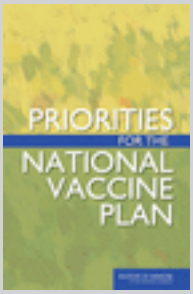

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PRIORITIES FOR THE NATIONAL VACCINE PLAN

Committee on Review of Priorities in the National Vaccine Plan

Board on Population Health and Public Health Practice

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"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

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This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Linda Rosenstock,** Dean, UCLA School of Public Health. Appointed by the National Research Council she was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

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APPENDIXES*

*Appendixes A-F are available on the CD in the back of the book and at http://www.nap.edu/catalog.php?record_id=12796. Appendixes G and H are printed in the book and are also available online at the URL provided.

Summary

The National Vaccine Plan is required by Title III in the 1986 National Childhood Vaccine Injury Act (NCVIA).[1] A plan was first released in 1994 and was updated by a draft plan issued in November 2008 (HHS, 1994, 2008). The National Vaccine Program Office (NVPO), located in the Office of the Assistant Secretary for Health in the Department of Health and Human Services (HHS), solicited broad input from stakeholders, including the public, when drafting the plan. NVPO also asked the Institute of Medicine (IOM) to convene a committee to "prepare first a letter report[2] on its review of the 1994 plan" and then to prepare a "report with conclusions and recommendations about priority actions within the major components of the draft new plan" (see Box S-1).

This report, *Priorities for the National Vaccine Plan*, aims to identify a set of actions the committee believes merit primary attention as NVPO and its partners finalize and implement the National Vaccine Plan. Strategic plans typically linked with budgets and resources are rarely sufficient to support every activity that planners may consider important and needed. Although the 2008 draft plan does not provide information about the potential costs of implementing its objectives and strategies, the committee defined "priority actions" as actions that take precedence among many competing claims for resources. The committee made 18 recommendations about "priority actions" distributed among the plan's five goals, and two additional recommendations, one of which refers to the scope of the National Vaccine Plan

[1] See Appendix C.

[2] The letter report was released in June 2008 and is available from the National Academies Press (http://www.nap.edu) and in Appendix D.

BOX S-1
The Charge to the Committee

The federal government issued "Disease Prevention through Vaccine Development and Immunization, The US National Vaccine Plan" in 1994. The Institute of Medicine will convene an ad hoc committee to evaluate the 1994 National Vaccine Plan and then review and make recommendations regarding an update of this National Vaccine Plan. The committee will hold workshops[a] with national expert stakeholders in medicine, public health, and vaccinology to review a publicly available, draft update of the Plan. The committee will prepare a letter report of the evaluation of the 1994 Plan, and a report with conclusions and recommendations about priority actions within the major components of the draft Plan.

[a] The IOM Committee on Review of Priorities in the National Vaccine Plan conducted its work between March 2008 and November 2009, including five information-gathering meetings with national stakeholders in Washington, DC, Chicago, Seattle, and Irvine.

and another that reflects NVPO's role as a crucial ingredient in implementing the plan and ultimately ensuring that its objectives are achieved.

CONTEXT

Vaccination is a fundamental component of preventive medicine and of public health practice. The use of vaccines to prevent infectious diseases has resulted in dramatic decreases in disease, disability, and death in the United States and around the world. The contemporary national vaccine program[3] is extraordinarily complex in all aspects, from research and development of new vaccines to financing and reimbursement of immunization services. As a medical product, preventive vaccines occupy a unique niche because they are given to healthy individuals, they are purchased in large volume by the federal government as part of the Vaccines for Children entitlement program, and government public health agencies at the federal and state level make policy decisions about how best to use vaccines to protect the public's health. Similar considerations inform policy for global vaccine efforts.

In the latter part of 2009, the political, economic, and social environment presents both opportunities for and challenges to strengthening the U.S. system for developing, manufacturing, regulating, distributing, funding,

[3] In this report, the committee uses *national vaccine program* in lower case to denote the vast and complex network of actors and actions related to vaccines and immunization, and uses *National Vaccine Program* (per the 1986 act) when referring to the governmental agencies that have responsibilities related to vaccines and immunization.

and administering safe and effective vaccines for all people. The Introduction highlights key issues in the health care delivery system and in society, and also comments on the significance of the evolving 2009 novel H1N1 influenza pandemic.

THE HISTORY OF THE PLAN

The NCVIA called for the Secretary of Health and Human Services to serve as the director of the National Vaccine Program,[4] for a plan outlining the activities of the program to be updated annually,[5] an advisory committee to provide guidance to the secretary and the program, and a budget to support specific types of program activities. The act also listed nine responsibilities for the program and its director (Public Law 99-660, Title XXI, Subtitle 1, Section 2102):

1. Vaccine research
2. Vaccine development
3. Safety and efficacy testing of vaccines
4. Licensing of vaccine manufacturers and vaccines
5. Production and procurement of vaccines
6. Distribution and use of vaccines
7. Evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities
8. Coordinating governmental and non-governmental activities
9. Funding of federal agencies

Although the National Vaccine Program has had some great successes and there have been examples of effective coordination, neither NVPO (whose stated work is to provide "leadership and coordination among Federal agencies, as they work together to carry out the goals of the National Vaccine Plan") nor the plan have functioned as intended in the 1986 legislation. This report includes several case studies that illustrate gaps or limitations in the program's ability to perform important functions without the benefit of a strong, capable, and adequately resourced NVPO. These issues

[4] Although the 1986 legislation did not specify the placement of NVPO and its relationship to the Secretary of HHS, delegation of authority by the secretary led to placement of the office in the Office of the Assistant Secretary for Health (ASH), and made the ASH the head of the National Vaccine Program. The National Vaccine Advisory Committee (NVAC) charter states that "Pursuant to the Statement of Organization, Functions, and Delegations of Authority for the Department of Health and Human Services (46 FR 61318, dated December 2, 1977; as amended in 52 FR 23502, dated June 22, 1987), the ASH shall serve as Director of the National Vaccine Program."

[5] In 1998 the requirement for annual updates of the National Vaccine Plan was repealed by Public Law 105-362, Title VI, § 601(a)(1)(H), Nov. 10, 1998, 112 Stat. 3285.

and some of the reasons NVPO has never become what it was intended to be are discussed in Chapter 6.

GENERAL COMMENTS ABOUT THE 2008 DRAFT PLAN

The committee found that the lack of a coherent vision in the draft plan may be linked with an apparent sense of ambiguity about whether the plan should serve as (a) a collection of ongoing and planned activities that many agencies are already undertaking followed by an assessment of accomplishments at a later date; or (b) a list of critical needs and gaps that require coordinated attention by specific agencies or combinations of agencies and stakeholders; or (c) both a and b? A vision statement could resolve this ambiguity and guide the plan's drafters, and the stakeholders who contribute to and will help implement the plan, in identifying the plan's desired outcomes.

It is understandable why the plan's drafters chose to include both activities that are part of existing strategic plans and are certain to be accomplished in the near future, and activities that are novel, not necessarily represented in any other planning document, and require multi-sectoral coordination and collaboration. However, the committee suggests that NVPO consider distinguishing between objectives or strategies that are likely to be accomplished regardless of their placement in the National Vaccine Plan and those that are unique to the plan and require coordination among agencies and with non-government stakeholders in order to be achieved.[6] The committee's recommendations about "priority areas within major components of the plan" refer to the latter type of objectives and strategies. Additionally, the forthcoming implementation plan NVPO will prepare after finalizing the strategic plan would be strengthened by a clear explanation of how the indicators in each goal relate to the objectives and strategies in that goal (Strikas, 2008).

Below, chapter summaries and recommendations are provided in the order in which they occur in the report with one exception. In view of the importance of NVPO's coordinating function, which is covered in the report's final chapter (6), the overview of coordination appears first.

CHAPTER 6: COORDINATION

The history of NVPO and the National Vaccine Plan, and how it has influenced interagency coordination and coordination with stakeholders, is reviewed in the sixth chapter. The office's authority and its human and financial resources have not matched its responsibilities, and the committee

[6] W. Orenstein, 2007 NVAC meeting (NVAC, 2007).

found that this mismatch has resulted in missed opportunities for the National Vaccine Program, and in NVPO's inability to fully meet its statutory duties.

Coordination is at the heart of the plan's purpose, which is "to promote achievement of the National Vaccine Program mission by providing strategic direction and promoting coordinated action by vaccine and immunization enterprise stakeholders" (HHS, 2008). For this reason, supported by a request from the National Vaccine Advisory Committee (see Appendix B), the committee considered NVPO's coordinating role with regard to the plan, including intragovernmental coordination and coordination with external stakeholders, in addition to considering the individual elements of the plan.

Although coordination is not always possible or even necessary, there are areas where it is critical. For example, using a vaccine research agenda to spur the efficient development of priority vaccines requires intersectoral coordination at a high level. Building a structured way of identifying and addressing emerging safety information where appropriate, useful, and realistic, requires input from multiple agencies and external stakeholders. Each agency has its own fairly distinct responsibilities in the area of vaccines and vaccination. However, some areas require coordination to reduce inefficient duplication of effort, and in other areas, one agency's efforts may not be enough to reach an important goal.

Because vaccines and immunization constitute a major public health matter that involves multiple government agencies and has great importance to the public's health, an effective coordinating entity is needed, and effectiveness is dependent on authority and funding commensurate with the task at hand. However, the committee finds that NVPO, which was envisioned by the 1986 statute to serve as this entity, currently lacks the authority, influence, and profile needed to do so. Recently, NVPO has been given and has seized the opportunity to play a crucial coordinating role with regard to H1N1 pandemic influenza vaccine safety (HHS, 2009; NVAC, 2009a; Vellozzi, 2009). This example illustrates NVPO's potential as coordinating entity in the face of a major challenge to the National Vaccine Program.

Recommendation 6-1: The Secretary of HHS should actively demonstrate the Department's support for the National Vaccine Plan by:

(1) clarifying its primacy as the strategic planning tool applicable to all federal agencies with roles in the National Vaccine Program, and

(2) allocating the resources necessary to assure robust planning and implementation, with coordination by the National Vaccine Program Office.

CHAPTER 1: VACCINE DEVELOPMENT

Developing and manufacturing most[7] vaccines involves using living organisms and presents unique technical and regulatory challenges. Both industry and regulators are risk averse, and progress in regulatory science in general has been slow; as a result a "tried and true" paradigm characterizes some aspects of vaccine development and regulation (Goldberg and Pitts, 2006; Poland et al., 2009). Furthermore, some barriers to innovation stem from administrative and communication challenges at the interface between regulators and industry, not from concerns about safety, efficacy, or immunogenicity.

Recommendation 1-1: The National Vaccine Plan should incorporate improvements in the vaccine regulatory process that reflect current science and encourage innovation without compromising efficacy and safety.

Improvements include:

- Strengthening communication with vaccine developers through more frequent workshops and guidance documents.
- Revising procedures and standards for developing, licensing, and producing vaccines for infectious diseases that encourage flexibility and innovation.

In order to ensure that the Food and Drug Administration (FDA) can promote vaccine development while protecting safety, the agency must have funding and staffing commensurate with its responsibilities to identify, develop, and apply the best and most current science to the regulation of vaccine products.[8]

There currently is no ongoing, evidence-based process by which vaccine candidates are identified as priorities shared among various stakeholders. Such a process can accelerate the development of vaccines by identifying the need and the likely market, and should be accompanied by a concerted effort to employ modern techniques to reach the goal of new and improved vaccines.

Recommendation 1-2: The National Vaccine Plan should incorporate the development of an evidence-based approach for prioritizing new and improved vaccine candidates by targeted disease and

[7] Newer synthetic sub-unit vaccines are an exception.

