquire and analyze safety data has improved significantly over the past few years. Great progress has been made in digitizing some of the major adverse event reporting systems and improving the timeliness of data collection, including the VAERS. In 2015, FDA and CDC fully implemented eVAERS, an electronic reporting system for manufacturers. By the end of 2017, CDC and FDA expect to complete the VAERS website updates and database architecture changes to accommodate electronic reporting by consumers, health care providers, and manufacturers. When these steps are complete, electronic reporting is expected to rise from the current 25 to 30 percent to more than 75 percent.

Several federal agencies, including FDA and CDC, were also noted for providing global leadership on vaccine development. For example, FDA collaborated with other national regulatory authorities to develop the WHO guidelines on the Nonclinical Evaluation of Vaccine Adjuvants and Adjuvanted Vaccines. The WHO Expert Committee on Biological Standardization adopted the guidelines in October 2013. Likewise, CDC has provided technical support to develop the WHO's Global Vaccine Safety Blueprint that will assist low- and middle-income countries develop the capacity for vaccine safety assessments and responses. Stakeholders felt that the breadth, depth, and quality of vaccine safety reports published over the past five years are indicative of the USG's commitment to vaccine safety.

3.1.3 Achievements Toward Goal 3: Support Communications to Enhance Vaccine Decision-Making

Collaboration was an overarching theme in the achievements mentioned for Goal 3. The collective, cooperative efforts of stakeholders throughout the vaccine ecosystem, including both federal and nonfederal stakeholders, has helped improve the recognition of vaccines as an issue of importance and increased the prominence of vaccines as a policy and advocacy issue. The National Cancer Institute at NIH supports continued research to improve HPV vaccines and

HPV vaccine uptake, including support of The President's Cancer Panel's report titled Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. Although stakeholders were quick to note that HPV vaccination rates are still far from ideal, they did note that the comprehensive communication approach taken with the HPV vaccine was an excellent model and one that will likely lay the groundwork for improved HPV vaccination rates. This model is guided by CDC, which is working with several partners and stakeholders to improve HPV vaccine coverage. CDC has awarded cooperative agreements to 22 state and local immunization programs to help increase HPV coverage through implementation of strategies targeted at immunization providers, including development of jurisdiction-wide joint initiatives with immunization stakeholders. CDC has also funded several national partner organizations that are undertaking activities to improve HPV vaccine coverage. In 2015, CDC with the American Cancer Society (ACS) convened a National HPV Roundtable to bring together a network of organizations involved in cancer prevention, immunization, health care delivery, and public health to discuss barriers to HPV vaccination and develop pilots to address them. CDC, by funding ACS and other partner organizations, can focus on systems barriers and challenges that remain because of health disparities and the misperceptions of providers and consumers on the risks and benefits of HPV vaccination. Stakeholders believe that the information gathered through such nationwide projects will guide future efforts and ultimately increase vaccination rates and save lives.

In 2014, CDC published a paper in the Morbidity and Mortality Weekly Report *on the benefits of the Vaccine for Children (VFC) program since its implementation in 1994. The findings from this paper included analysis of both immunization coverage and the economic impact of the VFC program in the United States. Coverage for the childhood vaccine series was near or above 90 percent for much of the period. Modeling estimated that among children born between 1994 and 2013, vaccination would prevent an estimated 322 million illness, 21 million hospitalizations, and 732,000 deaths over the course of their lifetimes at a net savings of $295 billion in direct costs and $1.38 trillion in total societal costs. The impact of this work has further justified continued prioritization of childhood vaccination as a preventive measure. (NIH Office of Science Policy, 2016).*

3.1.4 Achievements Toward Goal 4: Ensure a Stable Supply of, Access to, and Better Use of Recommended Vaccines in the United States

Significant progress has been made against Goal 4 in the 2010-2015 timeframe. Passage of the Affordable Care Act helped reduce the financial and systems barriers to vaccination, including a provision for first-dollar coverage for adult vaccinations among eligible health plans. The promotion of NVAC's Standards for Adult Immunization Practices, (NVAC, 2014a) and development of HHS's first National Adult Immunization Plan will also help improve coverage rates among adults, particularly in light of the work federal agencies are doing to promote implementation of the adult standards. For example, the Indian Health Service (IHS) and CDC partnered to develop a video on the implementation of the Standards for Adult Immunization Practices in the IHS. The IHS also partnered with the Northern Plains Tribal Epidemiology Center and HHS Region 7 to develop a video public service announcement on adult immunizations — specifically, influenza — for use in clinical waiting rooms through Good Health TV, a subscription-based health education channel targeting Native Americans that is currently in place in more than 90 IHS and tribal clinics across the United States.

The improved access to and acceptance — by both consumers and payers — of vaccine being administered in nontraditional settings such as pharmacies and public health departments, has helped reduce the systems barriers to vaccination. Together, these achievements have helped improve vaccine coverage rates across the lifespan and among special populations, such as pregnant women. These achievements also helped ensure that pediatric vaccine coverage rates remain high.

In addition to the achievements made in reducing consumer financial and systems barriers to vaccination, advances in health IT have enabled better tracking of vaccine coverage rates. Among health IT achievements, adoption of scanable, two-dimensional (2-D) bar codes will enable more comprehensive tracking of vaccines. By providing important information about the vaccine unit, such as the lot number and expiration date, 2-D bar codes have the potential to improve safety tracking. This technology also lays the foundation for more advanced forms of clinical decision support. The development of IIS query and response standards has increased the interoperability of IISs and laid the groundwork for improved and efficient bidirectional communication between systems.

For the past several years, FDA, the American Academy of Pediatrics, and CDC have been working together to enable the use of 2-D bar codes on vaccines. The market shift began in 2011, when FDA issued guidance that opened the door for placing alternative symbology on vaccine products, stating that FDA would consider exemption requests from vaccine manufacturers who request use of 2-D bar codes containing, for example, the expiration date in lieu of linear bar codes. This has had a significant impact on the adoption of 2-D bar code scanning and demonstrates the collaborative efforts of key industry players. U.S. vaccine manufacturers have introduced 2-D bar codes on the majority of products currently shipping. The adoption of 2-D bar codes will help improve vaccine ordering, distribution, and tracking systems, both for routine use and in times of public health emergency. Providers who use 2-D bar codes have also acknowledged the potential for time savings.

Finally, several significant achievements have enabled the safe delivery of vaccines, even during a public health emergency response. CDC has developed new storage and handling guidelines as well as training that will help improve the availability and quality of vaccines. Expanded seasonal influenza vaccine supply, a result of both increased demand and capacity-building for pandemic preparedness, was a major achievement during the past five years. This greatly improved production capacity has gone a long way toward ensuring sufficient supply in the event of an emergency.

3.1.5 Achievements Toward Goal 5: Increase Global Prevention of Death and Disease Through Safe and Effective Vaccination

Globally, one of the top achievements that stakeholders noted during the Mid-course Review was the endorsement of the GVAP in 2011 at the 65th World Health Assembly. Stakeholders highlighted the monitoring and evaluation in the GVAP annual report that identifies and flags areas at risk or off course. This approach was highly praised as attention is brought to the areas in most need of additional support.

Stakeholders also noted that the global immunization coverage rate is the highest it has ever been. The work that Gavi is doing to introduce new vaccines to developing countries was highlighted as a significant achievement and a major contributor to improving global vaccine

coverage rates. Since 2010, USAID has provided country-tailored technical assistance to 22 countries, including Gavi proposal development and preparations for new vaccine introduction. USAID country-level bilateral projects have also supported routine immunization system strengthening and service-delivery activities, with the aim of optimizing the agency's global investment in Gavi for vaccine purchases and health systems strengthening. For example, in 2013 to 2014, USAID supported the deployment of two new life-saving vaccines in Tanzania — pneumococcal conjugate and rotavirus — marking only the second time a low-income country has executed a dual launch of vaccines. USAID supported this significant effort beginning almost a year in advance of the official launch, supporting cold chain assessments, developing learning materials, conducting training, revising and distributing management tools, and developing communications strategies and key messages. Through contributions to the Government of Tanzania, coverage rates are expected to reach 80 to 90 percent, with an anticipated decline in mortality to follow. In 2015, USAID pledged an additional $1 billion to Gavi over four years, subject to congressional approval, in support of the Gavi strategy to immunize an additional 300 million children and save 5 million lives by 2020.

CDC's Global Immunization Division (GID) provides support across most phases of the vaccine life cycle globally, from research, innovation, and evaluation to global immunization policy development. For example, CDC GID and the Division of Viral Diseases serve as principal investigators on studies with industry to develop microneedle patches for vaccine delivery, a technology that could help with global vaccine distribution by simplifying cold chain requirements. They have used collaborative strategies to improve vaccine acceptance, such as working with Voice of America in Nigeria to provide journalists with training to improve the quality and frequency of media reporting on vaccines. CDC GID is also a co-lead on Strengthening Surveillance and Response in Central Africa, a multicountry project centered in Africa that supports integrated disease surveillance and response for VPDs.

Equally important to the progress that has been made in increasing coverage rates is the work that has been done to improve the global public health capacity that supports the immunization enterprise. For example, USAID has supported the training of thousands of district and front-line health workers around the globe on various topics of immunization, such as estimating target population, vaccination coverage, and dropout and wastage rates; performing vaccine stock management; developing and using coverage monitoring charts; and preparing reports. Not all global elimination efforts are progressing as well as hoped, but the polio elimination effort has made significant progress, particularly in Africa, where there has been one year without a single case and one strain, Type 2, has been eliminated and declared eradicated globally.

3.2 Opportunity Areas Identified by Stakeholders

A primary goal of the Mid-course Review was to identify three to five opportunity areas primed for major progress in the next five years. Although the goals, objectives, strategies, and priorities initially set forth in the 2010 Plan remain important, the opportunity areas identified through the Mid-course Review identify where additional focus could result in significant achievements within the next five years.

During the focus group sessions and one-on-one interviews, stakeholders were asked to prioritize and rank the 10 opportunity areas that emerged from the initial data-collection effort (see Section 2.3, Validation and Prioritization of Findings, for details of the methodology). There was strong consensus among federal and nonfederal stakeholders on the prioritization of the top five opportunity areas. As shown in Table 2, there is a clear segregation of the average scores, with lower being better (see Appendix B: Synthesis of Achievements and Opportunity Area Methods for details), between the top five and bottom five opportunity areas. Three of the opportunity areas were ranked among the top five selections by all three focus groups, albeit not in the same order. These three opportunity areas, the first three in Table 2, all focus on the overarching goal of increasing immunization coverage.

