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Opportunities for the Next Administration

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Sustaining the Global Commitment to Life-saving Immunization

Opportunities for the Next Administration

Maria Schneider, Julie Becker, and Adam Williams¹

For just a few dollars a dose, vaccines save lives and help reduce poverty. Unlike medical treatment, they provide a lifetime of protection from deadly and debilitating disease. They are safe and effective. They cut healthcare and treatment costs, reduce the number of hospital visits, and ensure healthier children, families and communities.²

Executive Summary

U.S. leadership and funding for global immunization efforts have accelerated over the past 15 years. The returns have been substantial. U.S. efforts—primarily through Gavi, the Vaccine Alliance—have contributed to the immunization of 500 million children and the prevention of approximately 7 million deaths from measles, diphtheria, pertussis, rotavirus, and other diseases. The U.S. Agency for International Development (USAID) provides technical support and funding to strengthen immunization delivery systems, and additionally, a U.S. network of partners has played a pivotal role in the research and development of two-thirds of all new vaccines globally.

Yet 1.5 million children under five years of age still die each year from vaccine-preventable diseases, which account for approximately 20 percent of child mortality. Enormous gaps in coverage remain within and among countries in the developing world. Moreover, Gavi's long-term ability to transition countries from aid recipients to full funders of their domestic immunization efforts is uncertain. This uncertainty puts at risk the global capacity to maintain effective immunization programs and introduce new vaccines, the very reason Gavi was established.

For the next administration, global leadership on immunizations is just as important as funding. Stakeholders identified three priority areas where the United States should intensify efforts to keep life-saving immunizations front and center globally:

¹ Maria Schneider is an executive vice president of Rabin Martin. Julie Becker is an executive vice president of Rabin Martin. Adam Williams is a senior associate at Rabin Martin.

² Seth Berkley, "Vaccines: The Biggest Bang for the Buck in Global Health," *Huffington Post*, December 19, 2011, http://www.huffingtonpost.com/seth-berkley-md/vaccines-the-biggest-bang_b_1015390.html.

- 1) Leveraging the U.S. government's influential role on the Gavi Board to sustain and improve global vaccine coverage and support successful country transitions to full ownership of domestic immunization programs
- 2) Stimulating private-sector investment and supporting product development partnerships to accelerate the research and development of new vaccines for the developing world
- 3) Reducing inequities in coverage through efforts to reach the most vulnerable populations

Methodology

The findings in this paper are based on interviews with 36 experts in women's and family health. They are current and former U.S. government officials, Gavi officials, leaders of large NGOs and faith-based groups, and representatives from the private sector. Experts were asked to assess the value of the U.S. role in global immunization efforts, which U.S. programs and investments have been most successful (and which have missed the mark), and why. They were also asked to identify key areas of focus for the incoming administration in the area of global immunizations.

Global Context for U.S. Investment

Historical Background

After the formation of the World Health Organization (WHO) and related organizations such as UNICEF in the 1940s, dedicated vaccine programs were initiated around the world. Several effective vaccines were introduced in the 1950s and 1960s (smallpox, diphtheria, tetanus, pertussis, polio, measles, mumps, and rubella). Since then, efforts to scale up the reach of these and other vaccines around the world have met with global support. Great strides were made in immunization globally in the 1970s and 1980s. This progress was followed by a period of stagnation in the 1990s, and then a resurgence of interest in the 2000s.

The United States has been, and continues to be, a driving force in global immunization initiatives through its bilateral programs and multilateral support. To appreciate fully the extent and impact of U.S. involvement, it is helpful to look back at the story of smallpox, a disease that threatened 60 percent of the world's population and killed every fourth victim before interventions began.³

The success of a large-scale smallpox vaccination program, implemented by USAID in 20 West and Central African countries in 1965, prompted the WHO to launch an ambitious campaign that spanned the 1960s and 1970s with the support of USAID and the Centers for Disease Control and Prevention (CDC) and culminated in the last naturally occurring case of

³ World Health Organization, "The Expanded Programme on Immunization," http://www.who.int/immunization/programmes_systems/supply_chain/benefits_of_immunization/en/.

smallpox in Somalia in 1977.⁴ This success led the WHO to expand its immunization program to include poliomyelitis, diphtheria, measles, tetanus, pertussis, and tuberculosis under the Expanded Programme on Immunization (EPI), which was launched in 1974 with the goal of dramatically increasing vaccination rates among children in developing countries.

More recently, the U.S. government has demonstrated substantial and consistent involvement and leadership, particularly over the past 15 years, notably through bilateral programs, bilateral engagement at the national level through coordinating committees, founding investments in the game-changing Gavi, and significant investments in global health vaccine research and development efforts (described later). These efforts are also contributing to the Decade of Vaccines—a 10-year effort, established in 2010, to extend the full benefits of immunization to all—which produced the Global Vaccine Action Plan.

Global Immunization Priorities

Child immunization efforts have focused on 14 diseases that are some of the most common causes of disability and death globally: diphtheria, pertussis, tetanus, measles, polio, tuberculosis, hepatitis B, Haemophilus influenzae type B (Hib), rubella, meningococcal disease, pneumococcal disease, rotavirus, Japanese encephalitis, and yellow fever.

The Millennium Summit of the United Nations, convened in 2000, prioritized increasing access to these immunizations. MDG 4 identified the key role of immunizations for reducing child mortality. Vaccines in development also have the potential to help diseases targeted by MDG 6 (combat HIV/AIDS, malaria, and other diseases). International commitment to the MDGs launched major efforts to extend immunization access to children in the most underserved areas, primarily in Africa and Asia, as well as fast-track the development of new vaccines.

Building on the MDGs, in September 2015, countries around the world adopted the SDGs, a set of high-level goals to end poverty, fight inequalities, and tackle climate change. Goal 3 focuses on health, with a target of ending all preventable deaths of newborns and children under the age of five by 2030. In addition, the targets focus on improving access to vaccines and supporting research and development for vaccines focused on diseases that disproportionately affect low-income countries.

Global Progress to Date

Efforts over the past 15 years to increase equity in immunizations in areas of the world most affected by vaccine-preventable diseases have achieved significant measurable success. Under-five mortality rates plummeted by more than a third from 2000 to 2015, largely attributable to the reduction in deaths from pneumonia, diarrhea, and measles. Reduced death rates for these diseases among children under five represented nearly half the gains in child survival.⁵

⁴ F. Fenner et al., "Smallpox and Its Eradication," World Health Organization, 1988, <http://whqlibdoc.who.int/smallpox/9241561106.pdf>.