[8] "The non-user fee part of CBER's budget request for FY 2009 is $158 million, an increase of just under $3 million, or a mere 1.9 percent over FY 2008" (Richards, 2008).

develop specifications for high-priority vaccines to accelerate their development.

Specifications, such as target population, will differ for each vaccine, and defining them would increase predictability for manufacturers, reduce financial risk, and perhaps cost. The evidence to be considered would include disease burden and feasibility, and would incorporate data or guidance available from prior published work linking research and funding levels to national priorities.[9] An approach to priority setting may include the following:

- Supporting disease burden studies (e.g., morbidity and mortality) when needed for vaccine prioritization.
- Employing outcome measures that capture both survival gains and quality-of-life improvements.[10]
- Employing cost-effectiveness analysis.
- Consider technical and scientific feasibility of vaccine development as a prioritization criterion.

The committee found that the vast majority of National Institutes of Health (NIH)-supported peer-reviewed vaccine research is investigator-initiated and that coordination among federal agencies and with academic and private sector stakeholders could be strengthened. Furthermore, some examples of innovative and productive intersectoral collaboration come from a history of public-private partnerships, from the World War II era collaborations between the Department of Defense, industry, and academia, to contemporary development of vaccines for global health through product development partnerships.

Recommendation 1-3: The National Vaccine Plan should incorporate creation of a strategy for accelerating development of high priority vaccines that (a) engages all relevant institutes within NIH and the Department of Defense, academic investigators, and private sector partners; and (b) adapts lessons learned from past and present innovative public-private partnerships.

[9] See, for example Gross et al., 1999; Neumann et al., 2005.

[10] Quality-adjusted life years, or QALYs, have been suggested for use in the United States for priority setting in vaccine development (IOM, 2000). Disability-adjusted life years, or DALYs, have been suggested for use internationally. However, it is important to note that both measures have their proponents and critics, and that there are other measures of health outcome that could be used to inform a process of priority setting.

This coordinated outcome-focused approach to vaccine development would need to be periodically reassessed to maintain appropriateness.

The distinction between preventive vaccines against infectious disease and other preventive therapeutic vaccines apparent in the 1986 law is not a reflection of 21st-century vaccine science. The committee believes that as long as the statutory requirements are met by the National Vaccine Program, there is nothing that prevents the Secretary of HHS from expanding the program's mission or finding other ways to link HHS policy and strategy across vaccine categories.

Recommendation 1-4: Future iterations of the National Vaccine Plan should include classes of vaccines (such as therapeutic vaccines and vaccines against non-infectious diseases) beyond those expressly enumerated in the statute, and the Secretary of HHS should explore how best to assign responsibility for coordination in this area.

This broader view of vaccines recognizes the potential value of new vaccines beyond the "traditional" role of preventing infectious diseases and positions the federal government to support coordination on and encourage the broader application of scientific and technologic breakthroughs related to non-traditional vaccines.

CHAPTER 2: VACCINE SAFETY

Taking every step necessary to maximize vaccine safety is as important as endeavoring to derive the greatest disease-prevention benefits that vaccines can provide. Because vaccines are given to large numbers of healthy people, safety is a great concern and is addressed through a system (consisting of many agencies and stakeholders) that collects vaccine safety data, generates hypotheses, and conducts studies to evaluate safety hypotheses.

Recommendation 2-1: The National Vaccine Plan should establish a process to identify potential vaccine safety hypotheses for further basic, clinical, or epidemiologic research through annual review of data from the Vaccine Adverse Event Reporting System (VAERS), the Vaccine Safety Datalink (VSD) project, the Clinical Immunization Safety Assessment (CISA) network, and the Vaccine Injury Compensation Program, and from information available from sources outside the United States.

There is no coordinated vaccine safety research agenda or a periodic, systematic process to prioritize a safety research agenda for the nation

(Klein and Myers, 2006; NVAC, 2009b). Although the Centers for Disease Control and Prevention (CDC) Immunization Safety Office (ISO) has its own research agenda, what is also needed is a national vaccine safety research agenda to help guide and coordinate the efforts of all federal agencies and various stakeholders that conduct activities related to vaccine safety research.

Recommendation 2-2: The National Vaccine Plan should emphasize the development and publication of a framework for prioritizing a national vaccine safety research agenda that spans all federal agencies and includes all stakeholders, including the public.

The scientific criteria of such a framework for prioritization might include, but are not limited to:

(a) Assessment of the nature and extent of existing evidence for a possible association of an adverse event with a vaccine.
(b) Determination of the individual or public health burden of potential adverse events following immunization.
(c) Consideration of the feasibility of scientifically rigorous study of a safety concern.
(d) Assessment of biological plausibility of a causal association between an adverse event and a vaccine.

A national research agenda would call on other agencies, such as NIH (which has historically played a limited role in vaccine safety research), CDC, and FDA, and non-federal stakeholders (such as providers who work with special populations, and vaccine manufacturers) to assume joint responsibility and work collaboratively on high-level challenges in vaccine safety research.

An NVAC-affiliated advisory entity dedicated to vaccine safety has the potential to play a role both as an independent source of guidance on vaccine safety issues and by offering a forum for dialogue on the subject of vaccine safety.

Recommendation 2-3: The National Vaccine Plan should include the establishment and scope of work of a permanent NVAC vaccine safety subcommittee to:

(a) provide guidance on the activities described in Recommendations 2-1 and 2-2 in a public and transparent manner;

(b) provide guidance about the identification and evaluation of potential safety signals; and

(c) publish on a biennial basis a review of potential safety hypotheses; current vaccine safety activities including those of pre- and post-licensure studies, VAERS, VSD, and CISA; and planned priorities for research.

To facilitate rapid response to a safety signal, the subcommittee might convene a relevant array of experts to advise the government and partners on a course of action. For example, neurologists could be convened to discuss the biological mechanisms of a given neurological event, and epidemiologists could discuss studies VSD could undertake.

Recommendation 2-4: The National Vaccine Plan should incorporate concrete steps to expand and strengthen vaccine safety research, including:

- **enhanced funding for CDC's Immunization Safety Office activities, including support of extramural research;**
- **enhanced funding for FDA's safety monitoring activities; and**
- **expansion of NIH vaccine safety activities to include research portfolios, funding through requests for proposals, program announcements, and creation of a study section dedicated to vaccine safety research.**

Funding could be allocated to each agency to support activities that implement the identified priorities as appropriate to each agency's research capabilities and strengths.

CHAPTER 3: COMMUNICATION

The desired outcome of the work of the National Vaccine Program and of the National Vaccine Plan is a population protected from vaccine-preventable death and disease. Society itself has changed in the speed with which information—and misinformation—are transmitted, as well as in an increased patient role in the patient-clinician relationship. Simply promoting the use of vaccines no longer meets the needs of individuals and families seeking to make informed decisions amidst a maelstrom of conflicting messages.

The committee found no evidence of an overarching vaccine communication strategy for the National Vaccine Program. Instead, communication regarding vaccine safety has been largely reactive to crises, and has been

conducted by a small and under-resourced staff at CDC.[11] The universe of vaccine information, science, safety research, quality control, and policy decision making is large and complex. Both health care professionals and the public poorly understand many aspects of the system. Pertinent information needs to be communicated in a strategic and comprehensive manner to reach the overarching goal of informed decision making.

Recommendation 3-1: The National Vaccine Plan should incorporate the development of a national communication strategy on vaccines and immunization targeting both the public and health care professionals. Such a strategy should:

(a) Reflect current research on communication;[12]

(b) Describe how relevant government agencies will coordinate and delineate primary responsibility for specific components and audiences;

(c) Anticipate, plan, and support rapid response to emerging high-profile scientific, safety, policy, or legal developments;

(d) Provide the right information to the right individual(s) or group(s) in the most appropriate manner, with attention to literacy, linguistics, and culture of the target audience(s); and

(e) Receive adequate support of dedicated human and financial resources.

Communication cannot be an afterthought; it requires upfront investment, planning, and implementation. A communication strategy will need to be multi-tiered, with the federal government playing a role in coordinating and directing the overall message, with adequately resourced state and local public health agencies and the medical community on the frontlines.

The committee also finds that there is no coherent effort to apply existing communication science to shape a research agenda that could inform the national vaccine communication strategy.

Recommendation 3-2: The National Vaccine Plan should incorporate a process for identifying research needs to inform the national communication strategy, including research on how the public obtains information about vaccines and immunization, perceives risks, and makes decisions concerning vaccination in the contemporary information environment.

[11] For further discussion see Chapter 3.

[12] See Recommendation 3-2.

A stronger, adequately funded and staffed NVPO could support interagency coordination in the area of communication in part by helping to identify communication needs that span the entire National Vaccine Program.

GOAL 4: VACCINE USE AND SUPPLY

Goal 4 in the draft National Vaccine Plan—ensure a stable supply of recommended vaccines, and achieve better use of existing vaccines to prevent disease, disability, and death in the United States—covers an extraordinarily broad set of issues. The National Vaccine Plan does not provide a clear and coherent vision for Goal 4 (e.g., all adults and children have access to all vaccines recommended by the Advisory Committee on Immunization Practices [ACIP]) nor does it describe the prerequisites for the effective use of vaccines. The committee has suggested a reframing of the goal.

The draft plan contains an objective that addresses supply issues, and the recommendation below reflects the committee's agreement that this area rises to the level of a priority.

Recommendation 4-1: The National Vaccine Plan should include the development and implementation of strategies to assure a stable and adequate vaccine supply for public health preparedness and recommended routine use purposes.

A gap in the draft Goal 4 is the lack of objectives or strategies linking health care financing with health services performance measures to induce and enable providers to seek out, stock, and administer ACIP-recommended vaccines.

Recommendation 4-2: The National Vaccine Plan should include the development of strategies to eliminate financial barriers such as unreasonable cost-sharing by patients who are unable to afford out-of-pocket costs for vaccines and provider payment mechanisms that discourage full and meaningful participation in the delivery of immunization services.

Recommendation 4-3: The National Vaccine Plan should emphasize the application of research and best practices in the organization and delivery of immunization services to improve patient access (such as location and hours) and service efficiency and quality (such as improved provider knowledge and decrease in missed opportunities for vaccination).

Recommendation 4-4: The National Vaccine Plan should encourage the exploration of non-traditional approaches to disease surveillance, monitoring vaccine safety, and assessing vaccine coverage. Such approaches might leverage the increasing ubiquity of the internet and wireless data services, personal communication devices, and social networking facilities.

Recommendation 4-5: Given the importance placed on the national adoption of certified, interoperable health information technology and electronic health records, the National Vaccine Plan should ensure active involvement of NVPO and relevant partners in the planning and implementation of the national health information initiative.

This involvement should include:

- Assuring the development and adoption of standards necessary for effective immunization clinical practice and population surveillance systems;
- Assuring that the definition of "meaningful use" considers immunization practice and reporting;
- Facilitating use of vaccine-related data by all public health partners (e.g., state and local public health departments); and
- Assuring that all public health partners have the expertise and resources to participate in the initiative.

Such efforts would include ongoing attention to needed resources, integration across diseases and programs, and ongoing financial technical assistance.

Recommendation 4-6: The National Vaccine Plan should include strengthening the public health infrastructure to support vaccine delivery, measure immunization practice and performance, intervene to address disparities in access to immunization, and respond to emerging infectious disease threats.

Efforts to strengthen the public health infrastructure could include:

(a) Development of capacity in all health departments to assure the delivery of immunization services to underserved populations in all communities or during an emergency.[13]

[13] See Recommendation 4-7 on the implications of health care reform.