Table 2: Opportunity Areas as Ranked by the Stakeholder Focus Sessions (Presented in Order from Highest Ranked to Lowest Ranked)

Opportunity Area Ranked By Stakeholders	Average Score (Lower Is Better)
Strengthen health information and surveillance systems to track, analyze, and visualize disease, immunization coverage, and safety data both domestically and globally.	2.50
Foster and facilitate efforts to strengthen confidence in vaccines and the immunization system to increase coverage rates across the lifespan.	2.75
Eliminate financial and systems barriers for providers and consumers to facilitate access to routinely recommended vaccines.	3.50
Strengthen the science base for the development and licensure of vaccines.	3.50
Facilitate vaccine development.	4.25
Increase coordination, collaboration and knowledge sharing among related parties and disciplines.	7.25
Improve the transparency of the vaccine safety system and the entire vaccine enterprise to policymakers, the public, and providers.	7.50
Improve scientific knowledge about why and among whom vaccine adverse events occur.	7.75
Support the strengthening of immunization systems globally through policies, practices, and partnerships.	7.75
Improve surveillance for VPDs, and strengthen health information systems to monitor vaccine coverage, effectiveness, and safety both domestically and globally.	7.75

Two other opportunity areas — *strengthen the science base for the development and licensure of new vaccines* and *facilitate vaccine development* (listed fourth and fifth in Table 2) — also garnered clear consensus. Two of the three focus groups, including one federal and one nonfederal focus group, ranked these two opportunity areas among their top five. Both of these opportunities focus on improving the process for bringing new vaccines to market.

During the prioritization process many stakeholders thought that a few of the opportunity areas could be consolidated. Accordingly, some of important themes from areas that were not selected have been incorporated into the top areas. Table 3 summarizes these opportunity areas, including descriptions of possible activities, challenges, and what stakeholders suggested success could look like by 2020.

Table 3: Summary of Opportunity Areas: Description, Challenges, and Characteristics of Success as Identified by Stakeholders

Opportunity Area	Description	Challenges	Characteristics of Success
Strengthening health information and surveillance systems to track, analyze, and visualize disease, immunization coverage, and safety data both domestically and globally	• Increasing and improving use of IISs, electronic health records (EHRs) and interoperable technology • Increasing decision support tools for consumers and providers (e.g., forecasting) • Improving infrastructure to support global safety data • Developing tools and technology for real-time global surveillance of infectious disease patterns and vaccine coverage data • Strengthening capabilities to use health IT to enable end-to-end vaccine tracking	• Enabling bidirectional communication between IISs and EHRs • Getting the necessary legal documents in place to facilitate data sharing across jurisdictions • Interoperability between systems • Presenting data in a manner that facilitates decision-making • Making data available to all relevant stakeholders, including consumers • Making data available in real time	• Bidirectional communication between EHRs and IISs, increasing the amount and robustness of data stored in IISs; use of EHR and claims data to provide granularity to specific populations (e.g., vaccine coverage by geographic location, race/ethnicity, age) • Reducing barriers that limit connectivity to IISs • Increasing decision support tools available to make data actionable • All stakeholders, including consumers, providers, and third parties like schools, can access immunization data • All countries have a system for spontaneous reporting of adverse events following immunization (AEFIs) and investigating those that are serious
Fostering and facilitating efforts to strengthen confidence in vaccines and the immunization system to increase coverage rates across the lifespan	• Ensuring that providers have the tools necessary to effectively educate and communicate the benefits and risks of recommended vaccines • Pragmatic studies that evaluate education and communication materials in real-world settings, including their impact on behavior • Improving adherence to the Advisory Committee on Immunization Practices (ACIP)-recommended schedule	• Identifying under-vaccinated populations • Lack of metrics to facilitate understanding of vaccine confidence, particularly among different socioeconomic populations • Fostering vaccination acceptance in special populations, such as pregnant women, the elderly, and immune-compromised individuals • Communicating an increasingly complex schedule to providers and consumers • Addressing misperceptions about the benefits and risks of vaccination • Ensuring that vaccination remains the societal norm	• Robust coalition building at the local level (e.g., supporting local community groups to disseminate key messages about vaccines) • Increasing toolkits and resources available for providers • Tailoring communications and messaging to reach special populations (e.g., pregnant women) • Decreasing geographical pockets of low vaccine coverage

Opportunity Area	Description	Challenges	Characteristics of Success
Eliminating financial and systems barriers for providers and consumers to facilitate access to routinely recommended vaccines	• Identifying and addressing financial barriers that limit a provider's ability to offer vaccines • Improving accessibility of vaccines for consumers • Reducing financial barriers for Medicare and Medicaid beneficiaries	• Reducing financial and process barriers for providers to offer vaccines • Providing consumers access to their immunization records so that they know which vaccines they need • Addressing differences in coverage between states under Medicaid • Different rules applying to vaccines covered under Medicare Part B and Part D, which may affect access and affordability • Ensuring that vaccines are available at a time and location convenient for consumers • Not all providers are considered "in network," thereby reducing access to vaccines, particularly in rural areas	• Resources exist to streamline the administrative process for providers to offer vaccines • Making all ACIP-recommended vaccines readily available to consumers • All providers are covered as in network for the purposes of administering vaccines for private health plans
Strengthening the science base for the development and licensure of vaccines	• Improving understanding of the host immune response • Improving understanding of pathogen biology and host-pathogen interactions • A more thorough appreciation of how aging affects the immune response (immune senescence) • Identifying new correlates of protection • Improving understanding of why and among whom adverse events occur • Lack of surveillance and burden of illness data	• Developing the knowledge base for targeted vaccine design • Addressing scope and complexity of the research required to improve understanding of the human immune response • Encouraging new activity and approaches to scientifically intractable challenges for vaccine development (e.g., universal influenza vaccine, human immunodeficiency virus [HIV], tuberculosis [TB])	• Availability of new vaccine-delivery methods • Improving existing vaccines (e.g., improving duration of protection for pertussis vaccines) • Licensing new and existing vaccines for use in pregnancy • Use of any identified correlate of protection in clinical development programs. • Understanding population differences in the human immune response and how to adjust for these differences • New vaccines in the pipeline against scientifically intractable problems/diseases

Opportunity Area	Description	Challenges	Characteristics of Success
Facilitating vaccine development	• Developing programs or incentives that reduce the risks of vaccine development • Identifying incentives to improve existing vaccines • Increasing public-private partnerships through phase 2 to reduce development risks • Implementing a process for prioritizing vaccine targets in light of changing environments and new opportunities	• Suboptimal global manufacturing capacity • Differences in regulatory requirements globally between different regulatory bodies • Infrastructure to support rapid vaccine development and delivery in a crisis (e.g., platform technologies)	• Shared risk-taking for vaccine development • Robust pipeline of vaccines in development • Decreasing the average amount of time needed to move vaccine candidates through the pipeline • Developing new models to address emerging infectious diseases • Converging global regulatory standards • Infrastructure in place to support research globally, including understanding the effectiveness and demand for vaccines

Sections 3.2.1 through 3.2.5 present a fuller description of each opportunity area, with examples of the types of planned or ongoing activities that support each opportunity. Although none of the five opportunity areas focuses exclusively on global issues, all the top five opportunity areas are relevant globally. Sections 3.2.1 through 3.2.5 discuss the global implications of each opportunity area.

3.2.1 Strengthen Health Information and Surveillance Systems to Track, Analyze, and Visualize Disease, Immunization Coverage, and Safety Data Both Domestically and Globally

Stakeholders consistently stressed the importance of surveillance as a top need for the coming five years. The need for timely and accurate data is critical for most aspects of the work that needs to occur in the immunization ecosystem and is essential for decision-making. The types of surveillance data needed include tracking the prevalence of VPDs, immunization coverage, and vaccine safety both domestically and globally. Advances in the health IT arena will enable tracking of such data with greater accuracy and timeliness than ever before.

Health IT will continue to be a major policy issue over the next five years, and the immunization community should take advantage of that momentum. Chief among the issues discussed on this topic was the interoperability among data systems so that vaccination histories are accurately recorded. Stakeholders felt the availability of vaccination services in nontraditional settings will only continue to grow. This, combined with an increasingly mobile population in which individuals may receive care across jurisdictions, underscores the importance of ensuring that data systems are fully interoperable, with near-real-time access to information so that patients and their health care providers have up-to-date information about which immunizations an individual has had and which they need.

With a concerted effort, many stakeholders thought that IISs capable of sharing immunization data in near-real time could be achieved within the United States in the next five years. In fact, many stakeholders in the health IT arena are already working to make this vision a reality. For example, the Office of the National Coordinator for Health Information Technology (ONC), in collaboration with NVPO and CDC, has launched the Public Health Immunization Pilot Project, an effort developed to address the need to share immunization information across jurisdictional boundaries. The project will create a transport hub, and participating pilot sites will be able to exchange immunization data across jurisdictional boundaries through this centralized hub using adopted and recommended standards for interoperability. The initial pilot will include five states and provides a model that could be used to enable cross-jurisdictional immunization data sharing nationwide. The challenges to implementing a fully interoperable health information system are not strictly technical, however. There will also need to be infrastructure (e.g., technical support) and incentives to encourage robust adoption by the provider community. IISs are an important tool that can improve immunization surveillance. The information they contain is critical during a VPD outbreak response and for safety surveillance.

Obtaining timely demographic information about the unvaccinated is important, particularly for diseases like influenza that have a peak season. To address the need to identify pockets of unvaccinated individuals and better understand the geographical and socioeconomic barriers to vaccination, the U.S. Centers for Medicare & Medicaid Services (CMS) and NVPO partnered to create an interactive influenza vaccination map. This map allows researchers and health care providers to easily visualize and track influenza vaccination rates for Medicare fee-for-service beneficiaries in near-real time using claims data. Information is updated weekly during influenza season; available for every state in the United States; and searchable by demographics, age group, and zip code. The data provided through this tool allow researchers and providers to take more targeted interventions to increase influenza vaccination rates.

Real-time health data are also critical for monitoring the use of vaccines and other health interventions during large-scale public health emergencies. The PHEMCE's Medical Countermeasure (MCM) Monitoring and Assessment Integrated Program Team recently identified the need to continue analyzing EHR data to assess the use of medical countermeasures (including vaccines) in response to a public health emergency such as a pandemic or bioterrorist attack. During an emergency, data may be limited. Ideally, data from EHRs and other preexisting research may contain important signals used to assess safety and effectiveness of MCMs used outside clinical trials during an emergency response.

Globally, there is a need to ensure that appropriate infrastructure is in place to perform postlicensure surveillance for adverse events. The lack of postlicensure surveillance infrastructure can make it difficult or prohibitively expensive for manufacturers to introduce new

vaccines destined for use primarily or exclusively in developing countries. Some work is already underway to address this need. For example, USAID is helping to build the AEFI monitoring system in several countries. USAID provides training for health workers on AEFIs, ensures the availability of AEFI forms at health facility levels, helps develop reporting systems for AEFIs, and assists with the integration of AEFI reporting systems with VPD surveillance systems.

Global surveillance infrastructure needs extend well beyond AEFIs, however. Much of the work being done for disease-elimination initiatives, such as the Global Polio Eradication Initiative (GPEI), depends on a strong surveillance network to ensure prompt detection to prevent potential outbreaks. Without a strong surveillance network, many of the successes of GPEI, including the 99-percent decrease in polio cases since 1988, would not have been possible. As the lead U.S. scientific agency in GPEI, CDC's GID will continue to support epidemiologic and laboratory surveillance, immunization system strengthening, and training of in-country health care professionals to use real-time data for decision-making, with the goal of finishing the job to eliminate polio. Likewise, USAID continues to support polio-eradication activities that contribute to GPEI, with current annual funding of $59 million. USAID provides financial and technical assistance in support of polio endgame objectives, targeted to the three remaining polio endemic countries (Nigeria, Afghanistan, and Pakistan in 2016), outbreak countries, and countries at high risk of importation. The majority of USAID support is directed at surveillance and outbreak response, communications, social mobilization, and supplementary immunization activities. USAID's approach also emphasizes engagement with local and international nongovernmental organizations (NGOs) and communities, with a particular focus on hard-to-reach, mobile, cross-border, and refugee populations.