⁵ Li Liu et al., "Global, Regional, and National Causes of Child Mortality in 2000–12, With Projections to Inform Post-2015 Priorities: An Updated Systematic Analysis," *The Lancet* (September 30, 2014).

Nevertheless, each year pneumonia and diarrhea, together with malaria, are still responsible for one-third of the deaths of children under the age of five, most of which occur in the developing world. The most common types of pneumonia and rotavirus (causing severe diarrhea) are vaccine-preventable. Pneumococcal diseases, which are responsible for nearly a million deaths annually, are the leading cause of death in children under five. In some developing countries, the rates of infant deaths due to pneumonia are estimated to be as high as 20 percent.⁶

At this time, only one malaria vaccine is available for limited use. Research on several vaccines is underway but a highly effective, WHO-recommended malaria vaccine for widespread use is years away.⁷

Tremendous Progress on Polio, but Eradication Not Yet Achieved

The push to eradicate polio, begun in 1988, has yielded a 99 percent reduction in the disease incidence. In 2015, WHO declared that polio was no longer endemic to Nigeria, which as recently as 2012 had accounted for more than half of all polio cases worldwide.^a Polio transmission currently remains endemic in just two countries (Afghanistan and Pakistan), where 73 cases were reported in 2015.^b Until poliovirus transmission is interrupted in these two countries, all countries remain at risk of polio, especially vulnerable countries with weak public health and immunization services.

^a World Health Organization, "WHO Removes Nigeria from Polio-Endemic List," September 25, 2015, <http://www.who.int/mediacentre/news/releases/2015/nigeria-polio/en/>.

^b Centers for Disease Control and Prevention, "Update on CDC's Polio Eradication Efforts, March 18, 2016, <http://www.cdc.gov/polio/updates>.

More Focus Needed on Measles and Rubella

In the Western Hemisphere, endemic measles and rubella have been eliminated, and globally, deaths from measles have dropped by 79 percent. Measles and rubella can be prevented with two doses of a safe, effective, and inexpensive vaccine. However, progress has not been as robust as expected, and in 2014, measles still killed nearly 115,000 children per year—mostly children less than five years of age.^a

^a World Health Organization, "Measles Fact Sheet, No. 286," March 2016, <http://who.int/mediacentre/factsheets/fs286/en>.

Globally, smallpox is the only disease affecting humans that has been eradicated worldwide. Polio eradication, which is within sight due to concentrated and well-coordinated global efforts, with critical participation from the United States, could be a historic second. Experts interviewed expressed hope that measles could be third in line.

⁶ World Health Organization, "WHO Position Paper on Pneumococcal Vaccines 2012," http://www.who.int/immunization/position_papers/PP_pneumococcal_April_2012_summary.pdf.

⁷ Given the vaccine's efficacy, the WHO recommends countries conduct pilot projects in targeted regions of malaria vaccine (RTS,S/AS01 vaccine), the only candidate malaria vaccine that is currently available.

Key Programs and Partnerships—What’s Moving the Dial

Gavi, the Vaccine Alliance

In addition to U.S. immunization support provided through USAID, CDC, and other agencies, U.S. government investment in Gavi, a public-private partnership and funding mechanism for expanding vaccine access in poor countries (see box), has remained strong across administrations. Gavi is hailed as the most successful U.S. immunization investment.

In 2000, President Clinton made the first U.S. pledge to Gavi; this donation of \$47 million, paid in 2001, was the first public funding received by the organization.⁸ In the 2000s, the George W. Bush administration considered immunizations key to child health as part of the Child Survival and Health Grant Programs, through which USAID uses a strategic partnership model to engage and build the capacity of civil society with host-country governments and the private sector. While policies and high-level statements from U.S. leaders did not highlight global immunizations as a top priority, the Bush administration did support Gavi when it was first established, starting a path toward the U.S. government’s highest-impact investment in immunizations.

Much of U.S. involvement in global immunizations through the course of the Obama administration has been through steadily growing contributions to Gavi. At the same time, the United States has also prioritized immunizations more broadly through greater advocacy and statements from government leaders about the value of vaccines, more openness to engaging with the private sector, a focus on both innovation and delivery, and overall increased integration of immunizations into key government blueprints and initiatives.

Large Funding Commitment

In 2015, the United States committed \$200 million to Gavi, the largest annual contribution from the United States to date (Figure 1). In a show of strong commitment, the administration has requested \$235 million for Gavi in 2016, and has pledged \$1 billion for the period 2015–2018, subject to congressional approval.⁹ According to a USAID spokesperson, this large pledge will assist Gavi in the accelerated rollout of the pentavalent, pneumococcal, and rotavirus vaccines, thereby addressing the leading causes of the world’s two biggest childhood killers—pneumonia and diarrhea.¹⁰

⁸ Henry J. Kaiser Family Foundation, “The U.S. & Gavi, the Vaccine Alliance: Overview,” March 18, 2015, <http://kff.org/global-health-policy/fact-sheet/the-u-s-and-the-gavi-alliance/>.

⁹ Gavi, “United States of America: Proceeds to Gavi from Donor Contributions & Pledges (2011–2015), as of 30 June 2016,” <http://www.Gavi.org/funding/donor-profiles/united-states/>.

¹⁰ Gavi, “Key Outcomes Resources Assured for 2016–2020,” <http://www.gavi.org/Library/Publications/Replenishment/15-Replenishment-report---summary/>.

Gavi, the Vaccine Alliance—A Model for Scaling up Access and Introducing New Vaccines

Gavi, the Vaccine Alliance (Gavi) is an international coalition of partners with the goal of accelerating uptake and use of underused vaccines in developing countries, and decreasing the time it takes to provide access to new vaccines. The Alliance includes national governments (both donor and recipient countries); international organizations such as UNICEF, WHO, and World Bank; philanthropic institutions, such as the Bill & Melinda Gates and the Rockefeller Foundations; the private sector, represented by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA); and research and public health institutions. Since 2000, Gavi has contributed to the immunization of 500 million children and the prevention of approximately 7 million future deaths.