(b) Development of greater public health capacity to identify deficits in access to immunization services.[14]

(c) Assistance to states to eliminate barriers to the full use of all appropriate personnel in vaccine administration due to restrictions on licensure and scope of practice.

Health care reform legislation will ideally include monitoring immunization and achieving targets as a measure of success. Deficiencies in immunization rates would trigger specific corrective plans. The following recommendation assumes the passage and enactment of national health care reform legislation.

Recommendation 4-7: The National Vaccine Plan should incorporate rapid and comprehensive assessment of the outcomes of national health reform and their implications for the nation's vaccine and immunization priorities.

Specifically, NVPO, as "owner" of the plan, could contribute by:

- Participating in implementation efforts related to the expanded health insurance access for the population.
- Participating in implementation efforts related to the design of health insurance coverage and cost-sharing features, administrative matters affecting the actual provision of vaccines, and standards and procedures governing the measurement and reporting of health plan performance.
- Promoting the integration of health plan performance and operations with community public health policy and practice in order to assure (a) the availability of community-wide information about population immunization status, disparities in access, and areas of need; (b) access to immunization services; (c) public health agency analytic, management, and other needed capabilities; and (d) the ability of public health workers, health insurers, and health care providers to mount a joint response to emerging public health threats.
- Promoting strategies for assuring the full immunization of those who remain uninsured.

CHAPTER 5: GLOBAL VACCINE ISSUES

Many of the issues relevant to Goals 1 through 4 of the draft plan apply to global needs as well—research and development of needed vaccines such as malaria and HIV, safety of vaccines and surveillance of adverse events,

[14] See Recommendation 4-5 on health information technology.

communication needs at user and provider levels, and vaccine use including supply issues.

The health infrastructures in many low- and middle-income countries do not adequately support use of needed vaccines. Causes include inability to pay for vaccines, inadequate infrastructure (ranging from public health laboratories to refrigerators), lack of providers or paraprofessionals to administer vaccines safely, and lack of systems to monitor vaccine use and potential adverse events. Without adequate infrastructure, funding for vaccines alone will not get vaccines to those who need them most.

Recommendation 5-1: The National Vaccine Plan should call for the engagement of U.S. federal agencies and partners to support immunization capacity-building to implement new vaccines in low- and middle-income countries through the provision of expertise and financial resources necessary to incorporate new vaccines, strengthen immunization infrastructure, and achieve higher levels of vaccination. One infrastructure component requiring specific attention is the development and implementation of surveillance systems for vaccination, disease burden, and vaccine safety that are innovative and appropriate for developing countries.

Differential pricing—that is, matching prices to a nation's ability to pay—can increase global access to vaccines while providing incentives for innovation.

Recommendation 5-2: The National Vaccine Plan should endorse active U.S. engagement in the development of global policy frameworks to further global adherence to differential pricing in order to ensure access to needed vaccines in all countries.

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Introduction

The 2008 draft National Vaccine Plan was prepared by the National Vaccine Program Office (NVPO) in the Department of Health and Human Services (HHS) with input from other departments and agencies (HHS, 2008). The plan consists of 5 goals, 36 objectives, and 156 strategies. The Institute of Medicine (IOM) Committee on Review of Priorities in the National Vaccine Plan was convened to review the plan and to make recommendations regarding priority actions in the major components of the plan (see Charge to the Committee below). For ease of reference, the committee organized its report according to the five goals, which are listed in Table I-1 along with the chapters in which they are discussed. Each chapter contains recommendations and rationale for a set of priority actions.

CHARGE TO THE COMMITTEE

The National Vaccine Plan originates in the 1986 National Childhood Vaccine Injury Act (NCVIA) that also established the National Vaccine Program (and by extension, the National Vaccine Program Office) and the National Vaccine Advisory Committee (NVAC).

The act asked the Secretary of HHS to "establish in the Department of Health and Human Services a National Vaccine Program to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines"[1] (NCVIA) and called on the program director to "prepare and issue a plan for the

[1] Public Law 99-660, 42 U.S.C. 300aa-1, § 2101 1986; see Appendix C.

TABLE I-1 National Vaccine Plan Goals

Goal		Chapter
1	Develop new and improved vaccines	1
2	Enhance the safety of vaccines and vaccination practices	2
3	Support informed vaccine decision making by the public, providers, and policy makers	3
4	Ensure a stable supply of recommended vaccines, and achieve better use of existing vaccines to prevent disease, disability, and death in the United States	4
5	Increase global prevention of death and disease through safe and effective vaccination	5

implementation of the responsibilities of the Director" and stated that the plan (which originally was to be updated annually)[2] would

> establish priorities in research and the development, testing, licensing, production, procurement, distribution, and effective use of vaccines, describe an optimal use of resources to carry out such priorities, and describe how each of the various departments and agencies will carry out their vaccine functions in consultation and coordination with the Program and in conformity with such priorities. (Public Law 99-660, Title XXI, Subtitle 1, Section 2103:3757)

The first National Vaccine Plan was issued in 1994. The plan was updated by NVPO in 2008 at the request of the Assistant Secretary for Health, and NVPO subsequently began to gather stakeholder input on the plan. As part of the process, NVPO asked the IOM to convene an ad hoc committee and gave the committee a two-part charge. The committee was asked to first "prepare a letter report on its review of the 1994 plan" and then to "hold workshops with national expert stakeholders in medicine, public health, and vaccinology to review a publicly available, draft update of the Plan" and prepare a "report with conclusions and recommendations about priority actions within the major components of the new draft plan" (see Box I-1).

The 1994 National Vaccine Plan had four goals: (1) to develop new and improved vaccines; (2) to ensure the optimal safety and effectiveness of vaccines and immunization; (3) to better educate the public and members of the health professions about the benefits and risks of immunizations; and (4) to achieve better use of existing vaccines to prevent disease, disability, and death (HHS, 1994). The plan also offered 26 objectives and more than 70 strategies for achieving those objectives. In addition, 14 anticipated

[2] In 1998 the requirement for annual updates of the National Vaccine Plan was repealed by Public Law 105-362, Title VI, § 601(a)(1)(H), Nov. 10, 1998, 112 Stat. 3285.

BOX I-1
The Charge to the Committee

The federal government issued "Disease Prevention through Vaccine Development and Immunization, The US National Vaccine Plan" in 1994. The Institute of Medicine will convene an ad hoc committee to evaluate the 1994 National Vaccine Plan and then review and make recommendations regarding an update of this National Vaccine Plan. The committee will hold workshops[a] with national expert stakeholders in medicine, public health, and vaccinology to review a publicly available, draft update of the Plan. The committee will prepare a letter report of the evaluation of the 1994 Plan, and a report with conclusions and recommendations about priority actions within the major components of the draft Plan.

[a] The IOM Committee on Review of Priorities in the National Vaccine Plan conducted its work between March 2008 and November 2009, including five information-gathering meetings with national stakeholders in Washington, DC, Chicago, Seattle, and Irvine.

outcomes, only one of which was measurable, were offered as a basis for judging the success of the plan.

To address the first part of its charge the committee authored a letter report addressed to HHS (and published in June 2008) briefly reviewing the 1994 plan and providing guidance on developing the new plan. As the committee noted in its letter report (see Appendix D), the 1994 plan contained almost no measurable objectives or indicators, and its content was largely a reflection of then current activities of relevant HHS agencies. Given that "[c]haracteristics of the 1994 plan [made] it difficult to attribute specific activities to plan objectives," the committee did not attempt to link accomplishments to the plan (IOM, 2008). In the letter report, the committee examined changes in the broader social, policy, and economic context of vaccine development and immunization, and highlighted several areas in which noteworthy progress has been made, particularly by federal agencies. The committee acknowledged that progress in developing and delivering vaccines has benefited from essential contributions by other stakeholders, including researchers, manufacturers, state and local public health agencies, and health care providers. Based on this review of the 1994 plan, the committee offered guidance to NVPO and its partners on key process and content areas to be considered in developing the update to the National Vaccine Plan. The complete letter report can be found in Appendix D.

This report, *Priorities for the National Vaccine Plan*, responds to the second part of the committee's charge, highlighting major themes that emerged from meetings with expert stakeholders and offering a series of

recommendations about priority actions in the major components of the draft National Vaccine Plan. The committee deliberated at length about the relationship between NVPO and the plan and the implications of NVPO's current limited resources and status for its ability to ensure and support successful implementation of priorities reflected in the plan's goals, objectives, and strategies. NVPO, the entity that was to be the main coordinator on vaccine issues according to the vision apparent in the 1986 statute, was formed in 1988, and in less than one decade after the enactment of the NCVIA, NVPO became subject to funding and staffing cuts required by Congress (House of Representatives, 1995).[3] Chapter 6 provides an in-depth examination of the plan as a tool of coordination and NVPO as the structural entity charged with coordinating those efforts.

METHODS

The committee was charged with holding meetings with expert stakeholders to discuss the draft National Vaccine Plan and with developing "recommendations about priority actions within the major components of the draft new plan." Because of the wide range of subjects addressed and the varied level (for example, big-picture and broad versus low-level and detailed) represented among the objectives and strategies in the National Vaccine Plan (as well as input received from stakeholders and by NVPO and NVAC), the committee judged that it was neither feasible nor appropriate to use a quantitative priority-setting process.

The committee held information-gathering meetings on each of the five goal areas in the draft plan and reviewed material from the literature pertinent to each goal. Each meeting involved a wide range of stakeholders, as reflected in the agendas provided in Appendix F. After each meeting, the committee met in closed session and developed a list of themes and issues emerging from stakeholder input and from a review of the literature. Subsequently, the committee compared each of the five lists of themes and issues to each of the five goals in the plan; identified gaps and areas of overlap; further reviewed the literature pertinent to each set of themes; and applied several criteria to refine the list of themes and issues and to develop the recommendations described in each chapter. The criteria used included feasibility (financial and technical), potential impact on morbidity and mortality, and strategic opportunity (likely to require and motivate multi-stakeholder involvement).

[3] NVPO's budget was appropriated $9,631,000 in 1991, dropped annually between 1991 and 1994, and was cut sharply between 1994 and 1995 to approximately $1 million. The total staff began at 23, increased to 33, and dropped to 9 by 1996 (House of Representatives, 1995). It has remained at approximately this level since.

GENERAL COMMENTS ABOUT THE 2008 DRAFT PLAN

The committee believes that the plan would be strengthened by the addition of a clear vision statement about what the plan is or should be. For example, should the plan serve as (a) a gathering of many of the activities agencies are already undertaking, and then highlighting accomplishments at a later date, when some or many of those activities have been completed and objectives achieved; or (b) a short list of specific critical needs and gaps that require coordinated attention by specific agencies, or by various permutations of agencies and stakeholders; or (c) both a and b; or (d) something else?

The committee believes that the plan may serve these or other valuable functions. It is understandable why the plan's drafters chose to include both activities that are part of existing strategic plans and are certain to be accomplished in the near future, and activities that are novel, not necessarily represented in any other planning document, and require multi-sectoral coordination and collaboration. The committee suggests that NVPO consider distinguishing between objectives or strategies that are likely to be accomplished regardless of their placement in the National Vaccine Plan and those that are unique to the plan and require coordination among agencies and with non-government stakeholders in order to be achieved.[4] The committee's recommendations about "priority areas within major components of the plan" refer to the latter type of objectives and strategies. Additionally, the committee believes that the final (implementation) plan will be strengthened by a clear explanation of how the indicators in each goal relate to the objectives and strategies in that goal.

