Encouraging Vaccine Innovation: Promoting the Development of Vaccines that Minimize the Burden of Infectious Diseases in the 21st Century

Report to Congress



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National Vaccine Advisory Committee

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NVPO
NATIONAL VACCINE PROGRAM OFFICE

Vaccine Innovation Background

The National Vaccine Plan

- The National Vaccine Plan (NVP) is the nation's leading roadmap for a 21st century vaccine and immunization enterprise.

- The NVP has five overarching goals:

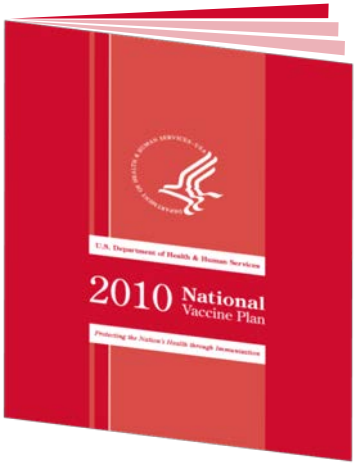
  Develop new and improved vaccines

  Enhance the vaccine safety system

  Support communications to enhance informed vaccine decision-making

  Ensure a stable supply of, access to, and better use of recommended vaccines in the United States

  Increase global prevention of death and disease through safe and effective vaccination



The NVP Mid-Course Review

The Mid-course Review of the National Vaccine Plan included 2 out of 5 priority opportunity areas related to innovation:

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

The NVP Mid-Course Review

The NVAC supported all 5 priority opportunity areas, and made additional recommendations related to innovation:

- The ASH should charge the NVPO, in coordination with relevant departments and agencies, to develop and validate new indicators within each of the 5 opportunity areas to ensure improved tracking of goals. The new indicators should include one that will track and report on U.S. government annual financial investments in vaccine innovation that support the development of (1) vaccines for established pathogens that have no vaccines, (2) vaccines for emerging pathogens, and (3) improved existing vaccines. The new indicators should also consider investments in vaccine delivery technologies.

- The ASH should charge NVPO, in coordination with other relevant departments and agencies, to begin developing strategies to (1) identify priorities for US government investments in vaccine-related innovations and (2) overcome barriers that inhibit innovation.

Report Background

Report Development

December 13, 2016
The 21st Century Cures Act is signed into law. A provision requires the HHS Secretary to submit a report on encouraging vaccine innovation

June 27, 2017
Panel discussion with experts in science, medicine, public health, vaccine safety, patient policy, consumer advocacy, and private sector industry

March 2018
HHS Secretary reviews and submits final report to Congress

Vaccine Innovation Steering Committee
On behalf of the Secretary, NVPO coordinates with ASPE, BARDA/ASPR, CDC, FDA, and NIH

Report Development
The VISC collaborates to develop the report

Report Requirements

Specifically, the report shall “review the current status of vaccine development and, as appropriate—

A. Consider the optimal process to determine which vaccines would be beneficial to public health and how information on such vaccines is disseminated to key stakeholders;

B. Examine and identify whether obstacles exist that inhibit the development of beneficial vaccines; and

C. Make recommendations about how best to remove any obstacles identified under subparagraph (B) in order to promote and incentivize vaccine innovation and development.”

Report Findings

Current Status of Vaccine Development

120+

vaccine candidates are currently under development

The U.S. vaccine enterprise is **well established** and has been **successful** at bringing innovative and new and improved vaccines to the market.

- **Many domestic and global partners are involved** such as government, industry, academia, non-profit, and private sector partners.
- **It is complex** including infectious disease surveillance, basic and applied research, product development, regulatory evaluation and licensure, recommendations for introduction and use, and vaccine uptake.

Current Status of Vaccine Development

Yet, the vaccine enterprise is at a turning point for 3 reasons:

The prevailing business model prioritizes vaccine candidates with large markets; yet market sizes are likely smaller for many remaining targets

Substantial investment is needed to address the scientific complexity of remaining targets

Uncertainty of the public health priority and demand of some targets may be unclear—increasing uncertainty of potential ROI and therefore investment risk of development

Current Status of Vaccine Development

The prevailing business model prioritizes vaccine candidates with large markets; yet market sizes are likely smaller for many remaining targets

- Some vaccines under development are expected to receive a recommendation for a subset of the population rather than a universal recommendation. For example, vaccines for persons undergoing elective surgery may only be recommended for use among that population.

- This presents several challenges, especially for small companies. The market for these products may be smaller and more difficult to estimate because of uncertainty about the population for whom the vaccine might be recommended and the expected level of utilization.