Gavi is not an implementing agency; rather, it relies on countries and partners to ensure that resources it provides are used to meet local needs. Gavi-supported countries develop proposals, which are reviewed by an independent expert panel for their technical soundness and recommended to the Gavi Board for approval. Gavi also explicitly incentivizes countries to achieve results to make sure that funds are used efficiently and effectively (e.g., performance-based funding for health system strengthening that links funding to immunization outcomes), and develops tailored indicators to measure performance and use of funds in addition to core indicators that are constant across all recipients.^a

There are three funding mechanisms for Gavi: the International Finance Facility for Immunization (IFFIm), which uses pledges from donor governments to sell bonds in the capital markets; the Advanced Market Commitment; and the Gavi Matching Fund for donations. Since 2000, IFFIm has raised \$5 billion from investors, which provides Gavi with the flexibility to access funds as they are needed, rather than depending on donor disbursements.

Gavi provides the great majority of its support to countries that meet certain conditions of financial need and disease burden, with 80 percent of funds going toward vaccine commodities (new and underused vaccines and accompanying injection equipment) and 20 percent of funds provided through cash grants meant to support countries' vaccine delivery systems as well as broader health systems strengthening.

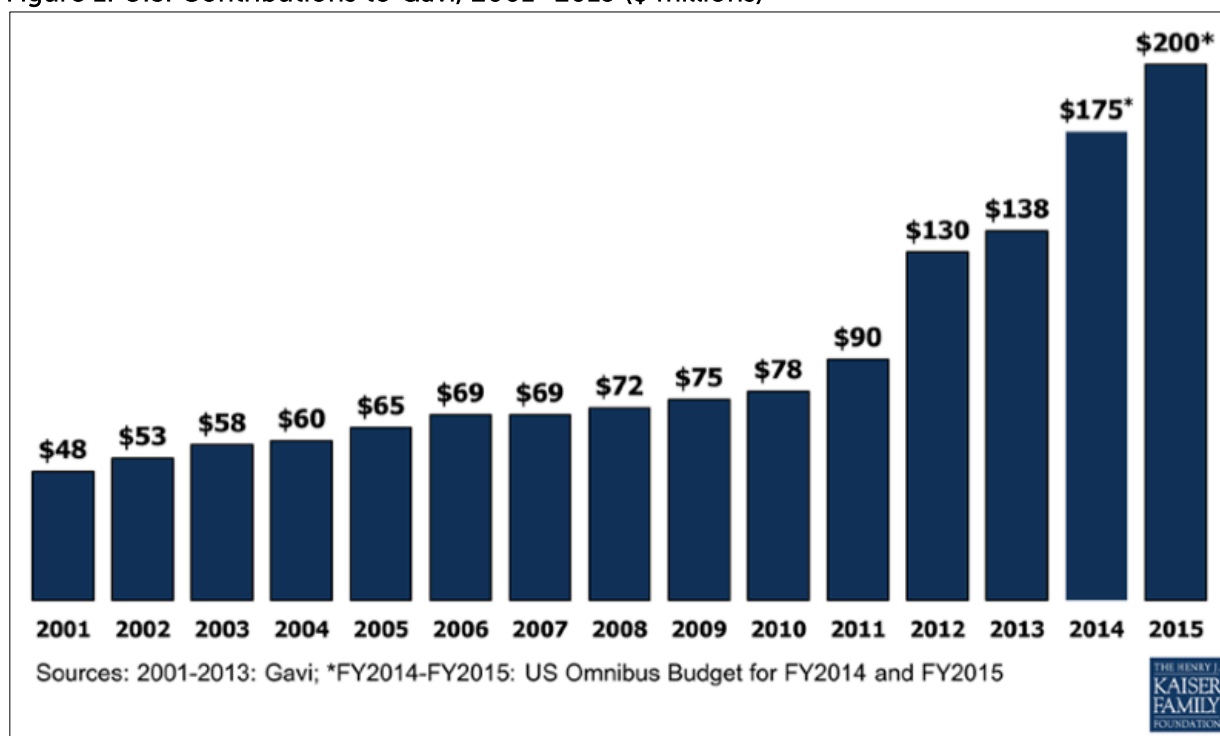
Recipient countries must share responsibility for funding their national immunization efforts through "cofinancing" requirements, which vary depending on country income level. As countries develop economically, their financial stake in their Gavi-supported immunizations must increase, and when national incomes rise above a certain threshold, they "transition" from Gavi eligibility and are no longer eligible to receive support, although they may benefit from manufacturers offering Gavi or similar prices for specific vaccines.

In 2016, five countries (Bhutan, Honduras, Mongolia, Sri Lanka, and Ukraine) will have transitioned from Gavi support and will be self-financing vaccines, and 16 others will be in the process of transitioning.^b There are many challenges and opportunities associated with the transition process, and Gavi has refined the process over time (examples of which will be highlighted later in this paper).

^a Gavi, "Performance Frameworks," <http://www.gavi.org/support/performance-frameworks/>.

^b Gavi, "Transition Process," <http://www.gavi.org/Support/Apply/Graduating-countries/>.

Figure 1: U.S. Contributions to Gavi, 2001–2015 (\$ millions)



Critical Importance of Board Membership

In addition to being a top government donor to Gavi, board membership enables the U.S. government to raise issues of interest and concern, provide operational oversight, and have a powerful voice in the organization’s investment decisions. In this way the United States can ensure good stewardship over how its investment is used.

The 28-member Gavi Board is composed of recipient countries, donors, implementing agencies, the private sector, and individuals. A rotating seat represents the combined constituency of the United States, Australia, the Republic of Korea, and Japan. Engagement through this country cluster gives the United States, as the largest donor, an important voice and empowers the U.S. government to influence priorities.

Value of Technical Assistance

USAID’s technical support in strengthening routine immunization services, through cold chain management, personnel management, training, program planning, and other areas, plays a crucial role in ensuring that both Gavi-financed immunization and other vaccines are delivered where they are most needed.¹¹ By providing direct support at the country level, USAID builds local capacity to vaccinate at scale.

¹¹ Richard Murray Trostle and Angela Shen, “Three Decades of USAID Investments in Immunization through the Child Survival Revolution,” *Emerging Microbes and Infections* 3, no. 2 (February 2014): e13.