3.2.1.1 What Success Will Look Like (Outcomes) in 2020

Stakeholders felt that strengthening health information systems would help ensure robust reporting and use of immunization data in IISs. The amount and completeness of the data available in IISs will increase, and the information will be available as machine-readable data in real time across jurisdictional lines. As consumers are able to access vaccines in more places (e.g., workplace vaccination events, pharmacies) and move geographically more frequently, it will be important to ensure that there is more bidirectional communication between EHRs and IISs. Bidirectional communication will ensure that providers can access current information available in IISs on a consumer's immunization history and send information back to the IIS after an immunization event so that the consumer's vaccination status remains current in the IIS. Immunization coverage data will be available to all who need them, including many that do not currently have access, such as preschools, consumers, and hospitals. An increasing number of records and systems will be in place to track immunizations across the lifespan and in special populations, such as pregnant women, but

Among state IISs, the Wisconsin Immunization Registry (WIR) provides an example of what can be achieved. The WIR houses individual immunization records that integrate information from birth and death records, public and private health providers, and parental records. As a tracking tool, it helps keep children on schedule for recommended immunizations. The WIR also records immunizations, contraindications, and reactions; validates immunization history and provides recommendations; produces recall and reminder notices; and manages vaccine inventory — all at no cost to providers. Consumers can also locate and retrieve their immunization record through the consumer portal at no cost.

additional resources — both human and financial — will be needed for state and local IISs to realize this goal. Adding a provider organization to an IIS can take several weeks, and many IISs have more requests from providers to access the IIS than there are resources in place to support the requests.

Achieving greater interoperability among health information systems will require additional incentives to help drive provider adoption of these systems. Stakeholders indicated the types of incentives that could be used to encourage provider use of IISs include:

- Financial incentives, such as increased reimbursement for providers connected to IISs or increased reimbursement for the administrative processes required to document immunization events.
- Maintenance of certification and licensures for providers tied to requirements for participation in IISs.
- Technical support that is readily available to providers at little to no cost.
- Availability of decision support tools that provide value to participating providers (e.g., forecasting).

To improve the interoperability of immunization data, the U.S. Department of Veterans Affairs (VA) has recently adopted the vaccine administration codes as specified by Health Level 7 data standards. All immunization data are now collected using a standard method that enables interoperability with other health care systems at all 1,500 VA sites nationwide, making it easier to track veterans' immunization records regardless of where in the VA system they are seen.

Making immunization information accessible is only the first step: Decision support tools that help make the data intelligible and actionable to a wide array of stakeholders will also need to be readily available. A broad range of decision support tools will be needed, such as those that help visualize vaccine coverage or disease outbreak data over a geographic area or forecasting tools that help ensure that providers know which vaccines a patient will need to receive at upcoming visits.

3.2.2 Foster and Facilitate Efforts to Strengthen Confidence in Vaccines and the Immunization System to Increase Coverage Rates Across the Lifespan

Although stakeholders consistently agreed that vaccination remained the social norm, many identified consumer confidence in vaccines as a concern, and there was a diversity of opinions on how best to address this challenge. Some thought that a coordinated national campaign with a commercial look and feel would be beneficial, while others emphasized the need for local coalition building and developing additional tools to help providers communicate the importance of vaccines across the lifespan. Many of the stakeholders engaged through the Mid-course Review also emphasized the need to address misperceptions, such as the erroneous impression that vaccines are only for vulnerable populations like children and the elderly.

There was consensus, however, that vaccine-related communications materials need to be tested in a real-world setting and evaluated for their ability to drive the desired behavioral change. Some stakeholders are already testing communication material for its acceptability to consumers. For example, in 2011 and 2013, CDC's influenza program conducted formative research to test the acceptability and clarity of influenza-related research with the general public, at-risk populations, and health care providers. The results from the focus group testing directly informed the revision of key communication materials for those audiences. Continuing

such studies, which evaluate the effectiveness of communication materials prior to release, will be critical.

In 2013 and 2014, CDC awarded 22 Prevention and Public Health Fund immunization awards to help improve HPV coverage. The awardees implemented a comprehensive communication campaign targeted at the public and implemented an IIS-based reminder recall for adolescents 11 to 18 years of age. They also implemented strategies targeted to immunization providers to increase knowledge of HPV-related diseases and improve skills needed to deliver strong, effective HPV vaccination recommendations. Seven of the participating jurisdictions observed statistically significant increases in the first- and third-dose coverage among females 13 to 17 years of age that ranged from 13.2 percent to 28.6 percent, as compared to the 2013 pre-implementation baseline. These successes provide a path forward for strengthening confidence in the future.

In addition to the federal government, support is needed from organizations that have existing ties to the target audience — specifically, health care providers and consumers. These organizations, including professional societies and consumer advocacy organizations, can use the trust they have already established with their constituents to effectively disseminate important information about the benefits and risks of vaccination. In fact, many professional societies and consumer organizations are already actively engaged in developing and disseminating best practices and communication materials about vaccinations to their constituents. For example, between January 2012 and December 2013, the Society for Adolescent Health and Medicine (SAHM) launched a grant program that funded 10 projects aimed at defining effective strategies for increasing vaccination in adolescents, promoting equal access, and disseminating strategies. The findings from these projects were published in an open access supplement of the "Journal of Adolescent Health" in May 2015 and are available on the SAHM website. Some of the cross-cutting themes and strategies that emerged from this work include:

- Increasing awareness among providers about the power of their recommendation to their patients is critical.
- Using technology to track immunization and sending reminders using multiple modalities are helpful.
- Developing culturally and linguistically tailored communication materials is important.
- There is a need to increase access through alternative settings such as mobile vans.

Like SAHM, ACS is active in disseminating key messages about the importance of vaccines and immunizations to providers and consumers. In collaboration with CDC, ACS has organized the National HPV Vaccination Roundtable, a national coalition of organizations that work together to prevent HPV-associated cancers and precancers by increasing and sustaining U.S. HPV vaccinations. The coalition includes government agencies, consumer advocacy organizations, professional societies, and vaccine manufacturers.

At the global level, USAID provides training to a network of community volunteers in several countries. The training covers key vaccination messages, including the benefits, risks, and safety of immunizations for the community.

In addition to consumers and health care providers, policymakers and elected officials are an important target for communication efforts, both domestically and globally. High-quality economic and cost-benefit analyses on vaccines and immunization are critical to ensuring that legislators and policymakers understand the importance of continued support for immunization programs. Ideally, such communication tools will be dynamic and allow for an analysis of alternatives. For example, CDC GID in collaboration with Kid Risk, Inc., has developed an integrated analytical model that answers high-stakes policy questions related to poliovirus risk management. These integrated modeling efforts have included simulations, decision and risk analysis, systems dynamics, and optimization to help policymakers understand the implications of their decisions. These integrated modeling efforts have helped motivate a faster response to polio outbreaks, leading to reduced response times and smaller outbreaks. These models have also helped make the economic case for continued investment in polio eradication by showing the value of prevention in terms of the health and economic outcomes. Moving forward, additional dynamic decision-making tools and communication materials will be needed to articulate the benefits and value of vaccines and immunization both domestically and globally.

CDC's influenza program has collaborated over multiple seasons with nonprofit and provider associations to increase influenza vaccinations in pregnant women. CDC develops targeted outreach communication materials and co-authors letters to providers annually. Collaborators for this work include:

- *American Academy of Pediatrics.*
- *National Foundation for Infectious Diseases.*
- *American Academy of Family Physicians.*
- *American College of Obstetricians and Gynecologists.*
- *American College of Nurse-Midwives.*
- *Association of Women's Health, Obstetric and Neonatal Nurses.*
- *March of Dimes Foundation.*
- *Society for Maternal-Fetal Medicine.*
- *National Medical Association.*
- *National Hispanic Medical Association.*

3.2.2.1 What Success Will Look Like (Outcomes) in 2020

Coverage rates across the lifespan will increase, lowering outbreaks of VPDs and decreasing geographic pockets of low coverage. Provider and public confidence in both vaccines and the entities involved in licensing, recommending, and monitoring vaccine safety will increase while the worry, concerns, and anxiety regarding vaccines, particularly with respect to safety, will decrease. Providers, parents, and the public will also support vaccines as an important and necessary part of our nation's health system. The types of strategies that will help achieve this end could include:

- Implementation of the recommendations in the NVAC confidence report.
- Continued investments and efforts to build the evidence-base for education materials and messages and to evaluate the impact of these efforts prior to use (including prior to use in a large-scale campaign).
- Coalition building at the local level.
- Connecting providers with the tools and resources that enable them to have effective dialogue and interaction with the full spectrum of parents, including those who are hesitant or lack confidence in recommended vaccines and vaccinations.

3.2.3 Eliminate Financial and Systems Barriers for Providers and Consumers to Facilitate Access to All Routinely Recommended Vaccines

As a result of the Affordable Care Act, there has been significant progress in reducing financial barriers to vaccination, but barriers for both consumers and providers remain. First, there are misperceptions among consumers and providers about which vaccines are now covered under the Affordable Care Act. Many consumers are not aware that ACIP-recommended vaccines are now fully covered, with no cost sharing for individuals who have eligible health insurance and receive vaccines at an in-network provider. Likewise, focus group participants raised the issue that many providers are not aware that Category B ACIP recommendations are also fully covered.

One systems barrier to vaccination is that consumers do not have direct access to their immunization records. Without this information, it is difficult for consumers to stay current on their vaccines and discuss with their providers which vaccines they may need to update. To address this challenge, CDC, ONC for Health Information Technology and the NVPO are exploring a solution with launching a pilot project called "MyIR" to give consumers free, on-demand access to state-specific official records, immunization history, and forecasting features. MyIR will aggregate all immunizations administered by providers across the state and enable consumers to add dependents to their account. The data from the first phase of the pilot showed that more than 54 percent of consumers who accessed their immunization record took action, either by scheduling an appointment to receive a vaccination or discussing it with their provider at their next scheduled appointment. These results illustrate that connecting consumers to their immunization data addresses a systems barrier to immunization.

Yet, financial barriers remain. Inconsistencies in Medicaid coverage between states continue to create challenges both for consumers and for providers. Similarly, certain gaps in Medicare Part B and Part D coverage may limit the affordability of some vaccines for Medicare recipients. For example, a recent study suggested that low enrollment of Medicare beneficiaries in Medicare Part D plans could contribute to lower zoster vaccine utilization among adults because of a lack of insurance coverage that could lead to substantial out-of-pocket costs (Hurley et al., 2014).

Finally, some systems barriers for providers will need to be addressed to improve routine access to vaccines. Providers, particularly primary care providers, are currently required to cover many preventive medicine topics during routine appointments. It needs to be easier for providers to cover vaccines as a prominent part of the preventive care discussion. Additional systems barriers for providers include:

- Ensuring that providers, particularly small practices, use savvy business practices to purchase and bill for vaccines.
- Making it simple for all providers, including nontraditional providers, such as pharmacies and state health departments, to be covered as in-network providers for the purposes of administering and billing vaccines.
- Developing guidelines and recommendations on the infrastructure needed for providers in their offices to offer vaccines (for example, refrigerators, back-up generators, etc.) so that healthcare provider groups do not have to spend time researching the requirements.