Current Status of Vaccine Development

Substantial investment is needed to address the scientific complexity of remaining targets

- New vaccine targets are more scientifically complex and challenging.
- The challenges presented may require substantial investment in new tools, standards, analysis methods, and other novel approaches to demonstrate safety and effectiveness.
- Challenging clinical trial design to evaluate safety and efficacy due to a variety of reasons including low incidence of disease; limited infrastructure in affected geographic areas; and lack of clarity in the understanding of at risk populations.

Current Status of Vaccine Development

Uncertainty of the public health priority and demand of some targets may be unclear—increasing uncertainty of potential ROI and therefore investment risk of development

- Public health priorities have historically been evident to stakeholders due to the clear disease burden of many infectious agents (e.g., polio) and public health demand for vaccines.
- The development of certain vaccines — for example, universal influenza vaccines and respiratory syncytial virus (RSV) vaccines for infants — is considered a high priority as reflected in the number of companies working on these vaccine targets.
- However, the public health priority for many remaining vaccine targets is less clear.

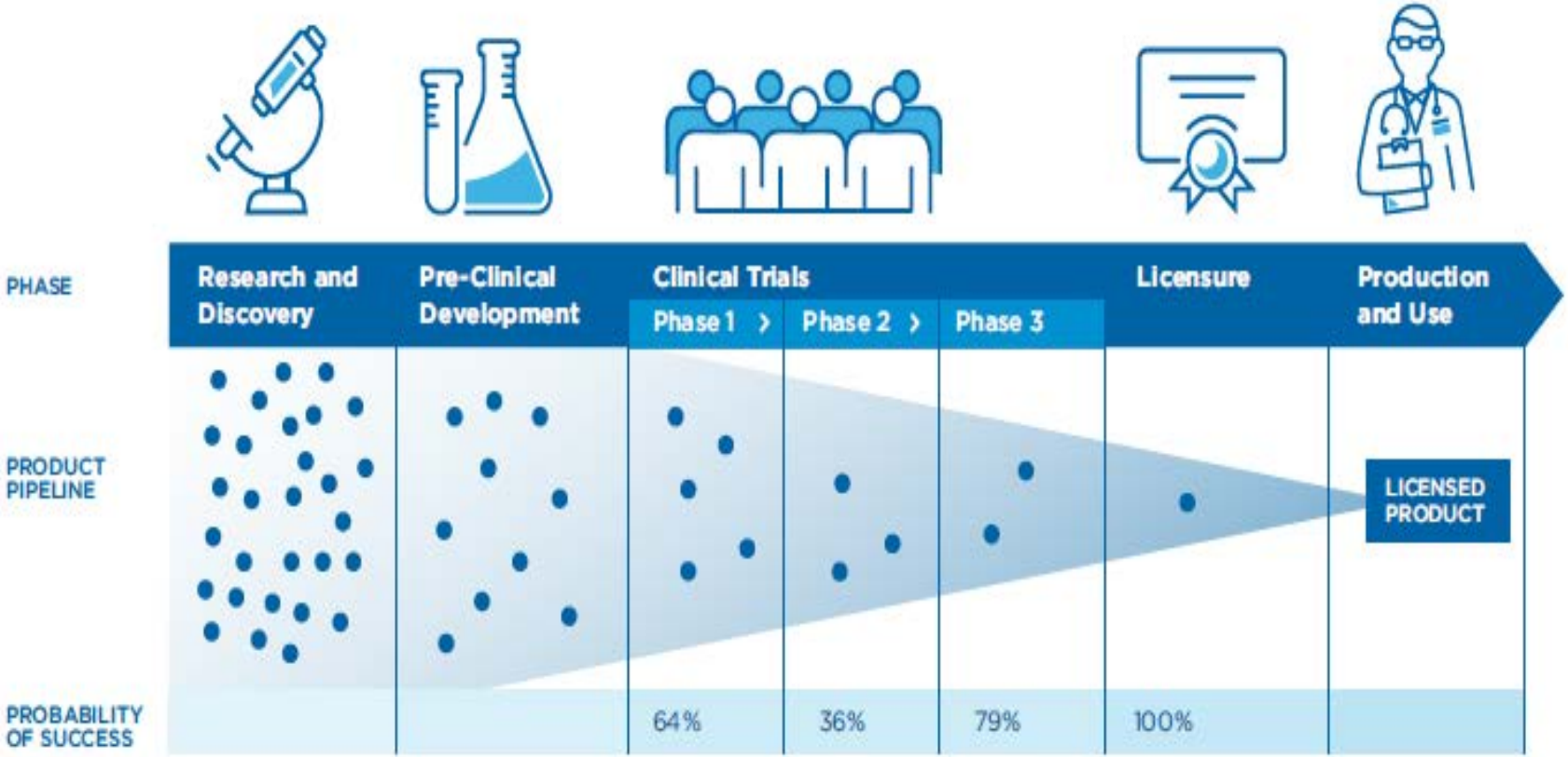
Current Status of Vaccine Development

Small and large companies are key to vaccine innovation.