Direct Gavi support to governments is also critical to vaccine delivery. For example, rollout of the 5-in-1 pentavalent vaccine, which protects against diphtheria, tetanus, pertussis, hepatitis B, and Hib, was accelerated with support from Gavi, and as of 2014 was being used in all 73 Gavi-supported countries. Many countries have also introduced pneumococcal and rotavirus vaccines into their immunization programs; 41 have been approved for rotavirus vaccine support and 58 have been approved for pneumococcal support as of November 30, 2015.¹²

Encouraging Private-Sector Involvement

As a result of increasing investments in Gavi by the United States and other donors, new suppliers have stepped up to provide reliable vaccines at prices sustainable in the global market. In 2001, there were five vaccine manufacturers supplying Gavi, only one of which was from an emerging market economy. By 2015, Gavi had more than doubled the number of suppliers, over half of which were from emerging markets.¹³

By expanding the number of suppliers of WHO-prequalified vaccines, Gavi has successfully increased supplies of older, underutilized vaccines, as well as negotiated lower prices for some of the more recent and more expensive vaccines, such as the rotavirus, HPV, and pneumococcal vaccines. In 2016, for example, GlaxoSmithKline committed to providing the pneumococcal vaccine at the lowest price ever (a reduction of 10 percent from the current price of \$3.40 per dose).¹⁴

Caution about Country Transition

While Gavi is seen to be a key success story of U.S. government investment in immunization, there have been and continue to be critiques of its performance. For example, Gavi's policy on country transitions (whereby transitioning countries ramp up funding over five years until vaccines and supplies are fully funded domestically) has been cited as "haphazard." Experts interviewed expressed concern about the variety of challenges countries will confront as they begin to transition even as Gavi and other stakeholders revisit financing, procurement, and other barriers.

Since 2011, 24 countries have entered graduation, with 16 expected to transition fully from Gavi support by the end of 2018. Despite improved economic indicators, these countries still face significant financial, leadership, and infrastructural challenges.

Experts claim that indicators for a country's readiness to transition from Gavi support (namely annual GNI per capita) do not take into account the full scale of need and may set up the transition process for failure. Some call the transition process itself "unrefined," with one

¹² Gavi, "Countries Approved for Support," November 2015, <http://www.gavi.org/results/countries-approved-for-support/>.

¹³ Gavi, "Developing Country Pharmaceutical Industry," <http://www.gavi.org/about/partners/developing-country-vaccine-industry/>.

¹⁴ See "The Bio-Pharma Industry and Society" (conference, CSIS, Washington, DC, March 17, 2016), http://csis.org/files/attachments/160317_The_Bio-Pharma_Industry_and_Society.pdf; Gavi, "Gavi Welcomes New Record Low Price for Pneumococcal Vaccine," March 17, 2016, <http://www.gavi.org/Library/News/Statements/2016/Gavi-welcomes-new-record-low-price-for-pneumococcal-vaccine/>.

expert summarizing the process as “adding a year here and a discount there but without a holistic, effective approach that has any hope of sustainability.”

Global Polio Eradication Initiative (GPEI)

The campaign to eradicate polio began with a World Health Assembly resolution in 1988. The agreement led to the formation of the GPEI, a public-private partnership headed by national governments and managed at the global level by the WHO, Rotary International, CDC, UNICEF, and the Bill & Melinda Gates Foundation. The United States has been one of the largest donor countries and has thrown its support behind the GPEI’s *Polio Eradication & Endgame Strategic Plan 2013–2018*, the goal of which is “to complete the eradication and containment” of all vaccine-related polioviruses.¹⁵ In addition to its GPEI involvement, the United States has also pursued bilateral engagement with polio-affected countries.

Building on the effective use of vaccines to eliminate polio in industrialized countries and Latin America, which served as the proof of concept for global eradication, the trajectory of polio elimination efforts since 1988 has included many successes.

Undoubtedly, the greatest achievements are the elimination of the wild poliovirus (WPV) from all but two countries (Afghanistan and Pakistan) and the declaration in 2015 that one of the three types of WPV had been eradicated globally. In spite of strong gains, however, efforts have fallen short of the original goal of global polio eradication by 2000. The conflict and resulting instability in Afghanistan and Pakistan have complicated vaccine delivery to those most in need.¹⁶ This insecurity threatens the possibility of polio eradication in the immediate future.

Nevertheless, as the world gets closer to achieving polio eradication, global stakeholders are beginning to think about “polio legacy planning.” The aim is to ensure that necessary polio functions are continued as long as they need to be and that after eradication the global health community makes a concerted effort to transfer effective assets, knowledge, and lessons learned from polio eradication to other health priorities.

Measles and Rubella Initiative

Another longstanding partnership is devoted to ending measles and rubella. As a founding member of the Measles and Rubella Initiative, the CDC, along with the American Red Cross and UNICEF, provides technical assistance for epidemiological and laboratory surveillance as well as funding to provide bundled measles vaccine and ensure safe immunization practices.¹⁷

¹⁵ Global Polio Eradication Initiative, “Polio Eradication and Endgame Strategic Plan 2013–2018,” <http://www.polioeradication.org/resource/library/strategyandwork.aspx#sthash.6Ueh0rIO.dpuf>.

¹⁶ Julie R. Garon and Walter A. Orenstein, “Overcoming Barriers to Polio Eradication in Conflict Areas,” *The Lancet Infectious Diseases* 15, 10 (October 2015): 1122–24.

¹⁷ Measles & Rubella Initiative: A Global Partnership to Stop Measles & Rubella, “Measles & Rubella Initiative,” <http://www.measlesrubellainitiative.org/>.

The initiative was established in 1988 and has had steady success. U.S. long-term engagement translates into a stake in continued progress and participation in the WHO's 2012–2020 Measles & Rubella Strategy, which aims to greatly reduce the incidence of measles and eliminate it by 2020. The strategy identifies 68 priority countries based on their relatively low level of routine vaccination coverage for measles and limited progress in introducing the rubella vaccine.