In this report, the committee uses *national vaccine program* in lower case to denote the vast and complex network of actors and actions related to vaccines and immunization, and uses *National Vaccine Program* (per the 1986 act) when referring to the governmental agencies that have responsibilities related to vaccines and immunization. Below, the committee highlights several dimensions of the national vaccine program that provide useful context for the plan. The committee also provides a minimalist illustration of many of the relevant federal agencies and stakeholders. Table I-2 is not comprehensive or complete, but may help to orient some readers to a complex network of actors. A more elaborate, but still incomplete illustration including federal advisory committees and depicting some of the relationships among various actors was originally provided in the committee's June 2008 letter report available in Appendix D.

[4] W. Orenstein, 2007 NVAC meeting (NVAC, 2007).

TABLE I-2 The National Vaccine Program: Government and Stakeholders

Stakeholders	Federal Government
The public: individuals and communities State, territorial, tribal, and local public health agencies Industry Academic research enterprise Primary care (part of the health care delivery system) Payers and Plans Community organizations National organizations and professional societies Foundations International and multilateral organizations	HHS *(includes NVPO)* CDC[a] CMS[b] FDA[c] HRSA[d] NIH[e] Department of Defense Vaccine Healthcare Centers Network Department of State U.S. Agency for International Development

[a] Centers for Disease Control and Prevention.
[b] Centers for Medicare & Medicaid Services.
[c] Food and Drug Administration.
[d] Health Resources and Services Administration.
[e] National Institutes of Health.

THE PURPOSE OF IMMUNIZATION

Vaccines have the capacity to prevent infectious disease in vaccinated individuals and to prevent their spread in populations and vulnerable individuals who cannot be vaccinated because of their age or health. Vaccines also serve a dual purpose: as medical interventions used with individuals (and, like all medical interventions, characterized by risks and benefits), and as public health interventions used in the population at large to prevent infectious disease outbreaks and reduce or eliminate disease, disability, and death.

Given the value of vaccination,[5] its enormous and continuing importance to public health and the complex issues of national health policy that it raises, the federal government's involvement is broad and deep, spanning virtually all aspects of the immunization enterprise, across multiple federal agencies and often involving collaboration with stakeholders. Public insurance programs such as Medicare, Medicaid, and the Children's Health Insurance Program finance the purchase and administration of vaccines for more than 100 million program beneficiaries. The Vaccines for

[5] The terms vaccination and immunization are sometimes used interchangeably. The committee uses vaccination to refer to the delivery of the vaccine to an individual, and immunization services to refer to the range of activities related to vaccination.

Children (VFC) program, a component of Medicaid, plays a crucial role in ensuring immunization access not only for children enrolled in Medicaid but also for uninsured, underinsured, and medically underserved children. Programs such as the Indian Health Service, federally funded community health centers and services of the Veterans' Health Administration in the Department of Veterans Affairs ensure access to immunization services for key populations including veterans, the uninsured, and children and adults whose health insurance does not cover vaccinations. The Centers for Disease Control and Prevention (CDC) plays a central role for the nation in measuring population immunization status and promoting access, while the Food and Drug Administration (FDA) and CDC are national stewards of vaccine safety surveillance and monitoring as well as for policies aimed at ensuring a safe and adequate vaccine supply. The U.S. Agency for International Development (in the State Department) promotes global vaccine access policy to improve the health of nations and directly funds research for diseases that affect developing countries. CDC also provides technical training and support in several areas of global immunization programs, including surveillance. The National Institutes of Health (NIH), the Department of Defense, and the Biomedical Advanced Research and Development Authority in HHS are instrumental in the development of new vaccine technology for both domestic and global needs. In its policy and planning roles, the federal government leads the nation in the development of policies for ensuring high levels of immunization in the population regardless of health insurance status. With enactment of national health care reform increasingly likely, the federal government would play the central role in translating reforms in coverage, payment, access, quality, and community prevention into improved vaccination outcomes.

Four ethical principles or values—beneficence, justice, public safety, and autonomy[6]—shape the way policy makers, health care providers, and individuals think about vaccines, and they also inform national and state immunization policies. Sometimes, these considerations give rise to conflicts and dilemmas. The imperative of protecting public safety sometimes requires government agencies to place limitations on personal autonomy. This is the case with state vaccine requirements for entry to school and child care, but similar examples may be found in the mandatory use of seat belts and child safety seats. The principles of beneficence and distributive justice have made vaccines a high national priority. For example, the federal government funds and administers the VFC program at a current cost of approximately $3 billion, with the aim of ensuring that children can receive vaccination

[6] Beneficence (and its corollary, non-maleficence), justice, and autonomy are widely acknowledged as fundamental ethical principles that guide the delivery of health care. Public safety or public benefit is a guiding principle in public health practice (Kass, 2001; Public Health Ethics Society, 2002).

without financial barriers (Shefer, 2008). These same principles also call for compensation of injuries through the Vaccine Injury Compensation Program (VICP) established in 1987 in accordance with the NCVIA in order to ensure that those who bear the burden of rare serious adverse events possibly caused by vaccines are compensated. The principles of public safety and beneficence also contribute to the motivation to develop new and improved vaccines to prevent diseases that cause suffering, result in higher rates of disease and death, and affect individuals' and society's economic well-being, including days of work missed due to vaccine-preventable disease and health care expenditures to treat serious sequelae of infectious diseases.

Risk and Benefit

As with all medical products, vaccines have risks and benefits, and government regulators in the Center for Biologics Evaluation and Research at FDA evaluate a vaccine's efficacy and safety before and after its licensure. At the time a company's Biologic License Application is reviewed by FDA, pertinent data are also presented to FDA's Vaccines and Related Biological Products Advisory Committee and to CDC's Advisory Committee on Immunization Practices (ACIP). Vaccines are licensed only if regulators are satisfied that they are efficacious and safe and have a favorable risk-benefit profile. However, it is important to note that there is no perfectly safe[7] or effective vaccine, and a vaccine's risk-benefit profile evolves over time as a result of growing knowledge about a product and changes in the environment in which a product is used. Four major types of studies in humans are conducted during a vaccine's lifecycle. Studies are conducted by manufacturers before a vaccine can be considered for licensure, and include the following: Phase I study in a small number of subjects to assess safety; study of safety and immunogenicity in Phase II; and large-scale, generally randomized controlled studies to assess efficacy and safety in Phase III. At the point of licensure, regulators may require additional safety studies after a vaccine is marketed and begins to be used in the general population (Phase IV studies). Also, after licensure, vaccines are released into the market after each batch is tested by FDA.

Balancing risks and benefits is complex. In general, studies are designed (i.e., statistically powered) primarily to assess efficacy and thus are only capable of detecting relatively common adverse events (the second generation rotavirus vaccine studies discussed in Chapter 2, which were designed to capture an adverse event previously identified, are an exception). Although

[7] The Code of Federal Regulations defines safety as "the relative freedom from harmful effects of the recipient when a product is prudently administered, taking into consideration the characteristics of the product in the relationship to the condition of the recipient at the time" (21 CFR § 600.3).

safety is equal in importance to efficacy, establishing absolute safety is impossible. Pre-licensure trials large enough to detect unexpected rare adverse events would be logistically difficult and would substantially delay introduction of a product that has been proven to save lives. Therefore, regulators and other public health agencies must rely on post-marketing vigilance to detect possible uncommon adverse events following immunization.

The vaccine safety system, although primarily organized and supported by the federal government, involves many non-government stakeholders that contribute to the system in one or more ways. The system includes vaccine manufacturers that are required to report within 15 days of detection serious adverse events following immunization, academic research centers and health care organizations that collaborate with government to conduct safety research (including investigation of safety concerns that arise), health care providers, and the public.[8] The Immunization Safety Office in CDC is a central component of the system, and in collaboration with FDA and other stakeholders, it supports an array of safety-related activities. The following activities are important to highlight:

- The Vaccine Adverse Events Reporting System, a passive surveillance system that receives reports of possible adverse events via mail, e-mail, fax, and web-based submission from vaccine manufacturers, health care providers, and the public, may detect "signals" (serious adverse events that might be associated with a preceding immunization) and be used to generate hypotheses;
- The Vaccine Safety Datalink project, which is a large linked database that integrates data on more than 8 million people enrolled in eight health maintenance organizations and conducts active surveillance and testing of vaccine safety hypotheses; and
- The Clinical Immunization Safety Assessment network based in several academic and clinical centers, which is equipped to provide basic science and clinical investigation of adverse events following immunization.

The vaccine safety system has a long and rich history that illustrates both the complexity of vaccine regulation and the capacity of the system to monitor safety and respond with speed and competence to evolving concerns. Chapter 2 provides an in-depth discussion of the system and offers a case study of the response to a safety concern that emerged in the wake of FDA licensure of the first rotavirus vaccine and expanded use in the population.

As noted earlier, the VICP provides compensation for conditions that might be adverse effects of vaccines. The compensation program is located

[8] A working group of NVAC has also been asked to review and make recommendations about the federal vaccine safety system, and the product of its information-gathering and deliberation is expected to be released in 2010.

BOX I-2
Pathways to Compensation in the Vaccine Injury Compensation Program

The first pathway to vaccine injury compensation is for individuals whose injuries are listed in the vaccine injury table.[a] The table, established as part of the 1986 legislation, recognized the potential of certain vaccines to produce specific injuries (i.e., there is medical and scientific evidence that the vaccine can cause the listed injury). If a vaccine identified in the table is administered and an injury listed in the table ensues, compensation is awarded. This process was intended to be non-adversarial or no-fault, swift, and simple. Individuals claiming an "on-table" injury need not demonstrate a causal link between the injury and the vaccine—the injury table is evidence that such a link has been established.

The second pathway for compensation recognized under the NCVIA is for individuals with an "off-table" injury, that is, an injury that allegedly is the result of a specific vaccine or vaccine ingredient but for which no scientific consensus about causality has been reached due to insufficient or conflicting evidence. The off-table pathway allows individuals who believe they have been injured by a vaccine to argue that the preponderance of evidence in that case is sufficient to warrant compensation even though it may fall short of the scientific standard for establishing a causal link between the vaccine administered and the alleged injury.

[a] The table is available on the VICP web site at http://www.hrsa.gov/Vaccinecompensation/table.htm.

in the Health Resources and Services Administration at HHS, and three federal government entities, HHS, the Department of Justice, and the U.S. Court of Federal Claims, play roles in the program (VICP, 2009). The 1986 law (NCVIA) requires that plaintiffs, called petitioners, first bring their case to the program before seeking compensation in civil courts and offers two pathways for awarding compensation (VICP, 2009; see Box I-2). Chapter 2 provides additional discussion of how information from the program can contribute to the safety research agenda, and Chapter 3 examines implications of the program's legal actions on communication about vaccine risks and benefits.

Communication

Society has changed, but the ways in which government communicates about vaccines have not kept up with those changes. Over the past three decades, there has been a great increase in the public's interest, expectations, knowledge (including faster access to information via the Internet),

and involvement in aspects of health care, including quality and safety, patients' rights, and research. In the past decade of the 20th century, multiple examples emerged of the "ubiquity of risk in modern industrial society" as a "central concern of U.S. politics, law, and popular culture" (Colgrove and Bayer, 2005). There is also a high level of sometimes confusing, conflicting, and inaccurate mass media and news media contributions to public beliefs about vaccines (this has been heightened during the implementation of the H1N1 monovalent influenza vaccine). In this environment, government agencies can no longer simply impart information as issues arise (i.e., reactive communication) or appear silent on questions about safety. The government (federal, state, and local public health agencies) needs to engage in dialogue with the public about vaccines and vaccine safety on an ongoing basis and to communicate factual information about vaccines and vaccination in a timely, complete, and clear way.