- Most vaccine candidates are developed by small companies that drive innovation in early stage development.

- During late stage development, products with a potential ROI attract large companies for investment.

- Only a handful of large companies have the resources and expertise to support late stage development.



Source: Biotechnology Innovation Organization, BioMedTracker, and Amplion. Clinical Development Success Rates 2006-2015.

Current Status of Vaccine Development

Large companies may face several vaccine development constraints:

- Limited resources leading to competition against investing in other pharmaceutical products that may have a higher ROI and lower risks.
- Capacity constraints related to the global market, which requires navigating multiple regulatory authorities and immunization policies, which may vary from country to country.
- Opportunity costs for investments in emerging priorities (e.g., Ebola virus vaccine).

Current Status of Vaccine Development

Federal agencies play a central role in vaccine innovation…

NIH	FDA	CDC	BARDA	NVPO
Supports and conducts basic research, translational research, and clinical evaluation focused on identifying vaccine targets and advancing novel candidates through the vaccine development pipeline.	Ensures a rigorous and extensive development program involving vaccine review and licensing, regulatory science and innovation, international collaboration, and post-licensure manufacturing and safety monitoring.	Identifies, controls, and prevents infectious diseases through surveillance, detection, and response; vaccine use recommendations; vaccine purchasing and service delivery; health communications; and post-marketing vaccine safety and effectiveness.	Develops and procures needed medical countermeasures through public-private partnership approaches: direct advanced research and development support, core services support, and leveraging investments in technologies.	Provides strategic leadership and coordination and oversees the National Vaccine Advisory Committee.

USG actions and policies can act as levers to promote vaccine innovation and address many challenges to continued vaccine innovation.

Innovation
Challenges & Opportunities

CHALLENGES TO INNOVATION

Limited understanding of the science to develop optimal vaccines

Challenging clinical trial design for specific populations

Converging regulatory requirements across countries

Uncertain return on investment (ROI) for new and improved vaccines

Limited understanding of the science to develop optimal vaccines

Opportunity

Enhancing scientific understanding of mechanisms involved in immune responses to infection and vaccination.

- NIH & CDC provide substantial support for studies to better understand key immunological characteristics of vulnerable populations.
- Federal investments in adjuvant discovery and development show promise in exhibiting different immune stimulatory properties—providing a toolbox for developers.
- Continued support for translational research and clinical vaccine development and evaluation can be critical for innovation products.

Challenging clinical trial design for specific populations

Opportunity

Using regulatory flexibility and novel scientific tool development.

- FDA's implementation of innovative and flexible regulatory mechanisms and pathways has ensured that approval of vaccine candidates keeps pace with technological and scientific advances.

- Novel scientific tools will be necessary to translate scientific discoveries into safe and effective vaccines. To this end, FDA has efforts underway regarding the development and use of novel clinical trial designs, including the use of biomarkers, innovative statistical analysis techniques, and real world evidence to facilitate vaccine innovation and development

Converging regulatory requirements across countries.

Opportunity

Enhancing global activities.

- Using FDA best practices to expand regulatory convergence may decrease the resources required by companies to engage in a global market. Examples include adoption of internationally recognized technical guidance documents or standards and scientific principles.

- Improving coordination with other countries such as agreement on clinical endpoints and assay and batch-release testing results

Uncertain return on investment (ROI) for new and improved vaccines.

Opportunities

Increasing surveillance and epidemiological studies.

- Epidemiological surveillance is critical to (1) assess disease burden that informs development targets, clinical trial design, and final target product profiles; and (2) identify needs for new vaccines or effectiveness concerns among existing vaccines.

- CDC gathers reliable epidemiological data to support clinical trial design and shape the final product profile of the vaccine.

- CDC and NIH support efforts to enhance global activities in surveillance as well as development of global clinical trial sites.

Uncertain return on investment (ROI) for new and improved vaccines.

Opportunities

Enhancing communication frequency and transparency with the USG and external stakeholders including industry.

- Continued communication between FDA and industry can decrease regulatory uncertainty by discussing data needed for a desired indication in the early stages of development.