According to the WHO Strategic Advisory Group of Experts (SAGE) on Immunization, progress toward reaching global goals has stagnated, requiring renewed focus and attention.¹⁸

Vaccine R&D

While Gavi and other groups focus on increasing access to and supplying vaccines, the development of new vaccines and improvement of existing ones is another vital effort involving public and private partners. U.S. engagement in global health vaccine R&D involves a network of industrial, academic, and governmental partners that have produced some two-thirds of all new vaccines worldwide over the past two decades.¹⁹ More than 20 different government agencies are involved in vaccine research, with the NIH playing a central role in work that underpins and accelerates vaccine development (see appendix).²⁰

Incentivizing R&D: Rise of Product Development Partnerships

Industry is a critical partner for government in commercializing and manufacturing effective vaccines. Unfortunately, there is an enormous funding gap for R&D of needed vaccines that target developing world diseases. Experts estimate that developing just one vaccine can cost more than \$500 million, and numerous diseases are potential vaccine candidates.²¹ This gap is due to the absence of a market to provide traditional incentives to pharmaceutical companies to invest the hundreds of millions of dollars and decades of time in such efforts.

In response to this need, an innovative funding mechanism for vaccine development, Product Development Partnerships (PDPs), has played a pivotal role over the past 15 years. PDPs are nonprofit organizations that have catalyzed and facilitated innovation by pooling government, philanthropic, private, and academic resources for research and development of new tools for diseases of the poor in developing countries. They limit the risk of individual financial investments in order to develop products that would otherwise not be brought to

¹⁸ World Health Organization, "Measles Fact Sheet, No. 286," March 2016, <http://www.who.int/mediacentre/factsheets/fs286/en/>.

¹⁹ National Vaccine Advisory Committee, "United States Vaccine Research: A Delicate Fabric of Public and Private Collaboration," <http://www.vaccinationcouncil.org/wp-content/uploads/2013/03/DELFAB.pdf>.

²⁰ Gregory K. Folkers and Anthony S. Fauci, "Vaccine Research and Development: The Key Roles of the National Institutes of Health and Other U.S. Government Agencies," in National Institutes of Health and National Institute of Allergy and Infectious Diseases, *The Jordan Report: 20th Anniversary: Accelerated Development of Vaccines 2002* (Washington, DC: U.S. Department of Health and Human Services, 2002), 80–86, https://www.niaid.nih.gov/sites/default/files/documents/jordan20_2002.pdf.

²¹ PATH, "Investing in Vaccines for the Developing World," April 2015, http://www.path.org/publications/files/VAC_investing_fs_2015.pdf; Stanley A. Plotkin, Adel A.F. Mahmoud, and Jeremy Farrar, "Establishing a Global Vaccine-Development Fund," *New England Journal of Medicine* 373 (July 2015).

market. The Bill & Melinda Gates Foundation has been the largest single funder of PDPs, which also receive funding from the World Bank, other foundations, and bilateral donors including USAID, which has consistently ranked among the top funders, and the NIH.²²

Development of the MenAfriVac Vaccine

One example of a critical PDP with tangible results and partners across sectors is the Meningitis Vaccine Project (MVP), a collaboration established in 2001 between PATH and the WHO funded by the Gates Foundation, with additional support from government agencies (USAID, CDC, and NIH), Gavi, UNICEF, and others. In partnership with Serum Institute of India Private Ltd., MVP developed MenAfriVac™, a low-cost vaccine specifically designed to curb meningitis A in Africa. Key U.S. government contributions included the donation of vaccine technology by the FDA, assistance from the NIH on negotiation of the technology transfer agreement, involvement of the CDC in the rollout, and participation of CDC-trained scientists in tracking spread of the disease.

In terms of products developed, the Global Health Technology Coalition hails the development and delivery of MenAfriVac™ as “a model for capacity building and scientific exchange between the United States and endemic countries” that will save an estimated \$570 million in the first decade since its introduction in 2011.^a Reinforcing this success story is the clear global desire for the vaccine, embodied in a plea from African leaders for help in ending this strain of meningitis, which previously was responsible for 85 percent of epidemics on the continent.

Unlike the vaccine it replaced, the new vaccine protects infants and prevents transmission, and is affordably priced for African countries.

^a Meningitis Vaccine Project, “Why Is There No Vaccine Suitable for Africa?,” <http://www.meningvax.org/needed-vaccines.php>.

Returns on U.S. Investment in Immunization

Immunization is saving the lives of children, yet this is just one of many benefits of U.S. investment in this area, as outlined below.

Smart Economics

From an economic standpoint, vaccines offer substantial value, with returns on investment as high as 18 percent, according to a Gavi-commissioned study by the Harvard School of Public Health, which analyzed spending on Gavi’s portfolio and its potential economic return.²³

Immunizations avert the cost of illness, treatment, and lifetime productivity loss due to death avoided and illness prevented. Healthier babies are more likely to grow into healthier children who are able to attend school and become more productive members of society, reaching their full potential. Instead of caring for a sick child and spending savings on medical bills, parents can work and have greater spending capacity. Further, while preventing childhood

²² Richard T. Mahoney, “Product Development Partnerships: Case Studies of a New Mechanism for Health Technology Innovation,” *Health Research Policy and Systems* 9 (2011).

²³ Gavi, “Vaccines Boost Economic Growth in Poorest Countries,” 2010, <http://www.gavi.org/library/news/roi/2010/vaccines-boost-economic-growth-in-poorest-countries/>.

illness is a key component of immunization, some vaccines (e.g., Hepatitis B and HPV) are given to children but prevent adult onset of illness.

In terms of cost savings, the United States recovers the \$23 million it invested between 1967 and 1979 on its campaign for smallpox eradication every 26 days by no longer having to vaccinate or treat the disease.²⁴ Research from Phase I of the Decade of Vaccines Economics project estimates savings of \$151 billion in global costs averted if immunizations were expanded in 72 of the world's poorest countries between 2011 and 2020.²⁵

A recent study reinforced the idea that vaccination is a "best buy" in global health by identifying that in 94 countries, every dollar invested in immunization between 2011 and 2020 was estimated to result in a \$16 return in relation to "cost of illness" (treatment and productivity costs) and a \$44 return when looking at the broader economic and social benefits of living a longer and healthier life.²⁶ The same study cited the measles vaccines as having the greatest return on investment, with \$58 dollars saved in future costs for every \$1 dollar spent.

Domestic Health Security

Protecting Americans from infectious diseases is a fundamental argument for the United States' longstanding priority on the reduction and elimination of vaccine-preventable diseases globally. The CDC's Global Immunization Division warns that although "VPDs such as polio, measles, and rubella have been eliminated in this country, the United States remains vulnerable to disease importations as long as they persist elsewhere."²⁷ In this globalized age, planes send passengers around the world in a matter of hours; disease can and does spread quickly.