3.2.3.1 What Success Will Look Like (Outcomes) in 2020

The desired outcome for this opportunity area is that recommended vaccines are readily available to all consumers. Vaccines will be available at the point of care, with no wait time, and no need to make a follow-up appointment to receive a vaccination. Stakeholders felt all consumers should have a provider within a 3- to 5-mile radius of their work or home who offers the ACIP-recommended vaccines they need. Some stakeholders are already taking action to address barriers that limit the accessibility of vaccines. For example, in 2015 the VA partnered with Walgreens to provide influenza vaccines to veterans enrolled in VA health care. Rather than having to go to a VA facility to receive an influenza shot, enrolled veterans could go to any of the more than 8,200 Walgreens sites nationwide and receive an influenza vaccination at no cost.

In addition to systems barriers, many stakeholders emphasized that the financial barriers to some vaccines, particularly for Medicare and Medicaid recipients, need to be addressed. Stakeholders expressed that all providers should also have in-network status with private health care plans for purposes of administering vaccines. Vaccines will be a prominent and integral part of preventive care and a routine part of well-visit appointments. For providers, offering vaccines will be straightforward, with guidelines and documentation available to assist them with equipment procurement, purchasing, and billing. Stakeholders highlighted the need for greater consensus building around what constitutes fair payment both for the cost of the vaccine and the time needed to administer and document it. Many provider professional societies are already taking steps to make this vision a reality. For example, the American Academy of Family Physicians has developed a suite of tools for providers that makes it easier to offer vaccines, including flowcharts, wipeable schedules, mobile apps, and pointers on coding to ensure payment for vaccination services. Likewise, the American College of Physicians offers webinars, quality-improvement guides, and a mentoring program that pairs seasoned immunization providers with providers who want to offer or expand their immunization services. Similarly, the American College of Obstetricians and Gynecologists has created toolkits for health care providers to promote HPV vaccination. The HPV provider toolkit includes tips and strategies for communicating the importance of HPV vaccination to different consumer demographics, a list of frequently asked questions, and a coding card that provides guidance on the Current Procedural Terminology codes to use for HPV vaccine administration.

3.2.4 Strengthen the Science Base for the Development and Licensure of Vaccines

Stakeholders felt that there have been significant scientific improvements over the past five years, but several scientific challenges still need to be addressed. First, for many of the infectious diseases not currently vaccine preventable, the vaccine targets are becoming increasingly complex because pathogens for which no vaccines exist are often difficult to target. New formulations for existing vaccines may also require new technologies for development, manufacturing, or vaccine delivery. In addition, several vaccines currently on the market could benefit from improved performance, such as influenza and pertussis-containing vaccines. In recognition of the limitations of such existing vaccines, some stakeholders are making a targeted effort to improve on existing products. ASPR/BARDA, for example, currently has three programs aimed at developing significantly improved influenza vaccines. In collaboration with CDC, NIH, and FDA, their program will look for new correlates of protection, use of adjuvants to improve performance, and different approaches (e.g., prime boost or live attenuated) that can be used to produce a broader spectrum of protection of longer duration among more age

groups. Additional work is needed to improve the overall understanding of how technologies like adjuvants can be used to optimize vaccine performance.

NIH is using protein structure-based design to improve vaccine development. By solving the structure of various surface proteins for infectious agents, a more targeted approach can be used to design vaccine candidates against these targets. The best example of this work is RSV, where several companies now have candidates under development based on the work done to characterize surface proteins.

Addressing scientific challenges will also require an improved understanding of the host immune response. To this end, NIAID has undertaken a large, collaborative research effort called the "Human Immunology Project Consortium" to develop the knowledge base. This program was launched in 2010 and renewed in 2015. Through the Human Immunology Project Consortium, vaccine responses of well-characterized human cohorts are studied using a variety of analytical tools to better understand the human immune system, its regulation, and the differences between responders and nonresponders. There is also a need to understand and adjust for differences in immune responses and vaccine effectiveness in special populations such as the elderly, where immune senescence is a major challenge, or during pregnancy. The knowledge and insight gained from this effort will be used to develop and evaluate new vaccines and immunization strategies that work in a greater diversity of individuals and help identify those at risk for an adverse event.

To advance the ability to identify those at risk for an adverse effect and improve understanding of the impact of vaccination in special populations it will be important to continue studying the science of vaccine safety. The data from many of the domestic vaccine surveillance databases, including VSD and PRISM, are already being used to evaluate the safety of vaccination during pregnancy. For example, CDC has initiated contracts with academic institutions and health systems to use VSD to evaluate the safety of immunization with seasonal influenza during pregnancy. Likewise, FDA's Sentinel PRISM Program has initiated two studies to evaluate whether there may be a relationship between immunizations administered during pregnancy and adverse pregnancy outcomes. The first study is to evaluate the risk of cleft lip and cleft palate; the second study seeks to evaluate the risk of spontaneous abortion (miscarriage). Moving forward, it will be important to continue to support these types of studies that evaluate vaccine safety in special populations.

In addition to supporting the science base for vaccine candidates targeting diseases that are important domestically, the USG needs to continue investing resources in diseases that primarily affect the developing world. For example, USAID's Malaria Vaccine Development Research Program is supporting a first-in-human trial at Walter Reed Army Institute of Research in collaboration with GlaxoSmithKline. The trial design includes a preliminary read-out through controlled human malaria infection. If efficacious, the vaccine could lead to co-formulation with RTS,S, the most clinically advanced malaria vaccine candidate to date.

3.2.4.1 What Success Will Look Like (Outcomes) in 2020

It generally takes more time to address scientific challenges than it does to address other types of barriers. Progress may occur more slowly, but with concerted effort, important scientific progress can be made in the next five years. Stakeholders felt the types of outcomes desired for this opportunity area include:

- Improving understanding of the person-to-person variability in immune response to vaccines.
- Providing new technologies for delivering vaccines (e.g., mists, patches, microneedles).
- Identifying of new or better correlates of protection.
- Developing vaccines for use in special populations, such as pregnant women.
- Improving the effectiveness of pertussis and influenza vaccines.

3.2.5 Facilitate Vaccine Development

In addition to scientific challenges, there are systems barriers that limit vaccine development. A diverse array of opinions exists on how to address the challenges that currently limit vaccine development. Most stakeholders, however, agreed that the following challenges need to be addressed:

- Models (funding and preparedness) for rapidly developing vaccines to address emerging diseases (e.g., the Global Vaccine Development Fund or WHO's R&D Blueprint for Action to Prevent Epidemics).
- Infrastructure for clinical trials in low-resource settings (e.g., research facilities, baseline data on infectious disease prior to vaccine introduction).
- Support for the "valley of death" between basic research and clinical development.

FDA is conducting research to better understand the rising rates of pertussis and response to vaccination. Recently, with its own funds plus support from NIH, FDA scientists reported results of a study demonstrating that the baboon provides an excellent model of clinical pertussis that will allow researchers to investigate how Bordetella pertussis *spreads in a population, how it is prevented by existing vaccines, and how those vaccines may be improved in the future. Specifically, FDA's findings suggest that although acellular pertussis vaccines may protect people against whooping cough, they may still become infected with the bacteria without getting sick and are able to spread the infection to others, including infants. FDA is now focusing on trying to understand how the vaccine can be improved so that it prevents infection and transmission.*

Some stakeholders are already working to address these challenges. For example, FDA continues to convene and co-sponsor public workshops to facilitate vaccine development against a wide variety of infectious diseases, including universal influenza, meningitis B, dengue, Ebola, and cytomegalovirus. These workshops are free and open to the public, attracting a wide array of stakeholders, including members of industry, biotechnology, and academic and patient advocacy groups. Often, these meetings are conducted in collaboration with NIH, CDC, and NVPO, and their purpose is to identify and discuss key issues related to the development and evaluation of vaccines for the infectious agent under discussion.

In addition, NIH offers a suite of preclinical services to the infectious disease research community. These services provide the community with access to microorganisms, research reagents, and developmental services that can fill knowledge gaps critical to scientific research and moving products along the development pathway. These services also act to lower the risk to potential commercial partners.

ASPR/BARDA is working to improve vaccine manufacturing capacity in the developing world so that the vaccine ecosystem can respond more quickly to emerging disease outbreaks. To date, 13 manufacturers in 12 developing nations have received technical and financial support from ASPR/BARDA to establish influenza vaccine manufacturing capabilities. Seven of these

manufacturers have licensed influenza vaccines for use in country, increasing the global manufacturing capacity for vaccines targeted against microbes with pandemic potential to more than 280 million doses to date.

In addition, ASPR/BARDA is developing a new approach to advanced development and manufacturing for vaccines against targets of high public health importance but low commercial value, including emerging infectious diseases. Domestically, an HHS-wide collaboration involving ASPR/BARDA, CDC, NIH, FDA, and industry and academic partners is underway to develop a comprehensive, integrated plan for manufacturing and timely delivery of vaccines against pandemic influenza strains. As part of the Seasonal Influenza Vaccine Manufacturing Improvement initiative, work is underway to develop better potency and sterility assays.

3.2.5.1 What Success Will Look Like (Outcomes) in 2020

As with the scientific challenges, stakeholders thought that progress against vaccine development barriers will likely proceed more slowly than in other opportunity areas. There was consensus among stakeholders that the barriers to developing vaccines need to be addressed for significant progress to occur in this area, particularly for emerging infectious diseases. Factors in the vaccine development model that need to be reconsidered include the funding models and incentive structures. Stakeholders also agreed that more public-private partnerships are needed, particularly between the discovery phase 1 and phase 2 clinical trials. If successful, the types of changes that could be observed in the next five years include:

- New vaccine development models with shared risk-taking.
- The development of a flexible strategy that delineates priority targets while remaining adaptable enough to account for changes in the environment, including emerging diseases.
- Identification and acceptance of new correlates of protection as efficacy endpoints.
- A robust pipeline, with multiple candidates at different stages for high-priority diseases.
- Additional support or a shortened timeline for product development through the early stages of clinical development.

3.3 INDICATORS

One of the main goals of the Mid-course Review is to identify indicators that can be used to provide a quantifiable way of measuring progress against each opportunity area. The indicators can be used in two ways. In opportunity areas where improvements are occurring, the indicators will provide a mechanism to document progress and communicate those achievements to the broader community. In contrast, for those areas where progress is stagnating despite concerted effort from related stakeholders, the indicators can be used to convey the lack of progress and potentially the need for additional resources.

For the Mid-course Review, indicators that another organization or agency is already using were given strong preference over new metrics for several reasons. Demonstrating feasibility and developing the data-gathering and analysis methods for new metrics can take two or three years. With the five-year timeframe for the Mid-course Review, this amount of development time for a new metric is not feasible. Another advantage of using preexisting metrics is that a system and resources are already in place to gather and analyze the data required. Using metrics already in existence also reduces the potential for duplication of effort and redundant reporting.