The landscape of immunization has also changed as successful vaccines have resulted in the disappearance or near-disappearance of the diseases that claimed the lives of many children and caused great fear among parents (although some diseases, such as pertussis, remain endemic, and others, such as measles, may be reintroduced into a community). The benefits of immunization appear less clear both as the memory of vaccine-preventable diseases recedes and as the incidence of many diseases decreases to the extent that some have become invisible in the community. Also, the sciences of vaccinology and vaccine safety are not characterized by absolute certainty; there are areas of uncertainty that are complex but require clear and timely communication. The complex work of communicating about risk and benefit and about the basis for immunization policy must be approached in a much more strategic, evidence-based, and effective form. The committee discusses communication and informed decision making (Goal 3 of the draft plan) in Chapter 3.

Elimination and Control of Vaccine-Preventable Diseases

The vaccine and immunization enterprise can be described succinctly as developing effective and safe vaccines, and using those vaccines to prevent disease. Both components involve the roles of and coordination between government and private sector actors. Chapter 1 of this report discusses vaccine research and development and recommends several priority actions in Goal 1 of the National Vaccine Plan. Chapter 4 discusses vaccine supply and use and recommends several priority actions in Goal 4 of the National Vaccine Plan.

Vaccine research and development involves government, especially NIH, academic research institutions, and industry (large pharmaceutical companies, biotechnology companies, and venture capitalists). With respect

to vaccines for global use, the array of actors is even broader, and includes philanthropies, varied multilateral entities, and formal public-private partnerships such as product development partnerships. Vaccine research and development has as its end-goal the production of effective and safe vaccines that confer long-term protection on those vaccinated. The path that leads from discovery to licensure and use, however, is lengthy (e.g., 10 years), challenging, and resource-intensive (WHO, 2006). Multiple factors lead to decisions about what is pursued in research and development, including public health need, market prospects and likelihood of a return on investment, and scientific and technological obstacles. Although manufacturers establish their own priority lists, there is no systematic national process for prioritizing candidates. Chapter 1 discusses research and development and the roles of NIH and FDA in greater detail.

Use of vaccines involves CDC, state, tribal, territorial, and local public health agencies, and the health care delivery system at all levels (providers, plans, payers). In the United States, the ACIP makes recommendations to CDC on the use of vaccines to prevent disease in all age groups. ACIP recommendations are considered in federal and state policies and funding decisions that largely aim to ensure that children receive all ACIP-recommended vaccines regardless of insurance status. Chapter 4 discusses the use of vaccines, including vaccine supply; use of vaccines for public health emergencies such as the ongoing H1N1 epidemic; public financing of vaccines through the VFC program and Section 317 (state discretionary funding for immunization); and immunization as an indicator of health care system quality and performance. In Chapter 5, the committee examines major issues in the global use of vaccines and makes recommendations about priority actions in Goal 5 of the National Vaccine Plan. Global issues include the different burden of disease caused by many pathogens for which there are no effective vaccines, and some considerable limitations in the infrastructure and capacity of low-income countries to manage and use existing vaccines. The reasons for both challenges include lack of financial resources. Novel partnerships between the public and private sectors have emerged in the past decade to address these challenges.

Federal Immunization Laws, Policies, and Programs

The Public Health Service Act and amendments to it, such as the NCVIA, form the foundation of federal immunization law and outline the responsibilities of government and to a lesser extent those of individuals. States make policy to support their role of ensuring immunization of the population (including financing immunization services and requiring vaccination for school entry), but the federal government strongly shapes national direction with regard to immunization. Amendments to Medicaid

in the 1993 Omnibus Reconciliation Act (Public Law 103-66) included the establishment of the Vaccines for Children Program, an entitlement program that provides free vaccine for children who are Medicaid eligible, uninsured, underinsured for immunization services (i.e., individuals whose insurance policy covers only some or no vaccines), or are American Indian or Alaska Native.

Vaccine cost, cost-effectiveness, and financing are among the important and complex considerations that inform policy decisions about the use of vaccines to prevent disease, disability, and death as a component of national and state public health policies. The use of vaccines has implications not only for the health of individuals and communities (i.e., in preventing spread of disease) but it also has multi-faceted implications for the health care delivery system, employers, schools, and parents. Vaccines have long been known to be cost-effective, and older vaccines (introduced before 2000) are also cost-saving. Newer, more expensive vaccines are cost-effective but not cost-saving. A 2008 NVAC report noted that the considerable increase in the cost of providing all ACIP-recommended childhood vaccines (a 336 percent increase in vaccines for males and 476 percent in vaccines for females) "has raised concerns about the ability of the current public and private vaccine delivery systems to maintain access to all vaccines recommended for routine use in children and adolescents without financial barriers" (NVAC, 2008). Medical practices, public health clinics and other settings where vaccination is administered also incur significant and growing non-vaccine costs that include counseling, storage, administration, and staff time. Reimbursement for these costs is frequently inadequate. At the global level vaccine financing issues are different than in the United States (see Chapter 5), but are similarly complex. NVAC, the IOM, and several professional societies such as the American Academy of Pediatrics have examined these interrelated problems of vaccine financing and have proposed solutions (AAP, 2007; IOM, 2000, 2003; NVAC, 2009).

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1

Development of New and Improved Vaccines

> *Vaccines are complex products and the science of vaccinology is difficult. To achieve the full promise of modern science and technology to prevent and treat disease by immunization, America's cooperative and collaborative relationships in vaccine research and development are interwoven into a fabric of innovation. This must be maintained and strengthened. It is important to understand the nature of these relationships to prevent inadvertent damage to this delicate fabric.* (NVAC, 1997)

In 1997, the National Vaccine Advisory Committee (NVAC) authored an article in the journal *Pediatrics* titled "United States Vaccine Research: A Delicate Fabric of Public and Private Collaboration," which provided a synopsis of the complexity and fragility of the U.S. vaccine enterprise at that time. The committee is not aware of an update of the 1997 article, but a contemporary overview would reflect a number of great advances and some areas in which considerable challenges in the efficient use of vaccines to prevent infectious diseases persist, including scientific hurdles and periodic shortages in vaccine supply (also discussed in Chapter 4) (Goldberg et al., 2002).

In this chapter, the committee briefly describes vaccine research and development and major themes that emerged at a meeting with stakeholders about this goal in the draft National Vaccine Plan. Based on those themes, a review of the objectives and strategies in the draft plan, and a review of the pertinent literature, the committee discusses gaps and opportunities in vaccine development and makes several recommendations on priority actions in Goal 1 of the draft plan, and a policy recommendation pertaining to the scope of the plan.

CONTEXT: THE CURRENT STATE OF VACCINE RESEARCH AND DEVELOPMENT

Although Goal 1 of the draft National Vaccine Plan is not titled "vaccine development and regulation," the two processes are profoundly intertwined; the outcome of successful vaccine development is licensure by the Food and Drug Administration (FDA) of safe and effective vaccines that will improve the public's health. Infectious disease vaccine development and regulation occur in a dynamic environment shaped by public health considerations and policies, scientific and technologic barriers, news media commentary, judicial decisions, and the multiple public avenues available for information exchange. A major challenge to the field is meeting the necessarily very high standard of safety for preventive vaccines used in healthy populations. Also, vaccines are generally used for large proportions of the population, for example, childhood vaccines for an entire birth cohort (e.g., 4 million newborns annually in the United States alone), and in hundreds of millions of people worldwide.

The pharmaceutical companies that produce vaccines "experienced a period of great contraction in the 1980s and 1990s"[1] (reasons that have been described include fear of liability, low profit margins, and low likelihood of recouping investment), but the first decade of the 21st century appears increasingly promising for the industry, as demonstrated by expansion in the number of manufacturers, a promising pipeline of potential new vaccines, and a changing view of the profitability of vaccines (Werble, 2009a,b). The industry conducts most of the applied and clinical research necessary for the further development and production of a vaccine.

The federal government supports vaccine research through several agencies including the National Institutes of Health (NIH) in the Department of Health and Human Services (HHS) and the more recently established Biomedical Advanced Research and Development Authority (BARDA), located in the office of the Assistant Secretary for Preparedness and Response (ASPR) also in HHS.[2] NIH funds basic and clinical vaccine research totaling an estimated $1.675 billion in 2009. The majority of vaccine-related research at NIH takes place in the National Institute of Allergies and Infectious Diseases (NIAID).

NIH and BARDA also represent two different and complementary approaches to vaccine development. NIH has long supported primarily an

[1] In 1967, 26 vaccine manufacturers were licensed by FDA, while in 2002, only 12 FDA-licensed vaccine manufacturers remained (Plotkin et al., 2008). According to the 2004 IOM report *Financing Vaccines in the 21st Century*, five companies made all vaccines routinely recommended for children and adults, and two were based in the United States—Merck and Wyeth (recently purchased by Pfizer, a U.S. pharmaceutical company), and the others were Europe-based multinationals.

[2] ASPR was created in 2006 by the Pandemic and All-Hazards Preparedness Act.

investigator-initiated approach, which is generally open ended and not targeted, while BARDA has taken a product-driven approach[3] to vaccine development. One example of BARDA's approach may be found in its June 2009 award of $35 million to a company that is expected to develop "recombinant influenza vaccines based on hemagglutinin genes or proteins (plasmid DNA, virus-vectors, peptides, subunit proteins and virus-like particles) . . . leading towards FDA-licensure and human usage" (BARDA, 2009).

The vaccine programs under BARDA also offer an example of the regulatory system's potential for flexibility. Specifically, FDA's promulgation of the so-called "animal rule"—regulations that describe the conditions under which efficacy data in animals may be submitted in lieu of data from human trials—has allowed BARDA and the companies it supports to evaluate the safety and efficacy of vaccines for biodefense for which human challenge with the pathogen would be unethical or unfeasible (Abdy et al., 2007; FDA, 2009d). (Clinical studies with humans are still needed to demonstrate a vaccine's safety and immunogenicity.)

Developing and manufacturing most[4] vaccines involves using living organisms and presents unique technical and regulatory challenges. Vaccine manufacturers may need to build or renovate a manufacturing facility specifically for the production of a given vaccine before that vaccine has been licensed. This results in a "sunk cost"—a cost that cannot be recovered if the vaccine is not licensed (Coleman et al., 2005). As part of the Biologic License Application, FDA evaluates the manufacturing process and facility (Landry and Heilman, 2005).

The vaccine regulatory process is also complex and difficult, requiring a high level of scientific expertise and sustained funding for its maintenance and enhancement. FDA's role in recent years has been shaped by two major events. In 2004, the agency announced its Critical Path Initiative, which is intended to bring about an infusion of scientific innovation into its work and spur the same in the companies that develop drugs, vaccines and other biologic products, and devices, with the ultimate goal of translating innovation into safe and effective products (FDA, 2004). FDA's effort to "modernize the scientific process" that transforms a discovery or proof of concept into a vaccine continues, and the agency publishes yearly compendia of activities it has undertaken or supports, in an effort to bring about the desired changes

[3] Requirements for BARDA's Project Bioshield include "solid clinical experience and/or research data" that support "a reasonable conclusion that the countermeasure will qualify for [FDA] approval or licensure within eight years after the date of a determination" (Hynes, 2007). The term "countermeasure" refers to vaccines, drugs, and other medical products intended to prevent or treat effects of bioterrorism.

[4] Newer synthetic sub-unit vaccines are an exception.