Protecting against both old and new diseases is important. Last year's Ebola outbreak in West Africa and recent influenza epidemics in Asia highlighted how rapid air travel and trade make geographic and economic borders meaningless in preventing the spread of infectious diseases. The current situation with the Zika virus is another powerful example.

Health Diplomacy

Preventing infectious disease provides an economic development advantage for low- and middle-income countries, where illness and disability can devastate families and communities and disease is a major factor contributing to impoverishment. Immunization is a part of the larger U.S. global development policy and agenda for 2030. As the world's largest economy, the United States has a responsibility to marshal its outstanding scientific and

²⁴ Fenner et al., "Smallpox and Its Eradication."

²⁵ Meghan L. Stack et al., "Estimated Economics Benefit during the 'Decade of Vaccines' Include Treatment Savings, Gains in Labor Productivity," *Health Affairs* 30 (June 2011): 1021–28, <http://content.healthaffairs.org/content/30/6/1021.full>.

²⁶ Sachiko Ozawa et al., "Return on Investment from Childhood Immunization in Low- and Middle-Income Countries, 2011–20," *Health Affairs* 35 (February 2016): 199–207, <http://content.healthaffairs.org/content/35/2/199.abstract>.

²⁷ Centers for Disease Control and Prevention, "Global Health—Immunization," <http://www.cdc.gov/globalhealth/immunization/>.

technological prowess to improve health, longevity, and prosperity in developing countries by helping to eliminate the morbidity and mortality from infectious disease.

Importantly, immunization also creates an opportunity to foster good will and improve health while strengthening diplomatic relations and bilateral collaboration since immunization requires buy-in, financial support, and cooperation from countries' local and national leadership.

Enduring Challenges

Gavi: Addressing Country Transition Challenges

Gavi's objective is to provide vaccines to the poorest countries, with the expectation that recipient countries will eventually "transition" toward self-sufficiency, ultimately purchasing commodities and funding immunization programs themselves. In theory, when countries transition, funding is freed up to expand coverage in other geographies, and to support the introduction of new vaccines into immunization systems. The rationale is that Gavi cannot continue to pay for old and underused vaccines, as well as the integration of new vaccines, for all countries. Further, Gavi has committed to donors that their funding will decrease as Gavi-eligible countries grow economically and transition.

If countries "transition" out of Gavi support entirely but stop funding domestic immunization programs, the negative health consequences—domestically and globally—are vast. But if Gavi allows countries to extend their transitions indefinitely, without additional funding and with more new vaccines being rolled out, Gavi's resources will be depleted quickly and the organization will no longer be sustainable.

In 2016, 16 countries in Africa, Asia, Eastern Europe, and Latin America will be transitioning from Gavi support, while 5 will have reached the end of Gavi support and will be self-financing vaccines.²⁸ However, such self-sufficiency is easier conceptualized than achieved and there are no "test cases" to learn from. One analysis summarizes the challenges graduating countries face, including "weak national agencies for vaccine purchasing, inadequate regulatory practices to ensure vaccine quality, inability to reach children in poor and remote communities, and insufficient budgeting by the government to meet the full cost of the vaccines after Gavi's funding support ends."²⁹

In advance of the recent Gavi replenishment conference, several industry partners that work with Gavi to produce vaccines made commitments to price reductions or price freezes on their products for countries graduating from Gavi-supported programs. GlaxoSmithKline, Johnson & Johnson, and Merck, among others, have promised to keep the prices at Gavi or

²⁸ Gavi, "Transition Process," <http://www.gavi.org/support/apply/graduating-countries/>.

²⁹ R4D, "Event: The Gavi Experience with Country Graduation: Overcoming Challenges to Sustainable Financing," January 30, 2015, <http://r4d.org/about-us/press-room/event-gavi-experience-country-graduation-overcoming-challenges-sustainable>.

UNICEF levels for 5 to 10 years once a country graduates, which eases the transition process somewhat.³⁰

Notwithstanding this private-sector support, Gavi needs to continue its work to ensure these commitments are fulfilled. At the same time, experts noted that Gavi could play an important role in supporting the development of systems to ensure sustainable delivery of immunizations even after countries have transitioned.

True Success Still Elusive: Equity Gaps in Immunization Coverage

Since 2000, the global community has rallied around the need to guarantee equitable vaccine access for all. But while there have been major gains during the past two U.S. government administrations, millions continue to die of vaccine-preventable diseases.

Access and equity persist as critically important and enduring challenges in immunization coverage. Vaccine-preventable diseases continue to be major contributors to maternal and child morbidity and mortality. The disparity between immunization rates in developing and most developed countries is vast.

Coverage rates also vary greatly between and within countries. For example, the WHO estimated global coverage of the Hib vaccine (preventing meningitis and pneumonia) to be 45 percent in 2012. Regionally, the WHO estimates Hib vaccine coverage at 91 percent in the Americas but only 14 percent in the Western Pacific and 11 percent in Southeast Asia.³¹

Contributing factors for such disparities include funding constraints, logistical challenges, such as maintaining cold chain storage in remote areas (e.g., islands, mountainous settings), and a lack of high-level support for routine immunization within countries.

It is not surprising that countries in conflict and those with fragile economies, heavier disease burdens, and poor health and supply chain infrastructure have immunization coverage rates that are still far short of the 2015 goal of 90 percent coverage. Under new targets for 2020, the Global Vaccine Action Plan aims to achieve ≥ 90 percent coverage nationally and ≥ 80 percent in every district, with polio eradication designated as the first milestone, and to accelerate research and development for new vaccines.³²

Likewise, despite advances in the global fight against measles, six countries (the Democratic Republic of Congo, Ethiopia, India, Indonesia, Nigeria, and Pakistan) account for 56 percent (or 11.5 million) of infants who did not receive the first routine measles vaccination in 2014.³³

³⁰ Gavi, "Private Sector," <http://www.gavi.org/pledging2015/private-sector/>.

³¹ World Health Organization/UNICEF, "Global and Regional Immunization Coverage (1980–2012)," July 2013, http://www.unicef.org/immunization/files/Global_immunization_coverage.pdf.