This section describes the 16 indicators that arose through the Mid-course Review. These indicators are posed for consideration because they could be used to monitor progress against the opportunity areas in the coming five years. Each opportunity area also includes at least one indicator that could be used to monitor progress globally. Further discussion and deliberation will be needed to finalize the list of suggested metrics presented in this section. Information about the baseline values and 2020 targets for the suggested indictors presented in this section can be found in Appendix D: Baseline Values and 2020 Targets for the Indicators.

3.3.1 Strengthen Health Information and Surveillance Systems to Track, Analyze, and Visualize Disease, Immunization Coverage, and Safety Data Both Domestically and Globally

The indicators recommended for this opportunity area (Table 4) are those that provide a measure of how well vaccine coverage and infectious disease incidences can be tracked both globally and domestically. Many of the vaccine coverage indicators rely on improved functioning of IIS and expanded IIS adoption, including the number of individuals who have records in an IIS and the number of providers connected to or capable of bidirectional communication with the IIS. The suggested indicators touch on both adult and pediatric populations. In addition to the three indicators focused on domestic issues, a fourth indicator serves as a measure of global disease surveillance capabilities.

Table 4: Suggested Indicators for Strengthening Health Information and Surveillance Systems

No.	Indicator	Entity Conducting Measurement	As a Measure Of…
1.1	The number of Advancing Care Information adopters that opt to fulfill the electronic reporting to IIS requirements to obtain Advancing Care Information certification (domestic)[2]	CMS with ONC	Number of providers capable of bidirectional electronic communication with their local IIS
1.2	Percentage of adults aged >19 years who have one or more immunizations recorded in an IIS (domestic)	IIS Annual Report, CDC	IIS adoption and use in adults
1.3	Increase the percentage of children aged <6 years whose immunization records are in a fully operational, population-based IIS (domestic)	Healthy People 2020, CDC	IIS adoption and use in children
1.4	Number of countries that have case-based surveillance for VPDs[3] (global)	GVAP, WHO Strategic Advisory Group of Experts (SAGE)	Global disease-tracking capabilities

[2] Advancing Care Information is a government program that offers incentives to providers that use EHRs in accordance with a common set of standards. This metric monitors the number of providers participating in the Advancing Care Information program that fulfill the participation criterion by electronically reporting immunization data to IISs (domestic only).

[3] Many developing countries have case-based surveillance for polio and measles, but no case-based surveillance exists for all VPDs.

3.3.2 Foster and Facilitate Efforts to Strengthen Confidence in Vaccines and the Immunization System to Increase Coverage Rates Across the Lifespan

The goal of increasing confidence in vaccines is ultimately to improve vaccine coverage, but vaccine coverage rates are affected by more factors than confidence, such as the strength of the provider recommendation, awareness of the disease and the vaccine that can prevent it, as well as the accessibility and affordability of the vaccine. As such, vaccine coverage rates are not a good indicator of vaccine confidence. Identifying metrics of confidence is a challenge that has yet to be addressed. At this time, few, if any, measures of confidence exist, and of the potential indicators identified, stakeholders could only agree on one (Table 5) as a potential surrogate measure of confidence. The percentage of children who have received zero doses of the recommended vaccines by 35 months of age reflects the number of parents choosing not to vaccinate their children. Moving forward, however, it will be important to develop metrics that are more precise measures of vaccine confidence across the lifespan for children, adolescents, and adults and in special populations such as the elderly and pregnant women. It will also be important to identify metrics that can be used to monitor vaccine confidence globally as well as domestically.

Table 5: Suggested Indicators to Strengthen Vaccine Confidence

No.	Indicator	Entity Conducting Measurement	As a Measure Of…
2.1	Decrease the percentage of children in the United States who receive 0 doses of recommended vaccines by 19 to 35 months of age (domestic)	Healthy People 2020, CDC	This metric is important for monitoring to ensure that the number of parents opting not to vaccinate at all does not rise.

3.3.3 Eliminate Financial and Systems Barriers for Providers and Consumers to Facilitate Access to Routinely Recommended Vaccines

The suggested indicators for this opportunity area are presented in Table 6 and address many of the barriers that limit the availability of vaccines at points of care and drive up the cost to consumers. Two of the indicators, 3.1 and 3.2, assess the availability of vaccines at two of the most common points of care for many consumers: the primary care provider and the pharmacy. Indicator 3.1, which measures the percentage of surveyed primary care providers who stock vaccines routinely recommended for adults, is indicative of whether the financial and systems barriers for providers to offer vaccines have been addressed. Indicators 3.3 and 3.4 are a measure of progress in addressing financial barriers to vaccination in a population where cost often represents a major barrier. One of the global metrics selected for this opportunity area focuses on measles elimination as a measure of vaccine access because measles vaccine uptake is often used as an indicator of the strength of a country's routine immunization system.

Table 6: Suggested Indicators for Financial and Systems Barriers That Limit Access to Vaccines

No.	Indicator	Entity Conducting Measurement	As a Measure Of…
3.1	Percentage of surveyed primary care providers who stock vaccines routinely recommended for adults (domestic)	CDC	Vaccine accessibility to consumers
3.2	Percentage of states and territories that allow pharmacists to administer all routinely recommended vaccines for adults aged >19 without a patient-specific prescription (domestic)	American Pharmacists Association	Vaccine accessibility for consumers
3.3	Percentage of state Medicaid programs that provide coverage of all ACIP/CDC-recommended vaccinations for adults and prohibit cost sharing (domestic)	CMS	Progress toward reducing financial barriers to vaccination
3.4	Increase the percentage of adults who are vaccinated against zoster (shingles; domestic)	Healthy People 2020, CDC	Vaccine coverage for older adults with a vaccine, where access and affordability remain a significant barrier
3.5	Increase coverage with the recommended number of doses of HPV for females by 13 through 15 years of age (domestic)	Healthy People 2020, CDC	Vaccine coverage for adolescents with a vaccine, where it has been difficult to obtain good coverage because of several system-level factors, including missed opportunities, misperceptions about vaccine (both provider and parental), the use of alternative sites (e.g., pharmacies), and costs (both to providers and consumers)
3.6	Percentage of pregnant women who report receiving influenza immunization during pregnancy (domestic)	Healthy People 2020, CDC	Addressing financial and/or systems barriers for providers such as obstetricians and gynecologists and other providers of adult vaccines
3.7	Number of WHO regions achieving measles elimination by 2020 (global)	GVAP, SAGE	Global measure of access, equity, and strength of routine immunization systems
3.8	Dropout rates between the first and third dose of diphtheria, pertussis, and tetanus (DPT) globally (global)	GVAP, SAGE	Global access to routine immunizations

3.3.4 Strengthen the Science Base for the Development and Licensure of Vaccines and Facilitate Vaccine Development

For purposes of identifying metrics, two opportunity areas — strengthening the science base and facilitating vaccine development — were considered together because they speak to different challenges for the same issue: vaccine development. Although the scientific challenges are different, both areas affect the ability to bring new vaccines to market and improve on existing vaccines.

As a measure of the ability to bring new vaccines to market, many stakeholders thought that the speed at which vaccines move through the development pipeline was a good indicator of progress, as is the number of vaccines in the pipeline. Often, vaccine candidates will make it through some of the early phases of the pipeline but fail to progress because there is not a sufficiently large market to drive further investment in the vaccine. As such, Indicator 4.1

focuses on the amount of time it takes to get a new vaccine through the pipeline as opposed to the number of entities in the pipeline (Table 7). Another important measure of progress is the number of vaccine candidates in the pipeline for diseases for which no vaccine is currently available (predominately because of scientific challenges). The ability to increase the number and developmental maturity of candidates against infectious diseases speaks to how much scientific progress has been made against infectious agents that have historically proven difficult to address. Four vaccines in this category are high priorities for the United States: universal influenza, HIV/acquired immunodeficiency syndrome (AIDS), malaria, and TB. Finally, in addition to vaccines, improvements in delivery technologies are important. New vaccine delivery technologies can confer many important benefits, from thermostable vaccines that simplify vaccine cold chain management, to patches and nasal sprays that can reduce the need for needles and syringes and may potentially allow for self-administration.

Table 7: Suggested Indicators for Facilitating Vaccine Development

No.	Indicator	Entity Conducting Measurement	As a Measure Of…
4.1	Average vaccine development timeline, from the preclinical phase to regulatory submission (domestic and global)	To be identified. The methodology that Pronker et al. (2013) used is particularly attractive because baseline data already exist for the last decade (1998 to 2009). The WHO development pipeline tracking malaria, RSV, HIV/AIDS, TB and enteric vaccines is a potentially rich source of data.	Progress toward bringing new vaccines to market
4.2	Number of vaccines in phase 1 clinical trials. The analysis will include the following infectious diseases: influenza (development of universal influenza vaccines), HIV/AIDS, malaria, TB, and pathogens for which no vaccines are currently on the market (domestic and global)	ClinicalTrials.gov[4], NIH	Ability to make progress against diseases that have historically proven scientifically intractable Provides a measure of how well R&D investments are aligned to public health needs
4.3	Licensure and launch of at least one platform delivery technology or the number of vaccine delivery technologies (devices and equipment) that have received WHO prequalification against the 2010 baseline (global)	GVAP, SAGE	Ability to bring new vaccine technologies to market Delivery technologies such as needle-free vaccines may have an important role in improving adoption and simplifying supply-chain concerns to make vaccines more accessible

[4] Clinicaltrials.gov is a database that contains all federally or privately funded clinical trials conducted under investigational new drug applications.

No one indicator has an explicit global focus, but all three indicators provide some measure of global progress either because they touch on diseases that are more problematic internationally than domestically or because they take into consideration challenges that are important globally as well as domestically (e.g., cold chain).

3.4 CONSIDERATIONS

The Mid-course Review is charged with refining the implementation activities of the NVP to address the challenges of the current vaccine landscape. The Mid-course Review collected insights from expert vaccine stakeholders across the entire vaccine enterprise, including the public, private, and nonprofit sectors, and several recommendations emerged. The considerations presented in this section are informed by the themes the stakeholder community provided. When possible during the course of the review, many of the considerations were validated through additional conversations with partner organizations.

Several recurring themes were identified and should be highlighted. Key among the considerations is a need for continued coordination across the broad vaccine ecosystem. NVPO performs this function now, and stakeholders perceived a continued need to coordinate because many critical components of the immunization enterprise fall across disciplines and to many partners. Collaboration has been the key to many of the successful achievements during 2010-2015. NVPO should continue to facilitate collaborative efforts and bridge public, private, and NGO activities to effectively move the enterprise forward. Stakeholders felt that NVPO should consider adjusting the structure of the NVP or future plans to focus at a higher level on goals that are paired with adaptable objectives. The current plan has 34 objectives and 147 strategies. This level of detail can shift to the Implementation Plan, which could be refreshed as objectives are accomplished and priorities shift. Many called out the GVAP as a model to consider when the NVP is updated.