(as an example, see Oliva et al., 2007).[5] In 2007, the FDA Amendments Act called for several changes that signal an even greater emphasis on science at FDA and are expected to lead to increased financial and human resources for the agency.[6]

THEMES FROM INFORMATION GATHERING

The committee gathered input from stakeholders and compared it to the objectives and strategies in Goal 1 of the draft plan; reviewed pertinent literature; and developed a series of themes indicating potential opportunities for improvement in vaccine development. These themes include (1) the role of the regulatory system; (2) the need for a priority-setting approach to vaccine research and development; (3) the need for coordination of research in vaccine development; and (4) the potential desirability of expanding the scope of the National Vaccine Plan to transcend the 1986 definition of vaccines as limited to prevention of infectious disease vaccines.

REGULATORY ENHANCEMENTS TO SUPPORT INNOVATION WHILE PROTECTING HEALTH

One topic not addressed by the existing Goal 1 objectives is the regulatory system that licenses vaccines and has the potential to facilitate or inhibit innovation.[7] The importance of addressing regulatory issues in the National Vaccine Plan was discussed at the committee's meeting with stakeholders on Goal 1 in the plan, and NVAC and the National Vaccine Program Office (NVPO) have received input from stakeholders on the subject of the interaction between regulators and companies seeking licensure of new vaccines (IOM, 2008; NVPO, 2009).

Despite some important scientific and technologic advances, change has been slow to occur in some areas of vaccine development. For example, an observation made by William Jordan and his colleagues at NIAID in the 1970s continues to be relevant today. They found that vaccine

[5] Recent examples of FDA-conducted research include development and evaluation of animal models needed to characterize the immune response to bacterial pathogens such as anthrax and pertussis and development of biomarkers indicating vaccine efficacy; development of assays to evaluate protection conferred by pneumococcal vaccine; and study of the antibody response against polysaccharide in the coat of bacterial pathogens such as pneumococcus and of the immunomodulatory effects of specific polysaccharides (FDA, 2009c).

[6] These include the creation of the position of Chief Science Officer and increased funding from fees manufacturers pay at major points during the regulatory application process.

[7] As an example, FDA's Critical Path Initiative was launched in 2004 "to create a framework for stimulating efforts to modernize the development, evaluation, manufacture and use of medical therapies and other FDA-regulated products" (FDA, 2009b).

> . . . development was hindered by the lack of investment to obtain a missing piece of scientific knowledge or technology. Just as the new molecular biotechnology was becoming available, there was an awareness of a lack of coordinated planning and funding to assure that each step in vaccine development followed as rapidly as possible the preceding one. Although the United States can point to major triumphs in vaccine development in the past 20 years, these old problems have not been eliminated. (HHS et al., 2002)

The *Jordan Report: Accelerated Development of Vaccines 2007*, a compendium of expert articles published by NIAID, noted that NVAC "called for review of existing cGMP [current Good Manufacturing Practices] requirements to assure they are science-based, potentially eliminate or modify those that are not, and allow for flexibility as long as it does not compromise the safety and efficacy of the vaccines" (HHS et al., 2007:22). It seems, based on stakeholder input that the committee received, that greater progress toward regulatory efficiency and flexibility (while preserving a focus on safety and efficacy) remains a concern (IOM, 2008).

The great, overarching challenge in bringing new and improved vaccines to market is that new vaccine development and regulation are closely linked processes that tend to be risk-averse.[8] Although there are examples of both industry innovation and agile, flexible regulatory approaches, including development of vaccines supported by BARDA and recent development of pandemic influenza vaccines, a considerable proportion of vaccine production and regulation is shaped by an old paradigm of what vaccines are and how they should be studied and regulated.

For various reasons, the regulatory process more easily tips toward the tried and true rather than toward innovation (Klein and Myers, 2006). Adjuvants are substances added to vaccines to enhance the immune response (FDA, 2009a), and they represent one of the new frontiers in vaccine development because of their potential effects ranging from strengthening immune response in some individuals (e.g., older adults) to achieving efficacy with smaller amounts of antigen. The challenges of testing and licensing vaccines containing promising new adjuvants have delayed consideration of those adjuvants by U.S. vaccine companies and regulators (Aguilar and Rodríguez, 2007). Also regulators continue to rely on classic randomized controlled trials despite the fact that they leave many unanswered questions about how a vaccine will work in real-life use (Poland et al., 2009). Finally, some newer vaccines to prevent diseases for which a vaccine already exists are simply reformulations or combinations of existing vaccines, which seems to suggest the existence of barriers to true innovation (Brennan and Dougan, 2005).

[8] These may include risk of failure for company, sunk costs that present a high threshold for entry into the vaccine market, and regulatory aversion to risk.

Several vaccines containing new adjuvants have been developed, and some are licensed for use in Europe,[9] but until October 2009, aluminum-containing compounds were the only adjuvant used in some FDA-licensed vaccines. (Cervarix, GlaxoSmithKline's [GSK's] newly approved HPV [human papillomavirus] vaccine contains the adjuvant ASO4 that combines aluminum hydroxide with monophosphoryl lipid A.) Although aluminum-containing adjuvants have been in use for 80 years, Aguilar and Rodríguez (2007) assert that were they newly discovered today, their side effects and toxicity could make them difficult to license by contemporary standards. Both FDA and the vaccine industry recognize the scientific challenges of evaluating new adjuvants, and FDA has begun to make progress with strategies to enable evaluation and licensure of adjuvants with favorable risk-benefit profiles. In 2008, an NVAC subcommittee report on dose optimization strategies suggested assuring that "FDA guidance on approaches to licensure path for novel adjuvant systems from regulatory agencies receives high priority in the Critical Path Initiative, with funding support as necessary, for expeditious publication" (Dekker et al., 2008:12). In its 2008 summary of Critical Path Initiative projects, FDA acknowledged "a severe shortage of analytical tools to evaluate new adjuvants," and an ongoing FDA project is focused on developing methods for preclinical evaluation of novel adjuvants using in-vitro screening methods (FDA, 2009b). The summary from a June 2009 World Health Organization (WHO) consultation meeting to inform the WHO Global Advisory Committee on Vaccine Safety and the Strategic Advisory Group of Experts on Immunization stated that "[o]verall, no significant safety concern or barriers to evaluating or using adjuvanted vaccines for the current H1N1 vaccine were raised" (WHO, 2009). The European Medicines Agency (EMEA) has established a process that allows vaccine manufacturers to submit preliminary applications using a non-pandemic strain with adjuvant. Once manufacturers replaced the strain in the vaccine with the pandemic strain (beginning in July 2009), they could resubmit their application and be granted approval in as little as five days if the agency was "satisfied that the extrapolation to the new strain was valid," but they would need to provide EMEA with new data after the vaccine begins to be used (Declan, 2009). An August 2009 FDA presentation described one of the objectives of clinical evaluation of H1N1 vaccines as "evaluat[ing] investigational adjuvants to provide data on their utility in dose sparing and enhanced immunogenicity" (Baylor, 2009). It is probably too early to tell whether adjuvants will be called for or to predict the direction of FDA's regulatory decisions regarding adjuvants for pandemic influenza vaccines.

Randomized controlled trials have been the gold standard in the regu-

[9] For example, the European Medicines Agency licensed an HPV vaccine adjuvanted with ASO4 in September 2007 and an H5N1 pandemic influenza vaccine adjuvanted with AS03 in September 2009.

latory process leading to the approval of vaccines (Poland et al., 2009). However, randomized controlled trials have limitations. For example, they may not represent results achieved with the actual use of vaccines—results obtained in healthy subjects typically enrolled in such trials may not be informative about the vaccine's safety and efficacy in populations that are heterogeneous with respect to age, health status, and genetics. Several stakeholders at the committee's meeting on Goal 2 in the draft plan (vaccine safety) mentioned related concerns, such as the fact that vaccines for pediatric use are studied in healthy children, who may not be representative of children with chronic and serious illnesses or other subgroups. Alternatives could include using randomized controlled trials to prove efficacy, evaluating surrogate markers, then evaluating surrogate markers in selected populations and/or conducting Phase IV (post-licensure studies) in such populations.

Some have argued that regulatory authorities are excessively risk averse, even when the risk is merely theoretical. Plotkin (2005b), for example, wrote that the 2003-2004 influenza vaccine was not adequately matched to the influenza strains circulating that season due to regulatory reluctance to allow use of a cell line that posed a "hypothetical" risk. Such occurrences are not only a regulatory and administrative matter, but may also negatively affect the public perceptions of the effectiveness of influenza vaccine in general.

Some of the regulatory barriers to vaccine development are not related to problems of vaccine quality, safety, or efficacy. Rather, they appear to be linked to organizational and policy matters, and may reflect bureaucratic obstacles rather than scientific processes and priorities (Miller and Henderson, 2007; Poland et al., 2009). Some regulatory barriers may relate to communication challenges between manufacturers and regulators (including FDA, the Office of Human Research Protections), misunderstandings, or procedural requirements that may be tangential to a study (Coleman et al., 2005; Glezen, 2006). Industry respondents to a qualitative study (of four pharmaceutical companies) found communication with European regulators much more "open" than with their American counterparts and this point has been echoed by others, including stakeholders informing this IOM committee at its December 2008 meeting (Coleman et al., 2005; IOM, 2008). One industry analyst wrote that "new technologies often languish because there's nobody inside FDA with sufficient time or resources to help them clear key scientific hurdles on the way to proving they are safe and effective" (Gottlieb, 2004).

There is an unmet need to translate the best of current science and technical innovation into the regulation of safe and effective vaccines. Although this is part of the mission of FDA's Critical Path Initiative, the 2009 budget for the initiative was only $5 million. The 2007 FDA Amendments Act also called for the establishment of the Reagan-Udall Foundation to

"modernize . . . product development, accelerate innovation, and enhance product safety," but the foundation's efforts to advance regulatory science has been delayed by congressional concerns about conflicts of interest on its board (Nature Reviews Drug Discovery, 2008).

A systematic approach could be used to assess and validate new technology that might replace older, time-consuming approaches currently used to ensure safety. One example relates to the testing of vaccines for the possible presence of adventitious infectious agents. It has been suggested that instead of using conventional culture methods, rapid and highly sensitive modern methods (some may already be in use in some cases) such as polymerase chain reaction and automated DNA sequencing could be used to detect such agents more quickly (Glezen, 2006). Another area in which improvement is possible is the use of bioassays used for testing vaccines. The animal tests used to assess the safety of older vaccines, such as whole cell pertussis vaccine (still used in the developing world) are decades old, and according to Milstien (2004) are neither precise nor predictive of a vaccine's safety in humans but continue to be required by some regulatory agencies.[10] Some animal tests, such as the abnormal toxicity test,[11] which remains in use in the United States but has been eliminated by most European regulatory agencies, are of questionable utility (Feigelstock, 2008; Milstien, 2004).

Because the topic of vaccine research and development is linked with issues in the goals pertaining to vaccine safety and vaccine use, several themes emerged from meetings of the committee with expert stakeholders on those goals in the draft National Vaccine Plan. Some stakeholders urged that the drafters of the National Vaccine Plan consider the need for improvements in information sharing among manufacturers, academe, and government, by addressing antitrust and intellectual property or proprietary considerations that are barriers to vaccine development and production. For example, industry scientists do not share failures that occur at the level of basic science and discovery, leaving others to unknowingly attempt the same or similar processes. Others called for facilitating the licensure of process improvements, novel delivery systems, and adjuvants. There were also discussions at two of the committee's meetings that focused on the importance of differentiating among the populations that may be given a vaccine. That is, the risk-benefit considerations for licensing products targeting certain populations at high risk from a vaccine-preventable disease (e.g., older adults, people with chronic conditions such as those on renal dialysis) may be different from those for vaccines intended for use in healthier populations. An additional theme pertained to furthering efforts to achieve international harmonization of regulatory requirements (e.g., to facilitate more rapid licensure in Europe

[10] See, for example, Kataoka et al., 2009, and Thalen et al., 2008.