³² Gavi, "Global Vaccine Action Plan. Annex 1: Recommended Indicators," http://www.who.int/immunization/global_vaccine_action_plan/GVAP_Annex1.pdf.

³³ Measles & Rubella Initiative, "Routine Immunization," <http://measlesrubellainitiative.org/learn/the-impact/routine-immunization/>.

Sustaining and accelerating progress in immunization coverage will require a concerted international effort over the next 15 years in order to achieve Goal 3 of the SDGs for 2016–2030 to “ensure healthy lives and promote well-being for all at all ages.”

Sustainable Development Goal 3: Relevance to Immunizations

- Ending preventable deaths of children under five years of age
- Ending the epidemics of AIDS, tuberculosis, malaria, and tropical diseases and combating hepatitis, water-borne diseases, and other communicable diseases
- Supporting the R&D of vaccines that primarily affect developing countries
- Providing access to vaccines
- Substantially increasing health financing and the recruitment, development, training, and retention of the health workforce in developing countries.^a

^a United Nations, “Sustainable Development Goals—Goal 3: Ensure Healthy Lives and Promote Well-Being for All at All Ages,” <http://www.un.org/sustainabledevelopment/health/>.

Insufficient Investment in R&D

Funding for vaccine R&D is inadequate and has been for years. For example, when the Ebola crisis was at its peak, NIH Director Francis Collins noted that if not for a decade of stalled government funding for research, NIH work on Ebola vaccines begun in 2001 might have produced a vaccine in time to have made a difference. To address urgent demand for action on Ebola, the NIH had to shift funds from other areas when no new funding was provided.³⁴

Although the private sector is the major developer and manufacturer of vaccines, the industry is understandably reluctant to invest in R&D for products for which the commercial market is small, as is the case with most new vaccines. As one expert from a pharmaceutical company commented, “The vaccine industry is not at a point where any of the big guys would be able to effectively run after these smaller target population conditions [Ebola, Zika, MERS].”

The U.S. government has made major investments and created multi-sector partnerships to help develop HIV, malaria, and dengue vaccines—including through product development partnerships. However, the United States could better leverage its investments through closer collaboration and coordination with the private sector.

Lack of Accountability

The 2015 Global Vaccine Action Plan Assessment Report identified two major problem areas stalling progress on vaccine access and immunization coverage: 1) insufficient funding for elimination strategies and their implementation for maternal and neonatal tetanus and for

³⁴ Sam Stein, “Ebola Vaccine Would Likely Have Been Found by Now If Not for Budget Cuts: NIH Director,” *Huffington Post*, October 12, 2014, http://www.huffingtonpost.com/2014/10/12/ebola-vaccine_n_5974148.html.

measles and rubella and 2) gaps in the accountability and translation mechanisms in the monitoring and accountability framework for the GVAP.³⁵

Seizing the opportunity to adjust course and reinvigorate progress at the midpoint of the Decade of Vaccines, the WHO's Strategic Advisory Group of Experts (SAGE) on immunization made several recommendations to address these two obstacles. Changes to the accountability process would encourage mutual accountability at all levels and common metrics for tracking progress. To strengthen healthcare delivery systems, SAGE outlined several measures requiring enhanced coordination and alignment of efforts among global, regional, and country partners.

Weak Supply Chains

Finally, supply chain effectiveness and equity go hand in hand as the countries with the lowest routine immunization coverage generally also face significant challenges with consistent vaccine cold storage, management, and distribution to hard-to-reach areas with poor health infrastructure.

Vaccine supply chains—already severely strained in the developing world—will become only more challenged during the next U.S. government administration, given expectations that several more vaccines will become available to low- and middle-income countries.

Opportunities for the Incoming Administration

According to experts interviewed, now is the perfect time for a new administration to strengthen U.S. investments in bilateral and multilateral efforts to harness the power of immunization to save millions of lives, improve immunization delivery systems, and support economic development around the world. Past accomplishments in expanding immunization coverage and eradicating disease, robust infrastructure, and the new SDG agenda for global development have created a strong foundation that can be built on and leveraged to amplify impact and reach. Specific opportunities highlighted by experts are described below.

Leverage Gavi Leadership Role, Particularly to Manage Country Transitions

Experts zeroed in on the U.S. government's "ideal" positioning to make headway on key immunization challenges through its role as an influential Gavi Board member. In this role, the United States can "put and keep difficult issues (around expanding coverage and increasing equity) on the table and help hold partners to account to deliver on both their commitments and Gavi's core mandate."

Country transition is the key issue of the day, and experts noted that the United States can help encourage discussions around how well Gavi is supporting these countries and whether

³⁵ WHO SAGE, "2015 Assessment Report of the Global Vaccines Access Plan," http://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2015_EN.pdf.

that support comes early enough. They agreed that the United States “has been good about pushing to date, but needs to keep pushing.”

The ultimate goal of U.S. efforts on immunization and overall global health is to support country ownership, a goal that has been endorsed by both donor organizations and recipient nations. Importantly, experts interviewed noted that as countries take a greater role in funding and running their own programs, the U.S. government, through its leadership in Gavi, would strengthen its return on investment by continuing to advocate for sustained involvement with these countries through the transition. In other words, “the U.S. government has both an opportunity and a responsibility to support countries when they are succeeding.”

Expand Product Development Partnerships to Stimulate Investment in Vaccine R&D

Currently, the lack of traditional market incentives means that there is limited attention to R&D for diseases that affect relatively small populations. But as we have seen with Ebola, Zika, and MERS (Middle East Respiratory Syndrome), there are devastating effects on women and children in particular when these diseases spread rapidly. New and expanded funding mechanisms are needed to encourage private sector investment in R&D, especially for neglected diseases.

The U.S. government should build on the success of PDPs to increase broader investment in vaccine R&D. As illustrated by the success of vaccines for measles, neonatal tetanus, and MenAfriVac™, developing the next generation of vaccines is a priority with potential for big payoffs in cost savings over time by reducing the burden of once rampant diseases on health systems. New vaccines already in the pipeline focus on typhoid, malaria, and dengue—major killers of women and children.

Beyond the development of new vaccines, innovations in science and technology could address challenges to delivery and administration of vaccines. For example, the problem of unreliable (or nonexistent) electricity for keeping vaccines cool could be addressed by the developments of vaccines that are stable at room temperature, or the development of cold storage that does not require electricity. Likewise, the availability of more oral vaccines could replace injections, making them cheaper and easier to administer by lower-skilled health workers.