Consideration 1: NVPO Should Continue to Coordinate and Convene Across the Broad Vaccine Enterprise

- NVPO, with its broad understanding of USG and private efforts across the vaccine enterprise, should continue to coordinate, particularly in those areas where coordination is most needed — for instance, convening when there are clear vaccine-related needs that cut across many disciplines or stakeholder groups.
- NVPO should represent the needs of the U.S. agencies that make up the NVP for federal resources to support the vaccine and immunization enterprise. Progress on the NVP should be used to support the agency budgetary requests to the Office of Management and Budget.
- NVPO will emphasize the importance of nonfederal stakeholders in this space and encourage as much collaboration as possible between federal and nonfederal stakeholders.
- The USG should expand its advisory participation in the global vaccine arena. The USG provides substantial financial support to global efforts, and its participation in global leadership is not proportional to the funding provided. Because NVPO has broad understanding across the entire U.S. enterprise, it could help play a role in advisory participation to NGOs and other multilateral organizations, such as WHO.

Consideration 2: Adjust the Structure of the NVP, the Implementation Plan, and Annual Reports

- Looking forward, a comprehensive plan such as the NVP should be high level to allow flexibility as conditions change over time. The granularity of objectives and strategies can be addressed at the Implementation Plan level.
- Annual reporting on the NVP should include accurate progress reporting to understand how the NVP is performing based on benchmarks, indicators, and metrics.
- More connection is needed between the priorities of the NVP and the emphasis of the Implementation Plan. The current Implementation Plan does not address many of the objectives and strategies in the NVP.
- Update the alignment of federal stakeholders assigned to the goals, objectives, and strategies in the NVP. Objectives have been accomplished and priorities have shifted over time. Reporting requests made to federal stakeholders should be refreshed to minimize the burden and align with the current mission of the agencies.

Consideration 3: NVPO Should Actively Support Efforts in the Five Opportunity Areas During the NVP 2016-2020 Timeframe

- All five goal areas of the NVP remain essential and federal agencies and NVPO should continue to support them.
- NVPO should facilitate progress in the Opportunity Areas (OAs) identified here. The OAs cross many stakeholder groups, both federal and nonfederal. NVPO should coordinate, facilitate, and encourage collaboration in the identified OAs to drive progress.
- NVPO should establish an active program to monitor progress in the OAs and the NVP as a whole.
- In a few instances, the suggested Indicators lack funding through the 2020 timeframe (e.g., indicator 4.1 vaccine-development pipeline). NVPO should identify a support mechanism for one or two indicators to gather the information that expert stakeholders need to understand the status of progress.
- In collaboration with the appropriate stakeholders, NVPO should facilitate development of metrics where none currently exists (e.g., vaccine confidence, tracking the vaccine development pipeline). In particular, identifying metrics for vaccine confidence is paramount and should be incorporated into the NVP Implementation Plan.

Consideration 4: NVPO Should Track and Support Policy Changes for Immunization

- Stakeholders noted several key areas where policy changes would drive immunization practices. Currently, no federal partner tracks legislation affecting immunization and the impact of those policy changes on the immunization enterprise.
- It is acknowledged that states, not the USG, are responsible for many of the mandates on immunization coverage. NVPO should understand the impact of forward-reaching policy adoptions at both the federal and state level and communicate those findings to federal partners.

Consideration 5: Global Efforts Should Be Maintained

- Infectious diseases are not confined by international boundaries. Keeping the U.S. population safe requires a deep understanding of global patterns of infectious disease, systems support to developing nations, and development of new and improved vaccines for established and emerging diseases.
- Although the OAs focus primarily on domestic immunization issues, expert stakeholders emphasized the need to support global activities.
- The USG should continue to support GVAP, WHO, and other international efforts to address the needs of the global vaccine enterprise.
- In the case of novel vaccines, it should be noted that even if development and large-scale manufacturing proceed favorably, numerous legal, regulatory, logistical, funding, communications, and policy challenges must still be addressed to facilitate mass international deployments. Activities may include assisting foreign national regulatory authorities or WHO to evaluate novel, unlicensed products.

4 CONCLUSIONS

At its inception, the 2010-2020 NVP was the first comprehensive national plan in existence, and the Mid-course Review was planned to course-correct as needed mid-way through the 10-year horizon. The NVP addresses critical challenges related to VPD and public health safety.

The Mid-course Review found that:

- All five goals are still key areas of focus for 2016-2020, and execution against the objectives of each goal should continue.
- Significant achievements have been made in each of the five goal areas since 2010; Goal 2, Safety, has had the highest level of progress, based on the opinion of expert stakeholders.
- Several areas are poised for significant progress in the next five years. Investing additional effort and resources in these OAs has the potential for major gains.
- Strong collaboration across the immunization enterprise is a frequent occurrence. These collaborative efforts have driven significant results in vaccine development, safety, surveillance, and enhanced immunization coverage.
- Cross-discipline stakeholder coordination is valued and facilitates progress by creating an environment in which thought leaders come together to set an agenda with benchmarks for vaccine progress.

CITATIONS

Access to Medicine Foundation. (2015). *Rapid access to investigational vaccines: An analysis of access provisions.* Haarlem, Netherlands: Delphi G. M. Coppens, Laurien A. Rook and Jayasree K. Iyer.

Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases, Viral Special Pathogens Branch. (2016). Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE) Q&A. Retrieved from http://www.cdc.gov/vhf/ebola/strive/qa.html

Izurieta, H. S., Thadani, N., Shay, D. K., Lu, Y., Maurer, A., Foppa, I. M., … Kelman, J. (2015). Comparative effectiveness of high-dose versus standard-dose influenza vaccines in US residents aged 65 years and older from 2012 to 2013 using Medicare data: A retrospective cohort analysis. *The Lancet Infectious Diseases, 15*(3), 293–300. doi:10.1016/s1473-3099(14)71087-4

Helfand, R. (2015) *Sierra Leone trial to introduce a vaccine against Ebola (STRIVE) Overview* [PowerPoint slides]. Retrieved from http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/UCM448002.pdf

Hurley, L. P., Bridges, C. B., Harpaz, R., Allison, M. A., O'Leary, S. T., Crane, L. A., . . . Kempe, A. (2014). U.S. Physicians' Perspective of Adult Vaccine Delivery. *Annals of Internal Medicine Ann Intern Med, 160*(3), 161-170. doi:10.7326/m13-2332

McLaughlin, J. M., McGinnis, J. J., Tan, L., Mercatante, A., & Fortuna, J. (2015). Estimated human and economic burden of four major adult vaccine-preventable diseases in the United States, 2013. *Journal of Primary Prevention, 36*(4), 259–273. doi:10.1007/s10935-015-0394-3

National Institutes of Health, Office of Science Policy. (2016). Childhood Hib Vaccines: Nearly Eliminating the Threat of Bacterial Meningitis. Retrieved July 20, 2016, from https://www.nih.gov/about-nih/what-we-do/impact-nih-research/our-stories

National Vaccine Advisory Committee. (2012). A pathway to leadership for adult immunization: Recommendations of the National Vaccine Advisory Committee. *Public Health Reports, 127*(2, Suppl 1), 1–42.

National Vaccine Advisory Committee. (2013). Protecting the public's health: Critical functions of the Section 317 Immunization Program — A report of the National Advisory Committee. *Public Health Reports, 128*(2), 78–95.

National Vaccine Advisory Committee. (2014a). Recommendations from the National Vaccine Advisory Committee: Standards for adult immunization practices. *Public Health Reports, 129*(2), 115–129.

National Vaccine Advisory Committee. (2014b). Enhancing the work of the Department of Health and Human Services National Vaccine Program in global immunization: Recommendations of the National Vaccine Advisory Committee. *Public Health Reports, 129*(5, Suppl 3), 12–85.

National Vaccine Advisory Committee. (2015a). Reducing patient and provider barriers to maternal immunizations. *Public Health Reports, 130*(1), 10–42.

National Vaccine Advisory Committee. (2015b). NVAC statement of support regarding efforts to better implement IIS-to-IIS data exchange across jurisdictions. *Public Health Reports, 130*(4), 332–335.

National Vaccine Advisory Committee. (2015c). Assessing the state of vaccine confidence in the United States: Recommendations from the National Vaccine Advisory Committee. *Public Health Reports, 130*(6), 573–595.

Pronker, E. S., Weenen, T. C., Commandeur, H., Claassen, E. H., & Osterhaus, A. D. (2013). Risk in vaccine research and development quantified. *PLoS ONE, 8*(3), e57755. doi:10.1371/journal.pone.0057755

APPENDIX A: DATA-GATHERING METHODS

Federal Stakeholder Data Review

In 2014-2015, NVPO contacted representatives at each of the 16 partnering federal agencies and departments assigned responsibility under the NVP to request a list of activities that have taken place over the past year in support of the NVP. The 2013 and 2014 NVP Annual Reports were also reviewed for relevant activities and achievements from prior years and used to help generate the comprehensive list of achievements. Federal data from the federal agency reports and annual reports were integrated into a data set, and then organized by the goal, objective and strategy each achievement most closely aligns to in the NVP. Two reviewers analyzed the data, highlighting key words and examples of collaboration. Common themes and gaps were synthesized. Highlights were selected based on inclusion in previous annual reports and the significance of new achievements put forward by the federal agencies as noteworthy activities. Gaps were determined by analyzing the data set for activities reported against each strategy.

Request for Information

To obtain input on top achievements from 2010 through 2015 and top opportunities for the 2016-2020 timeframe from nonfederal stakeholders, an RFI was released in the Federal Register (80 FR 61214) and on the NVPO website on Sept. 30, 2015, and open through Nov. 9, 2015. The RFI used a survey format with both Likert scale and free-text responses to gather information on significant achievements over the past five years (2010-2015), continuing gaps and future priorities. Specifically, for each of the five goals in the NVP, the RFI asked respondents:

- How strongly do you agree that substantial progress has been made against this NVP goal over the past five years?
- In the past five years, what do you believe have been the most significant achievements made in the field regarding this goal?
- In your opinion, what are the current gaps related to this goal?
- What do you think the top three priorities should be as they relate to this goal?
- What other priorities are important to you or your organization that might not have been covered in the original goals and objectives of the NVP?
- In the next five years, from your perspective, what are the three most pressing challenges facing the vaccine community?

Respondents were instructed to comment on as many or few goals as they felt comfortable, and a response was considered “complete” if they responded to one or more questions outside the optional “Organizational Information” section. In total, 38 complete responses were received; of those, 20 respondents opted to provide information about themselves or the organizations they represent. The individuals who responded to the RFI represented a broad range of stakeholders, including professional societies; academia; state, local and tribal public health agencies; advocacy groups; consumers; health care providers; international organizations; insurers; manufacturers; pharmacies and pharmacists; philanthropic organizations; or NGOs. The information these respondents provided about themselves and their organizations is provided in the following table.

Stakeholder Group	Information Respondents Chose to Leave on Themselves or Their Organization
Academia	*None*
Advocacy	• Voices for Vaccines • Adult Vaccine Access Coalition
Consumer	• Early childhood educator and concerned citizen • Nursing faculty and former public health manager
Insurers	• Health care service corporation • American Health Insurance Plans
Interested Industry	• Biotechnology Innovation Organization (BIO)
International Organization	• Sabin Vaccine Institute • PATH
Manufacturer or Distributor	• GlaxoSmithKline
Other	• National Association of County and City Health Officials • American Nursing Association
Professional Society	• Society for Adolescent Health & Medicine • American College of Obstetricians and Gynecologists • American College of Nurse-Midwives • American Academy of Pediatrics • The Gerontological Society of America • American Academy of Pediatrics, Department of International Child Health • Association of Immunization Managers
Public Health Department	• State health department

All responses were compiled for each question, including the free-text and Likert scale responses on progress made against the NVP objectives. Two reviewers evaluated and coded the free-text responses, pulling out key phrases, examples of collaboration and examples. Common themes and gaps were synthesized from the free-text responses and compared with the progress scores for each objective to determine whether they were in agreement, highlighting any discordant results.