[11] Product is injected into two guinea-pigs and five mice that are observed for 7 days (Milstien, 2004).

of a vaccine approved in the United States and vice versa) to accelerate the development and introduction for global use of new and improved vaccines and to reduce the cost of vaccine development.

Based on input from stakeholders, a review of pertinent literature, and its own deliberations, the committee found that there are aspects of vaccine development and regulation that can impede innovation without improving safety, efficacy, or immunogenicity, although recent changes at FDA suggest that the regulatory environment is strengthening its scientific foundations.

Recommendation 1-1: The National Vaccine Plan should incorporate improvements in the vaccine regulatory process that reflect current science and encourage innovation without compromising efficacy and safety.

Improvements include the following:

- Strengthening communication with vaccine developers through more frequent workshops and guidance documents, and
- Revising procedures and standards for developing, licensing, and producing vaccines for infectious diseases that encourage flexibility and innovation.

To ensure that FDA can play an optimal role in vaccine development, its Center for Biologics Evaluation and Research must have funding and staffing commensurate with its responsibilities to identify, develop, and apply the best and most current regulatory science to review of vaccine products.

PRIORITY SETTING IN VACCINE RESEARCH AND DEVELOPMENT

A second theme identified by the committee that is congruent with Objective 1.1 in the draft plan emphasizes the importance of developing and periodically updating a prioritized list of needed new and improved vaccines. Several industry stakeholders and academic researchers at the December 2008 meeting stated that if the government described the priority diseases for which vaccines are needed and any critical specifications for those vaccines, companies would be eager to deliver them. Previously, a 2003 NVAC report found that a unified approach to federal prioritization of vaccine development, so as to assure that public health needs are met, is an important component of vaccine development. An approach suggested in the 2003 report was for NVPO and NVAC to provide a mechanism for

a unified federal prioritization of vaccine development and distribution as specified in the 1986 enabling legislation.[12]

In 1985, IOM released two related reports titled *New Vaccine Development: Establishing Priorities Volume 1, Diseases of Importance in the United States* and *Volume 2, Diseases of Importance in Developing Countries* (IOM, 1985a,b). The committee that authored these reports developed a quantitative model that could be used by decision makers to prioritize the development of vaccines against a number of infectious diseases considered significant threats to public health. Several of the candidate vaccines considered in that report have been licensed since its publication and are now in use, including recombinant hepatitis B virus, hepatitis A virus, varicella zoster virus, *Haemophilus influenzae* b (Hib), rotavirus, and acellular pertussis vaccine. The other candidate vaccines remain at various points in the pipeline.

More than a decade later, NIH requested that IOM convene a new committee to assess the progress made since publication of the 1985 reports, to "discuss important barriers to vaccine research and development, and develop another quantitative framework for prioritizing vaccine development" (IOM, 2000). That committee selected 26 candidate vaccines and analyzed them using an "annualized value of the costs per quality-adjusted life year gained by a vaccine strategy." The candidate vaccines were then placed into four quartiles reflecting the extent to which a vaccination strategy would save money (I—most favorable, II—more favorable, III—favorable, IV—less favorable). The resulting report discussed how insufficient interest on the part of funders, such as private vaccine companies conducting research and development, can reflect concerns about profitability because of either poor market potential or possible costs due to liability for adverse events. "Stable and sufficient funding of basic research by the federal government, the use of creative funding mechanisms, and the creation of alliances between the public and private sectors are crucial to ensuring that effective, safe, and needed vaccines will be carried through the development stage into licensure" (IOM, 2000:124). A comparison of the 2000 IOM report to the update on vaccine development and research in the 2007 Jordan report (HHS et al., 2007) shows that of the three kinds of vaccines ranked in the first quartile (most favorable) based on strength of the evidence (cytomegalovirus, universal influenza, streptococcus pneumonia), none has been developed, and of the seven kinds of vaccines ranked in the second quartile (more favorable), only vaccines against HPV and tuberculosis have been developed and have received FDA approval.

The process of prioritization of candidate new vaccines also needs to

[12] The National Childhood Vaccine Injury Act.

include the Centers for Disease Control and Prevention (CDC). Landry and Heilman (2005) wrote that

> by engaging in early and wide-ranging discussions with companies, the advisory committees and the CDC staff can review broad criteria concerning future needs for and address what-if scenarios regarding candidate vaccines—e.g., if a respiratory syncytial virus vaccine had these characteristics, would it be considered for use in high-risk infants only or all newborns? The companies can often review early directions in research and development with the advisory bodies, although confidentiality because of the competitive forces of the marketplace will sometimes limit such discussions.

Similarly, Plotkin (2005b) has commented on the potential role of the Advisory Committee on Immunization Practices (ACIP) in a dialogue about setting vaccine development priorities:

> Public health authorities need to indicate which vaccines would be used if they were developed. The recent Institute of Medicine (IOM) report on priorities for vaccines is a signal example of what can be done, but to my knowledge it has never been discussed by the ACIP, nor has the ACIP indicated which of the priorities given by the IOM it agrees with.

The 2000 IOM report identified major gaps in data and research relevant to some infectious diseases of public health importance (e.g., *Treponema pallidum, Clostridium perfringens, enterococci*) and found that "research in fields such as epidemiology, health services research, health economics, human behavior, and even ecology" could help to advance vaccine development and program implementation. However, the committee that authored the 2000 report was surprised by a "lack of data and research in these fields, information that would have been useful to the committee in assessing disease burden" and "[i]n some cases, no significant new data had been published since that referenced in the 1985 IOM report on vaccine priorities, particularly national data on disease characteristics such as morbidity states and patterns of care" (IOM, 2000:124). The experience of the committee that authored the 2000 report may help to illustrate how a systematic, national process of priority setting could help identify areas in which research is needed and perhaps spur such research. For example, encouraging new targeted burden of disease studies, rather than repeating prioritization exercises using existing data, would further knowledge in the field and provide a more up-to-date basis for decision making.

Development of an HIV vaccine remains a critical priority for HHS and all stakeholders; the committee was surprised that the new draft plan did not mention an HIV vaccine. Another example of a currently unmet need that was mentioned at two or more stakeholder meetings is the emergence of difficult-to-treat bacterial infections, such as methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile*, as increasingly worrisome public

health problems that potentially could be addressed through the development of effective vaccines.

As noted above, the draft National Vaccine Plan includes identifying vaccine research and development priorities as an objective in Goal 1, but does not call for a formal, systematic process for priority setting. It was suggested at the February 2009 NVAC meeting that the plan elaborate on vaccine priorities for the United States and the products needed to address the lack of a systematic approach to vaccine development. An industry representative commented that from a commercial perspective, concerns remain about how—or whether—to develop vaccines for small or uncertain markets (NVAC, 2009). This sentiment—that it would be desirable and helpful if a government entity could identify which products should move forward—was also expressed repeatedly by stakeholders at this IOM committee's meeting on research and development. Although the committee recognizes that companies include additional factors, such as commercial potential, in their decision making, the committee has observed a level of agreement on the need for guidance toward a unified list of priority vaccines.

The committee found that there currently is no ongoing, evidence-based process involving all relevant stakeholders by which candidates are identified as priorities for vaccine development in industry and government programs. Such a process could accelerate the development of vaccines by identifying both the need and the likely market—linking priorities (vaccines with certain specified characteristics) to ACIP recommendations for use. The committee concurs with the draft plan's attention to prioritization of candidate vaccines and offers the following recommendation.

Recommendation 1-2: The National Vaccine Plan should incorporate the development of an evidence-based approach for prioritizing new and improved vaccine candidates by targeted disease and develop specifications for high-priority vaccines to accelerate their development.[13]

Such an approach would ideally involve government agencies and all relevant stakeholders and take place under the aegis of NVAC or a similar entity. The approach to priority setting may have some of the following attributes:

- Supporting disease burden studies (e.g., morbidity and mortality) when needed for vaccine prioritization;

[13] This recommendation refers to development of vaccines as defined by the 1986 act—vaccines to prevent infectious diseases.

- Employing outcome measures that capture both survival gains and quality-of-life improvements;[14]
- Use of cost-effectiveness analysis; and
- Consideration of the technical and scientific feasibility of vaccine development as a prioritization criterion.

A process for priority setting would be strengthened by incorporating evidence or guidance available from previously published work linking research and funding levels to national priorities.[15] Two parallel but separate processes are needed to prioritize vaccine targets for U.S. and global use, reviewing two different sets of burden of disease data, cost-effectiveness data, and other information. The committee recognizes that although quantitative ranking systems can inform, they are only one source of information in making policy decisions.

COORDINATION AND OVERSIGHT OF VACCINE DEVELOPMENT

A great deal of remarkably productive vaccine-related research takes place in the United States. However, the majority of NIH-supported research is comprised of investigator-initiated studies (NIH, 2009a,b). Such an approach is responsible for discoveries that may lead to new vaccines and, in the case of difficult scientific challenges (e.g., developing an HIV vaccine) may be necessary. On the other hand, proceeding from a list of priority vaccines to the development of those vaccines would benefit from a more planned and coordinated approach. For example, BARDA requests for proposals include detailed specifications for the vaccines needed (HHS, 2009).[16] A high level of coordination among stakeholders and pertinent government agencies would be beneficial in the development and licensure of vaccines identified in the process of prioritization described on preceding pages. Based on comments received at its December 2008 meeting on developing new and improved vaccines and on a review of relevant literature, the committee understands that barriers to coordination remain, although interactive dialogue has, indeed, been fostered among the relevant federal agencies, advisory committees, and industry.

[14] Quality-adjusted life years, or QALYs, have been suggested for use in the United States for priority setting in vaccine development (IOM, 2000). Disability-adjusted life years, or DALYs, have been suggested for use internationally. However, it is important to note that both measures have their proponents and critics, and that there are other measures of health outcome that could be used to inform a process of priority setting.

[15] See, for example, Gross et al., 1999, and Neumann et al., 2005.

[16] BARDA issued a request for proposals (RFP) in 2007 for advanced development of recombinant influenza vaccines based on hemagglutinin genes or proteins that may be manufactured in 12 weeks or less after the beginning of a pandemic with the goal of awarding contract(s) toward FDA licensure (HHS, 2009).

The 2009 H1N1 vaccine development effort provides an example of the potential of public-private coordination. Shortly after the recognition of the novel H1N1 outbreak, CDC prepared a vaccine seed strain and shared it with manufacturers. In April 2009 the acting CDC director stated that "HHS has also identified the needed pathways to provide rapid production of vaccine after the appropriate seed strain has been provided to manufacturers" and that as vaccine development progressed, "HHS operating divisions and offices including CDC, NIH, FDA, and ASPR/BARDA [would] work in close partnership" (Besser, 2009).

The committee found that the vast majority of NIH-supported peer-reviewed vaccine research is investigator-initiated and that coordination among federal agencies and with academic and private sector stakeholders could be strengthened. Furthermore, some examples of innovative and productive intersectoral collaboration come from the development of vaccines for global health, such as the approach of public-private product development partnerships (PDPs). Public-private partnerships such as PDPs have a long history both in the United States and in other countries. One example dates back to the World War II era collaboration among government, academia, and industry to develop the first licensed vaccines against influenza and pneumococcal pneumonia, improved vaccines against smallpox and tetanus, and other new or improved vaccines (Hoyt, 2006). Contemporary PDPs are involved in efforts to accelerate the development of an AIDS vaccine (e.g., the International AIDS Vaccine Initiative, IAVI) and vaccines for malaria and tuberculosis (TB) (e.g., the Malaria Vaccine Initiative, the Aeras Global TB Vaccine Foundation). (Chapter 5 provides additional discussion.)