Because R&D takes time (often decades), the Global Health Technology Coalition has recommended that the administration develop a long-term strategy to provide consistent and flexible funding for the CDC, the Department of Defense, the FDA, the NIH, and USAID, each of which plays a unique role within the R&D process. The coalition also recommends that separate funding should be allocated for global health emergencies and new and

emerging infectious disease threats, such as the Zika virus, so that agencies are prepared to respond without having to shift resources from other program budgets.³⁶

Step up Efforts to Reach the Most Vulnerable

The U.S. government—especially through its important role within Gavi—can lead the charge to support countries in closing the equity gap. Through technical support, better use of data, and sharper focus on vulnerable populations, the United States can help countries bolster efforts in regional pockets where coverage is minimal and help vaccinate at scale as well as in conflict zones and humanitarian settings.

As one expert from the private sector commented in reference to the Ebola crisis, “Only governments can solve the problem of vaccine uptake; the market can’t solve that. If we wait on a market solution, we will just get more of the same.”

In particular, USAID’s experience providing technical assistance is extremely valuable in ensuring that fewer children die from vaccine-preventable diseases. The global disparities in immunizations are directly related to weak health systems that do not have the supply chains to deliver vaccines, electricity or appropriate equipment to keep them cold, or the roads to transport them. As one advocate commented, “We have these powerful vaccines but it is about making sure that they are getting out in ways that are efficient and effective.”

The timing is ripe for greater investment here given recent disease outbreaks, porous borders, and the U.S. terror of pandemics. Building countries’ capacity to expand immunization coverage to the most vulnerable is essential for children’s health in these countries, but also globally. In the face of the global spread of disease, “There is a need to make sure there are responsible systems in countries to make sure disease doesn’t spread,” as one expert expressed.

Conclusion

Immunization has greatly reduced the burden of infectious diseases, improving and saving the lives of millions of children every year, and has provided a foundation for other health services and efforts to address childhood illnesses. The U.S. government has invested wisely in this “global health best buy” and serves as an important steward of global funds. In alignment with the SDG framework, the next 15 years offer the U.S. government pivotal opportunities to build on success by leveraging the U.S. leadership role with Gavi to help increase country ownership of domestic immunization programs; driving R&D innovation; and championing efforts to increase coverage and equity by focusing on the most vulnerable populations.

³⁶ Global Health Technologies Coalition, “2015 Policy Report: Meeting the Challenge, Seizing the Opportunity: U.S. Leadership Can Advance Global Health R&D,” <http://www.ghtcoalition.org/pdf/meeting-the-challenge-seizing-the-opportunity-us-leadership-can-advance-global-health-r-d-summary.pdf>.

Appendix A: Organization of U.S. Government’s Immunization Efforts

The U.S. government carries out its pivotal and multifaceted role in global immunization efforts through many different funding approaches and government agencies. U.S. efforts are both multilateral, through participation in international organizations and partnerships with governments, NGOs, and the private sector, and bilateral, through programs that work directly with other countries.

Working alone, neither the United States nor any agency or institution could have made a dent in increasing global immunization coverage and eradicating targeted diseases. Progress has been achieved through the five federal agencies contributing to immunization efforts, with respect to funding, infrastructure, and their own unique focuses, capabilities, and expertise.

CDC	The CDC’s Global Immunization Division provides technical assistance and surveillance support to country ministries of health, with a focus on eradicating polio, reducing measles deaths, and strengthening routine vaccine delivery.
USAID	USAID carries out its immunization strategy through a multipronged approach that combines flexibility with respect to type of assistance with a long-term focus on results. The agency adopted the self-proclaimed “system strengthening” approach following a decade of stalled progress and even decline in immunization levels in some countries in the 1990s. Focus shifted toward routine immunization systems and capacity building in target countries. To this end, USAID provided technical assistance and developed communications to incentivize health behaviors. The agency also pursued engagement at the community and country levels through bilateral, multilateral, and public-private partnerships.
FDA	The FDA is responsible for the regulation of a number of products in the United States, including vaccines and vaccine-delivery technologies, and is widely perceived to provide the global “gold standard” for health product regulation. In addition to regulating vaccines produced in other countries and used in the United States, it also supports the capacity of less developed countries to regulate the development and production of vaccines in their own countries. ³⁷
NIH	The NIH leads the charge for the United States on vaccine R&D investments. The NIH engages in global health through all of its 27 institutes and centers, with its National Institute of Allergy and Infectious Diseases (NIAID) playing a pivotal role in vaccine R&D for dengue fever, HIV/AIDS, malaria, tuberculosis, and other diseases.
DoD	In an effort to safeguard and improve civilian and military health in areas where troops may be deployed, the DoD conducts research into development new vaccines (e.g., malaria, dengue, Ebola and HIV). The DoD has been involved in the development of one of every four vaccines approved by the FDA in the last century. ³⁸

³⁷ PATH, “US Investments in Global Immunization: Leading Efforts to Improve Health and End Preventable Child Deaths,” https://www2.aap.org/international/immunization/pdf/US_Investments_Global_Immunization.pdf.

³⁸ Ibid.

Appendix B. Glossary of Abbreviations and Acronyms

DoD	U.S. Department of Defense
EPI	Expanded Program on Immunization
FDA	U.S. Food and Drug Administration
GAVI	Global Alliance for Vaccines and Immunizations
GNI	Gross national income
GPEI	Global Polio Eradication Initiative
GVAP	Global Vaccine Action Plan
Hib	Haemophilus influenzae type B
HPV	Human papillomavirus
IFFIm	International Finance Facility for Immunization
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
MDGs	UN Millennium Development Goals
MERS	Middle East Respiratory Syndrome
MVP	Meningitis Vaccine Project
NGO	Nongovernmental organization
NIAID	U.S. National Institute for Allergy and Infectious Diseases
NIH	U.S. National Institutes of Health
PDP	Product Development Partnership
SAGE	WHO Strategic Advisory Group of Experts on Immunization
SDGs	UN Sustainable Development Goals
UNICEF	UN Children's Emergency Fund
USAID	U.S. Agency for International Development
VPD	Vaccine-preventable disease
WHO	World Health Organization
WPV	Wild poliovirus