Stakeholder Interviews

The purpose of the stakeholder interviews was to gather information from nonfederal vaccine experts. A broad range of stakeholder groups was engaged through the interviews, including academia, industry, pharmacies and pharmacists, health care providers, philanthropic organizations and consumer groups.

The following table lists the organizations that were engaged through the stakeholder interviews. The names of the individual interviewees have been withheld to protect their anonymity because the interviews were intended to be non-attributable. Although interviewees were engaged for their expertise in a specific area, they were free to comment on any goal.

Organization	Engagement Method	Goal
Emory Vaccine Center	Individual interview	General
Emory University School of Public Health	Individual interview	General
Executive Advisor to Sanofi Pasteur	Individual interview	1
Biologics Consulting	Individual interview	1
Princeton University	Individual interview	1
GlaxoSmithKline/Novartis	Individual interview	1
Malaria Elimination Initiative, Harvard University	Group interview	1
PATH	Group interview	1
Johns Hopkins University Bloomberg School of Public Health	Individual interview	2
Institute of Medicine	Individual interview	2
Georgetown University	Individual interview	2
Merck & Co.	Group interview	2
Kaiser Permanente Center for Health Research	Group interview	2
Vanderbilt University Department of Pediatrics	Group interview	2
Dana-Farber Cancer Institute	Individual interview	3
Children's Hospital of Philadelphia	Individual interview	3
Columbia University Mailman School of Public Health	Individual interview	3
Tennessee Department of Health	Individual interview	4
University of Colorado Denver	Individual interview	4
Walgreens	Individual interview	4
Johns Hopkins University Bloomberg School of Public Health	Group interview	4
California Department of Public Health	Group interview	4
New York Department of Health	Group interview	4
WHO	Individual interview	5
Bill and Melinda Gates Foundation	Individual interview	5
Global Alliance for Vaccines Initiative	Individual interview	5
Center for Vaccine Ethics and Policy	Group interview	5
Centre for Immunization and Respiration Infectious Diseases, Canada	Group interview	5

Interviews took place with 27 individuals between Dec. 1 and Dec. 17, 2015. To encourage candid feedback, interviewees were told their comments would be non-attributable and reported in aggregate with other comments on a topic. Each interviewee was asked about specific goals based on their area of expertise, but they were free to comment on any goal or aspect of the NVP. The topics covered included achievements, gaps and priorities as well as specific questions around the themes that emerged from the RFI or prior interviews.

APPENDIX B: SYNTHESIS OF ACHIEVEMENTS AND OPPORTUNITY AREA METHODS

Prioritization of the Comprehensive List of Achievements

The list presented in the tables that follow contained 58 achievements that were highlighted in the RFI, federal data reports, or stakeholder interviews. These achievements were plotted in a Venn diagram by source (RFI, federal data reports, and stakeholder interview) to identify the similarities and differences. The list of the top achievements was compiled by pulling together the achievements noted by more than one data source and synthesizing common themes where applicable.

Goal 1: Develop New and Improved Vaccines

RFI and Federal Data Reports	Common Themes	Stakeholder Interview
• Development of vaccines for use during pregnancy • Advances in research tools such as development of standardized assays to measure vaccine efficacy and the use of in vitro biomimetics • Improvements to manufacturing capacity through the use of new technology to produce protection that lasts longer, uses less vaccine or produces a vaccine at a lower cost • Advances in vaccine delivery methods, such as intradermal delivery and use of adjuvants • Use of public-private vaccine development partnerships to address global health needs (e.g. MenAfriVac and ROTAVAC)	• New vaccines coming to market: HPV, meningococcal B, pneumococcal, H1N1 • Improvements in the influenza vaccine, including use of cell-based technologies, recombinant DNA, quadrivalent vaccines • Basic research performed at NIH to improve our understanding of the host immune system • Development of SMART vaccine tool	• Rapid development of an Ebola vaccine • Work done by the Vaccine Research Center at NIH • Work in RSV • Prioritization of adult vaccines

Goal 2: Enhance the Vaccine Safety System

RFI and Federal Data Reports	Common Themes	Stakeholder Interview
• Use surveillance data to detect, research and respond to AEFIs, such as Guillain-Barre syndrome, febrile seizures and intussusception • Global leadership from FDA on the use of new technologies to produce safer, more effective vaccines	• Adverse event databases are working well and producing good information, particularly VSD and PRISM • U.S. safety system is robust and generally working well, with good collaboration at the federal, state and local level	• Ability to rapidly acquire and analyze safety data during an emergency • FDA has done a remarkable job expediting the approval of vaccines and requiring post-licensure monitoring • NIH is awarding more grant funding to investigate safety • Vaccine safety publications — both the number and quality

Goal 3: Communications to Enhance Informed Decision-Making

RFI and Federal Data Reports	Common Themes	Stakeholder Interview
• Collaboration among immunization stakeholders to create and disseminate information on the importance of vaccines • Targeted outreach to providers • Culturally tailored communications and interventions to improve public awareness of the risks and benefits of vaccination • Increase in the consumer-focused, publically available information on the internet • Targeted campaigns and outreach to improve HPV vaccination rates among adolescents • Use of social media	• HPV is a success story in progress and a model for how to take a comprehensive approach	• Getting vaccination on the policy and advocacy agenda as an issue of importance • Greater public awareness of the importance of vaccines • Greater recognition among stakeholders that vaccines are an issue of importance • Shift in public opinion that has occurred as a result of disease outbreaks: without it, never would have passed new legislation in California

Goal 4: Supply, Access and Use of Recommended Vaccines

RFI and Federal Data Reports	Common Themes	Stakeholder Interview
• National Adult Immunization Standards have been particularly impactful in expanding vaccine access outside traditional settings • Research and modeling to improve the efficiency of existing immunization strategies • Among federal agencies that deliver health care (VA, IHS) use of health IT and EHRs to improve vaccination rates and monitoring • Expand the availability of vaccines through collaboration and extension of vaccine administration beyond traditional health care settings	• Improved manufacturing capacity, particularly for influenza and meningococcal B • Quality improvements and increases in production capacity from improved guidance on storage and handling from CDC • Reducing financial barriers: near-universal coverage for children and first-dollar coverage in the Patient Protection and Affordable Care Act • VICP and CICP are both working well	• Relatively high vaccine coverage rates, particularly the increase in coverage rates observed for adolescents • Universal vaccine coverage for all non-grandfathered clauses plus Medicaid expansion coverage • Better ability of government and manufacturers to respond to emergencies • Increased appreciation and learning from implementation science • Increased funding and focus on IISs, particularly for adults • Pandemic preparedness, particularly for influenza • Improving pharmacist privileges and patient acceptance of pharmacists as providers • Partnership between pharmacy and manufacturers • Reminder recalls for parents

Goal 5: Global Prevention of Death and Disease Through Vaccination

RFI and Federal Data Reports	Common Themes	Stakeholder Interview
• Endorsement of the GVAP from 194 countries at the 65th World Health Assembly • Capacity building in developing countries — surveillance, manufacturing and regulation • International collaboration to improve vaccination rates globally, particularly for meningitis A, HPV, rotavirus and pneumococcal disease • Progress against global eradication program objectives, notably rubella and measles	• Polio eradication in Africa: elimination of one strain, one year without a single case as well as significant improvements in control in India	• Globally, highest vaccine coverage rate ever achieved • Impact of conjugate vaccines on global VPD control and eradication • Progress to introduce new vaccines in developing countries by Gavi • Response to Ebola as both an achievement and an opportunity to do better

Synthesis of Opportunity Areas from the Comprehensive List of Opportunities

Beginning with the comprehensive list of opportunities identified during the data-gathering phase, three independent reviewers categorized opportunities that stakeholders mentioned by common theme. When the categorization was complete, reviewers met to compare the common themes identified from the stakeholder input, finalizing a Comprehensive List of Opportunity Areas for the 2016-2020 timeframe. The following table lists the 10 OAs that emerged from the initial data-gathering efforts. Note that they are numbered and listed by the goals they correspond to in the NVP, not by prioritization or importance.

OA ID	Opportunity Area	Corresponding Goals in the NVP
1	Increase coordination, collaboration and knowledge sharing among related parties and disciplines.	1
2	Facilitate vaccine development.	1
3	Strengthen the science base for the development and licensure of new vaccines, especially our understanding of the host immune system and correlates of protection.	1, 2
4	Improve scientific knowledge about why and among whom vaccine adverse events occur.	2
5	Improve the transparency of the vaccine safety system and the entire vaccine enterprise to policymakers, the public and providers.	2, 3
6	Foster and facilitate efforts to strengthen confidence in vaccines and the immunization system to increase coverage rates across the lifespan.	3
7	Eliminate financial and systems barriers for providers and consumers to facilitate access to routinely recommended vaccines.	4
8	Strengthen health information systems to track, analyze and visualize disease, vaccine coverage and safety data.	4, 5
9	Support the strengthening of immunization systems globally through policies, practices and partnerships.	5
10	Improve surveillance for VPDs, and strengthen health information systems to monitor vaccine coverage, effectiveness and safety both domestically and globally.	5

APPENDIX C: VALIDATION AND PRIORITIZATION OF FINDINGS METHODS

Focus Group Sessions

Focus group sessions were conducted to validate the top achievements and priorities identified through the initial data-gathering efforts. Between Feb. 1 and March 1, 2016, three focus sessions were conducted. Each focus session was held at the Hubert H. Humphrey Building and lasted two hours. To facilitate a robust dialogue, no virtual participation was permitted: In-person attendance was required. All three focus sessions covered the same content and agenda.

Focus Meeting Agenda

Each focus group session covered the following topics:

- Review the short list of Top 20 Achievements, 2010-2015.
- Review and rank the OAs for 2016-2020 by priority.
- For the top three to six OAs as ranked by the group, discuss what success looks like for each opportunity area and possible indicators of success.

Focus Group Participants

The focus groups were designed to obtain feedback from a diverse array of stakeholders, both federal and nonfederal. The first session focused on NVAC liaison organizations, with an emphasis on nonprofits and advocacy groups. The second focus session was for federal stakeholders, while the third session was primarily targeted at professional societies and provider groups. Eight to nine participants attended each session, and a full list of participating organizations can be found in the table below. The names of the participants have been withheld to protect their anonymity because the feedback received during the focus sessions was intended to be non-attributable. All focus groups were held at the Hubert H. Humphrey Building, located at 200 Independence Ave S.W., Washington, D.C. In total, 25 individuals representing 18 organizations and five federal agencies participated in the focus sessions.