- Regarding potential recommendations for use, improved communication between CDC and industry may help reduce uncertainty about implementation of new vaccine policy/programs.

- CDC has standardized ACIP working group guidelines so approaches and timelines for communicating with vaccine developers are more predictable.

Uncertain return on investment (ROI) for new and improved vaccines.

Opportunities

Improving vaccine uptake.

- Uptake of existing vaccines in a given population may predict uptake of new vaccines in that population.

- Ongoing efforts to improve vaccine uptake across the lifespan and among persons at increased risk for vaccine-preventable diseases or their complications should be sustained.

- Increasing uptake of currently available vaccines supports investments in new vaccines by increasing the projected market for new products.

Uncertain return on investment (ROI) for new and improved vaccines.

Opportunities

Public-private partnerships.

- For some high priority vaccine targets—like pandemic influenza preparedness or biodefense—public-private partnerships are central to facilitating development. BARDA successfully partners with industry to develop and procure vaccines against a range of threats.

- Development of vaccines or high-priority products with small markets or a low estimated ROI could benefit from public-private partnerships with federal support.

- USG investment could be leveraged to develop certain vaccines that would not be undertaken without incentives.

Summary

- The U.S. vaccine enterprise is **well established** and has been **successful** at bringing new and innovative vaccines to the market.

- **Focus** on the challenges in vaccine innovation and the benefit to individual and public health.

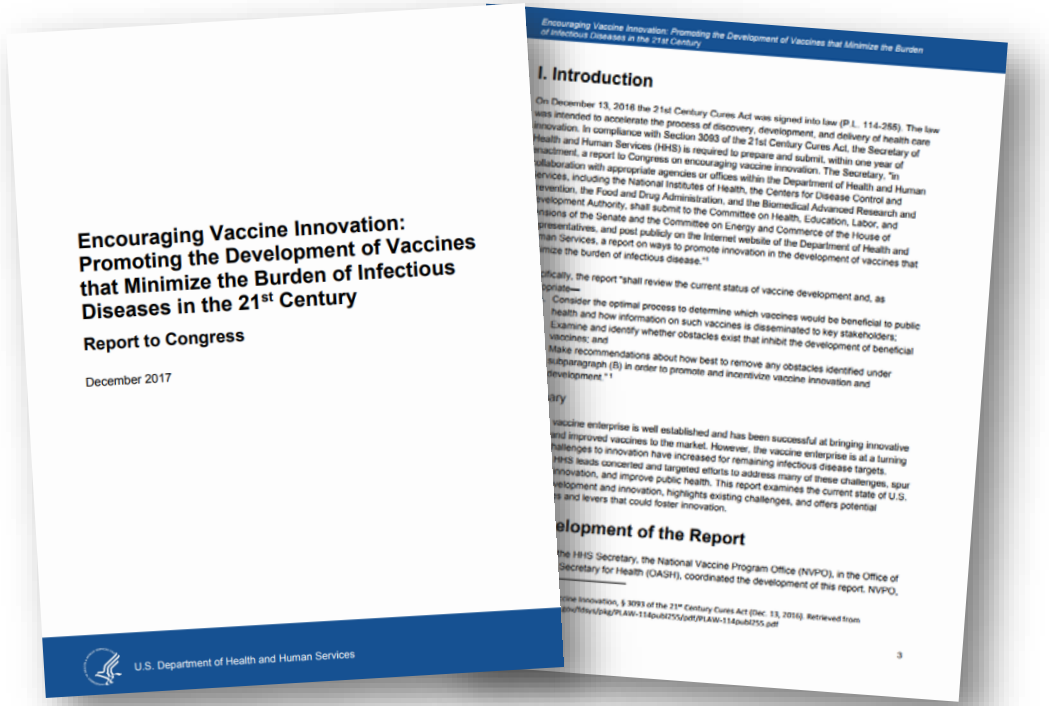
- **Federal agencies can play an important role** in addressing these challenges and spurring innovation.

Summary

Challenges	Opportunities
Limited understanding of the science to develop optimal vaccines	Enhancing scientific understanding of mechanisms involved in immune responses to infection and vaccination.
Challenging clinical trial design for specific populations	Using regulatory flexibility and novel scientific tool development.
Converging regulatory requirements across countries	Enhancing global activities.
Uncertain return on investment for new and improved vaccines	• Increasing surveillance and epidemiological studies. • Enhancing communication frequency and transparency with the USG and external stakeholders including industry. • Improving vaccine uptake. • Public-private partnerships.

Report Available: *https://www.hhs.gov/nvpo/featured-priorities/innovation/index.html*

View the Report



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Thank you!

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