Focus Session 1: Nonfederal Stakeholders, Emphasis on Nonprofits and Advocacy Groups (NVAC Liaison Organizations), Held Feb. 1, 2016

Organization
BIO
American Pharmacists Association
Association of Immunization Managers
American Immunization Registry Association
Association of State and Territorial Health Officials
Every Child by Two
National Association of County and City Health Officials
Arkansas Department of Health
Stanford University

Focus Session 2: Federal Partners,[5] Held Feb. 18, 2016

Organization
CDC, National Center for Immunization and Respiratory Diseases
NIH, NIAID
VA, National Center for Health Promotion and Disease Prevention
IHS, Headquarters
Health Resources and Services Administration (HRSA), Bureau of Primary Health Care
HRSA, Division of Injury Compensation Programs
CDC, Center for Global Health, GID
CDC, Office of Infectious Disease, National Center for Emerging and Zoonotic Infectious Diseases

Focus Session 3: Nonfederal Stakeholders, Emphasis on Professional Societies, Held March 1, 2016

Organization
Immunization Action Coalition
American Congress of Obstetricians and Gynecologists
American Medical Association
American College of Physicians
American Nurses Association
The Gerontological Society of America
Infectious Disease Society Association
American Academy of Pediatrics

Those federal partners that were unable to participate in the second focus group session provided input in one-on-one interviews. The following table lists the agencies and departments that participated in one-on-one interviews to provide their input on the top achievements and prioritization of OAs.

Agency	Departments Represented
CMS	• Center for Medicare • Center for Medicaid and Children's Health Insurance Program Services
DOD	• Immunization Healthcare Operations Section • Military Vaccine Agency • Vaccine Healthcare Centers Network
FDA	• Office of Vaccines Research and Review • Office of Biostatistics and Epidemiology • Office of Communications, Outreach and Development
ONC	• Office of the National Coordinator for Health Information Technology
USAID	• Office of Health, Infectious Diseases and Nutrition • Maternal and Child Health

[5] Several key federal stakeholders could not attend the focus group session on Feb. 18, 2016. To ensure that key federal stakeholders had an opportunity to provide input, our team met individually with liaisons from FDA, USAID, CMS, and the ONC either by phone or in person. A list of the federal stakeholders engaged through interviews can be found below.

The one-on-one interviews with federal stakeholders covered the same topics as the focus meetings as well as a few additional topics, as listed in the following agenda:

1. Introduction and backgrounds (10 minutes)
2. Review the objectives and implementation actions currently mapped to your agency under the NVP to ensure that they are still relevant for your agency's mission (20 minutes)
3. Review the draft List of Top Achievements (10 minutes)
4. Review and prioritize the draft List of Opportunity Areas (10 minutes)
    a. Do they reflect what you think the OAs should be for the coming five years, 2016-2020?
    b. Rank the top OAs by priority.
5. For the top three to six OAs (per your ranking), discuss the following questions (20 minutes):
    a. What will success look like for each OA?
    b. What metrics could be used to track progress against each OA?

Prioritizing Opportunity Areas

During the focus group sessions and federal stakeholder interviews, participants were asked to rank the 10 OAs identified during from the initial data-gathering efforts. The OA rankings from each focus session were aggregated and averaged. Rankings from the one-on-one interviews with the partnering federal agencies that could not attend the second focus session were aggregated and averaged with the rankings from focus session 2, the session targeted to federal stakeholders only. The OA rankings from the 10 federal agencies and 18 organizations that participated in the focus group sessions or federal interviews were averaged to arrive at the final ranking, with equal weight given to federal and nonfederal participants. A table showing how each focus session ranked the opportunity areas as well as the aggregate rankings can be found in below. The top priority as determined by the group is scored at "1," while the bottom priority is scored as "10" (the lower the number, the higher the priority).

OA ID	Opportunity Area	Nonfederal Rankings (Session 1, 3)	Federal Rankings (Session 2, Interviews)	Aggregate Ranking
1	Increase coordination, collaboration and knowledge sharing among related parties and disciplines.	4	10	6
2	Facilitate vaccine development.	7	1	5
3	Strengthen the science base for the development and licensure of new vaccines, especially our understanding of the host immune system and correlates of protection.	5	2	4
4	Improve scientific knowledge about why and among whom vaccine adverse events occur.	8	8	8
5	Improve the transparency of the vaccine safety system and the entire vaccine enterprise to policymakers, the public and providers.	6	9	7

OA ID	Opportunity Area	Nonfederal Rankings (Session 1, 3)	Federal Rankings (Session 2, Interviews)	Aggregate Ranking
6	Foster and facilitate efforts to strengthen confidence in vaccines and the immunization system to increase coverage rates across the lifespan.	3	2	2
7	Eliminate financial and sytems barriers for providers and consumers to facilitate access to routinely recommended vaccines.	2	5	3
8	Strengthen health information systems to track, analyze and visualize disease, vaccine coverage and safety data.	1	4	1
9	Support the strengthening of immunization systems globally through policies, practices and partnerships.	10	6	9
10	Improve surveillance for VPDs, and strengthen health information systems to monitor vaccine coverage, effectiveness and safety both domestically and globally.	9	7	10

Federal Stakeholder Engagement

After the focus group participants had prioritized the OAs and top achievements, federal stakeholders were engaged in one-on-one interviews to review and provide feedback on the OAs and top achievements. During the one-hour one-on-one meetings, federal stakeholders were presented with the prioritized list of OAs and asked to provide feedback on the draft language and discuss any ongoing or new projects the agency was undertaking that aligned to one of the prioritized OAs. Although the emphasis was on reviewing the prioritized list of OAs, federal stakeholders also had the opportunity to provide feedback on the prioritized list of top achievements and provide any examples of work they had done related to the top achievements. Finally, at this meeting the federal stakeholders also reviewed the draft list of indicators and provided feedback on which indicators, if any, would be most appropriate. The following table lists the agencies that participated in one-on-one interviews to provide their input on the top achievements, prioritized OAs and potential metrics.

Agency	Departments Represented
ASPR	• BARDA • Influenza Division
CDC	• GID • National Center for Immunization and Respiratory Diseases
CMS	• Center for Medicare
DOD	• Immunization Healthcare Operations Section • Military Vaccine Agency • Vaccine Healthcare Centers Network

Agency	Departments Represented
FDA	• Office of Vaccines Research and Review • Office of Biostatistics and Epidemiology • Office of Communications, Outreach and Development
HRSA	• Bureau of Primary Health Care • Division of Injury Compensation Programs
IHS	• Headquarters
NIH	• NIAID, Office of Scientific Coordination and Program Operations • NIAID, Division of Allergy, Immunology, and Transplantation • NIAID, Vaccine Research Center
ONC	• Office of Interoperability and Standards
USAID	• Maternal and Child Health
VA	• National Center for Health Promotion and Disease Prevention

During each of the one-hour one-on-one meetings with the federal stakeholders, the following topics were covered:

1. Purpose of the Meeting (10 minutes)
    a. Overview of the Mid-course Review process
    b. Vision for the final report
2. Review the OAs, 2016-2020, Prioritized by Stakeholders (20 minutes)
    a. Review the draft language
    b. Discuss any ongoing or new projects your agency is doing that align to an OA
3. Discuss the Metrics Under Development for the OAs (20 minutes)
    a. Review the draft list
    b. Discuss any other relevant metrics or indicators your agency may already be collecting
4. Review the List of Top Achievements Prioritized by Stakeholders (10 minutes)
    a. For those that touch on your space, are there any examples you would like to highlight?

APPENDIX D: BASELINE VALUES AND 2020 TARGETS FOR THE INDICATORS

The table below presents additional information on the suggested indicators from Section 3.3, Indicators. The additional information includes the baseline value and 2020 target, where available.

No.	Indicator	Entity Conducting Measurement	Baseline	Target
1.1	The number of Advancing Care Information adopters that opt to fulfill the electronic reporting to IIS requirements to obtain Advancing Care Information certification (domestic)[6]	CMS with ONC	73% of eligible hospitals were able to report vaccination to their local IIS (2014)	Not defined
1.2	Percentage of adults aged >19 years who have one or more immunizations recorded in an IIS (domestic)	IIS Annual Report, CDC	25% (CDC, 2012)	50%
1.3	Increase the percentage of children aged <6 years whose immunization records are in a fully operational, population-based IIS (domestic)	Healthy People 2020, CDC	75% (2008)	95%
1.4	Number of countries that have case-based surveillance for VPDs (global)	GVAP, WHO SAGE	67% of low-middle income countries have case-based surveillance system for inflammatory bowel disease and 53% for rotavirus diarrhea (GVAP, 2013)	75% of low-middle income for hospital-based sentinel site surveillance for inflammatory bowel disease and rotavirus diarrhea
2.1	Decrease the percentage of children in the United States who receive 0 doses of recommended vaccines by 19 months of age to 35 months of age (domestic)	Healthy People 2020, CDC	0.8% (2012)	Not defined
3.1	Percentage of surveyed primary care providers who stock vaccines routinely recommended for adults (domestic)	CDC	20% Internists and 31% of family practices	60%
3.2	Percentage of states and territories that allow pharmacists to administer all routinely recommended vaccines for adults aged >19 without a patient-specific prescription (domestic)	American Pharmacists Association	85% (American Pharmacists Association)	100%

[6] Advancing Care Information is a government program that offers incentives to providers that use EHRs in accordance with a common set of standards. This metric will monitor the number of providers participating in the Advancing Care Information program that fulfill the participation criterion by electronically reporting immunization data to IISs (domestic only).

No.	Indicator	Entity Conducting Measurement	Baseline	Target
3.3	Percentage of state Medicaid programs that provide coverage of all ACIP/CDC-recommended vaccinations for adults and prohibit cost sharing (domestic)	CMS	20% (CMS, 2012)	100%
3.4	Increase the percentage of adults who are vaccinated against zoster (shingles; domestic)	Healthy People 2020, CDC	6.7% (2008)	30%
3.5	Increase coverage with the recommended number of doses of HPV for females by 13 through 15 years of age (domestic)	Healthy People 2020, CDC	28.1% (2012)	80%
3.6	Percentage of pregnant women who report receiving influenza immunization during pregnancy (domestic)	CDC	52% (CDC, 2013)	Not defined
3.7	Number of WHO regions achieving measles elimination by 2020 (global)	GVAP, SAGE	0 of 5 WHO regions	5 WHO regions
3.8	The dropout rates between the first and third dose of DPT globally (global)	GVAP	2010 WHO/ UNICEF data	Decreasing trend
4.1	Average vaccine development timeline from the preclinical phase to regulatory submission (domestic and global)	To be identified. The methodology used by Pronker et al. (2013) is particularly attractive because baseline data already exists for the last decade, 1998 to 2009. The WHO development pipeline tracking malaria, RSV, human immunodeficiency virus/ acquired immune - deficiency syndrome (HIV/AIDS), enteric and tuberculosis is a potentially rich source of data.	To be determined	Not defined
4.2	Number of vaccines in phase I clinical trials. The analysis will include the following infectious diseases: influenza (development of universal influenza vaccines), HIV/AIDS, malaria, TB, and pathogens for which no vaccines are currently on the market (domestic and global)	ClinicalTrials.gov[7], NIH	To be determined	Not defined
4.3	Licensure and launch of at least one platform delivery technology or the number of vaccine delivery technologies (devices and equipment) that have received WHO prequalification against the 2010 baseline (global)	GVAP, SAGE	Not applicable	1 or more technologies

[7] Clinicaltrials.gov is a database containing all federally or privately funded clinical trials conducted under investigational new drug applications.