Recommendation 1-3: The National Vaccine Plan should incorporate creation of a strategy for accelerating development of high-priority vaccines[17] that (a) engages all relevant institutes within NIH and the Department of Defense, academic investigators, and private sector partners; and (b) adapts lessons learned from innovative past and present public-private partnerships.

This coordinated, outcome-focused approach to vaccine development would be periodically reassessed to ensure appropriateness. The strategy for accelerating vaccine development may be two-part: (1) high-level, cross-cutting needs for innovation in manufacturing processes and other aspects of technology, and (2) needs for new vaccines against specific diseases or new combination vaccines. The drafters of the plan could explore what

[17] Per Recommendation 1-2.

combinations of government agencies and stakeholders could best address these connected areas.

The very slow shift from egg- to cell-based production of influenza vaccine further illustrates the need not only for high-level prioritization of vaccine research, but also for strong government support of coordination to achieve those priorities. Hens' eggs have been used to grow influenza virus to make influenza vaccine for decades, although development of a cell-based vaccine has long been recognized as the way forward to improve vaccine production capacity. Despite the technical feasibility of producing a cell-based influenza vaccine, the shift from eggs to cells requires a substantial investment in licensing a new process that is costly, complex, and risky. The change also requires addressing scientific and regulatory questions about the safety, reactogenicity, immunogenicity of cell-based vaccine, while continuing to produce egg-based vaccine entails comparatively fewer financial or opportunity costs (although the availability of hens' eggs has been a limiting factor in recent years). The global concern about the potential of pandemic influenza and the concomitant need to facilitate rapid, large-volume production of influenza vaccine was one of the incentives for exploring different approaches to its manufacturing.

THE MEANING OF "VACCINE" IN THE 21ST CENTURY

The committee believes that the scope of the National Vaccine Plan could be broadened to include classes of vaccines other than vaccines intended to prevent infectious diseases. Such an expansion would recognize the fact that vaccines against infectious diseases are already benefiting from research and development efforts on other vaccine or vaccine-like entities, and that common immunologic platforms may be useful for different types of vaccines.

The language of the 1986 act is a clear reflection of its time. The purpose of the program described in section 2101 of the act is "to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines." In 1986, immunization and vaccines were quite firmly linked to or identified with infectious disease, and there was limited recognition of vaccines' potential role as therapeutic modalities or as preventive against cancer or other chronic conditions. The 1985 IOM report recommended a list of priority vaccines that included only vaccines against infectious disease agents. Fifteen years later, the IOM report *Vaccines for the 21st Century* (2000) reflected the broader understanding of vaccines and immunization and proposed a list of priority vaccines that included several therapeutic vaccines (e.g., for insulin-dependent diabetes mellitus, multiple sclerosis, and rheumatoid arthritis). Since 1986, vaccines have been licensed that help prevent hepatitis B and

human papilloma viruses that may cause cancers of the liver and cervix, respectively.

As Plotkin (2005a) wrote,

> Active immunization has heretofore been largely confined to infectious diseases, with some use of desensitization to treat allergies. Now consideration is being given to immunization against a wide variety of noninfectious diseases. Most effort is being directed against cancers, in which novel cellular antigens are often present.

Expanding the interpretation of vaccines and immunization in the statute would acknowledge the reality that the current vaccine landscape is broader than infectious disease vaccines; recognize the relevance of research advancing therapeutic and other non-traditional vaccines to the broader vaccine enterprise; and perhaps proactively position the federal government to support coordination and encourage wider utilization of what is learned in the entire field of vaccines. The committee acknowledges that developing a national vaccine plan is challenging and that a much broader scope would result if other types of vaccines were included under the plan's purview. However, the plan's statutory underpinnings imply a distinction between the "traditional" vaccines intended for prophylaxis against infectious disease and other types of vaccines (therapeutic, prophylactic against chronic disease) that is no longer useful. Coordination in this area may help to maximize the benefits of scientific discoveries, clarify regulatory expectations, and enable early consideration of the health care implications of new classes of vaccines. The committee does not believe that there is a federal government agency that currently oversees or coordinates work on other types of vaccines.

Recommendation 1-4: Future iterations of the National Vaccine Plan should include classes of vaccines (such as therapeutic vaccines and vaccines against non-infectious diseases) beyond those expressly enumerated in the statute, and that the Secretary of HHS explore how best to assign responsibility for coordination in this area.

The development, use, and evaluation of vaccines that depart from the traditional paradigm of preventing infectious disease could be strengthened if such vaccines were part of a broader national strategy.

The broader view of vaccines described above would recognize the potential value of new vaccines beyond the "traditional" role of preventing infectious diseases, and proactively position the federal government to support coordination on and encourage the broader application of scientific and technologic breakthroughs related to non-traditional vaccines.

GLOBAL VACCINES

Goal 5 in the draft plan calls for increasing "global prevention of death and disease through safe and effective vaccination." The goal and the objectives within it, together with an added explanation,[18] make it clear that research and development pertaining to vaccines for developing countries is included in Goal 1. Although, as the draft plan notes, scientific and technological approaches to developing vaccines for the developed and developing country markets do not differ, the ability to recoup investments and the existence of a viable market are strong determinants of manufacturer decision making about strains or serotypes of a microorganism that will be included in a given vaccine, and of the willingness to pursue development of vaccines for certain neglected diseases that affect large populations in low-income nations. Multinational firms have a strong incentive to move away from traditional vaccines that promise little or modest return on investment, and to focus their efforts on novel, more profitable vaccines for rich countries. As a result, vaccine development specifically for low- and middle-income countries is critically dependent on innovative financing mechanisms and delivery mechanisms for eventually available vaccines (see Chapter 5). It is important that the National Vaccine Plan includes objectives and strategies attentive to this challenging area.

There may be unique scientific challenges to developing vaccines for populations in some developing countries. For example, there is evidence that children in some geographic areas have a less robust response to oral polio vaccine, the first Hib conjugate vaccine, and some rotavirus vaccines (Poland et al., 2009). The problem of subgroup differences in immunogenicity (and similar examples) seems related to vaccine development for vulnerable populations (e.g., strategies 1.2.2, 1.4.7, or 1.4.8 in the draft plan),[19] but it is important that the plan make specific reference to these

[18] "Given the breadth of global immunization activities, some of the Objectives and Strategies relevant to this topic are included elsewhere in this Plan. All vaccine research and development are included under Goal 1 as the approach to achieving these objectives and the key stakeholders are not different for the United States and the rest of the world. By contrast, issues related to vaccine safety, communications, and program implementation are included under the Global Immunization goal as well as under other goals of the Plan. Whereas many of the objectives in these areas are similar for the U.S. and abroad, the strategies differ as internationally, U.S. stakeholders focus on partnerships and providing assistance rather than on direct implementation as described elsewhere in the Plan" (HHS, 2008:56).

[19] Strategy 1.2.2: Conduct and support expanded vaccine research to meet medical and public health needs of specific populations including neonates, infants, the elderly, pregnant women, and immunocompromised individuals; Strategy 1.4.7: Establish and strengthen partnerships to address urgent needs in vaccine research and development; and Strategy 1.4.8: Establish alternative development and manufacturing approaches to support licensure for those vaccines that have a limited market.

issues. Chapter 5 includes additional discussion of vaccine development for developing countries.

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2

The Safety of Vaccines and Vaccination Practices

The starting point for the contemporary vaccine safety system was the National Childhood Vaccine Injury Act (NCVIA) of 1986.[1] Enacted in the face of mounting public concern over both the safety of certain licensed childhood vaccines and the economic viability of the vaccine industry (Mariner, 1992), the act had two principal objectives. The first objective was to ensure that even as the public's health is protected through immunization, a system exists to compensate the small number of individuals who suffer injury thought to be caused by vaccines without the delays and costs associated with tort litigation. Simple fairness requires a mechanism to compensate those thought to be injured by vaccines that are properly manufactured and administered, that are recommended for universal use, and in some cases required by states for school entry to protect public health.[2] The other principal objective of the law was to create a climate of safety through adoption or expansion of optimal public health and clinical practices (e.g., monitoring vaccine safety, provision of printed patient information[3]) and the application of the best science to vaccine safety.

The fact that the founding of the National Vaccine Program (and by extension its executive entity, the National Vaccine Program Office [NVPO]) was among the desired outcomes in an act focused on vaccine safety is not

[1] Public Law 99-660, codified at 42 U.S.C. 201; see Appendix C.

[2] All states allow medical exemptions from school-entry vaccination requirements, 48 states allow religious exemptions from vaccination, and 19 states allow philosophical exemptions as well (NCSL, 2009).

[3] The law specifically requires the provision of Vaccine Information Statements.

coincidental. The act lists the program's nine responsibilities[4] with regard to intra-governmental coordination and coordination with stakeholders; most refer to the safety of vaccines and to adverse events. NVPO's coordinating role was and remains an essential part of the vaccine safety system established by the act. This chapter examines how the plan could enhance the vaccine safety system; a more extensive discussion of the coordination required to implement the National Vaccine Plan is provided in Chapter 6.

The first part of this chapter provides an overview of four major components of the 1986 legislation and their current status: (1) vaccine safety surveillance and research; (2) information and communication about vaccine safety (discussed in Chapter 3); (3) the program of compensation for injuries thought to be caused by vaccine; and (4) the National Vaccine Program and Plan. The second part of the chapter is organized around four recommendations about priority actions for vaccine safety in the National Vaccine Plan.

In the history of vaccine development and regulation, concern has focused on both vaccine efficacy (and correlates of clinical protection) and vaccine safety. Both vaccine efficacy and vaccine safety are relative: no vaccine is 100 percent effective or 100 percent safe. The use of vaccination has reduced the incidence of disease (and therefore the immediate threat to any individual) and, concomitantly, the burden of fear of disease-related morbidity, disability, and death. The lower risk of disease has understandably led to higher expectations of vaccine safety. The story of polio vaccine illustrates the evolving nature of a vaccine's risk-benefit balance and of the understanding of that balance as additional information on possible adverse events accrues and as disease incidence changes. In the 1950s when poliomyelitis was endemic in the United States, the benefit of live, attenuated poliovirus vaccine for the individual and the community was judged to greatly outweigh the risk of vaccine-associated paralysis, which occurred at a rate of about 1 case per 2.4 million doses distributed (CDC, 2009b). By 2000, when polio had been eliminated from the Western Hemisphere, this risk of vaccine-associated paralytic polio was judged no longer acceptable in the United States. An enhanced inactivated polio vaccine (IPV), first licensed by the Food and Drug Administration (FDA) in 1987, was ultimately recommended by the Advisory Committee on Immunization Practices (ACIP) in 2000 for exclusive use in routine immunization (CDC, 2000; Moylett and Hanson, 2004).

[4] The nine responsibilities include vaccine research, vaccine development, "safety and efficacy testing of vaccines," "licensing of vaccine manufacturers and vaccines," "production and procurement of vaccines," "distribution and use of vaccines," "evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities," "coordinating governmental and non-governmental activities," and funding federal agencies in implementing the National Vaccine Plan.

Interventions given to healthy persons to prevent disease are required to have a low risk-to-benefit ratio when compared to therapeutic interventions. Many childhood vaccines that are recommended for universal use by ACIP are required by states for attendance in licensed day care facilities and public schools, and thus administered to large segments of the population (e.g., nearly the entire annual birth cohort of more than 4 million children). Some adult vaccines are also universally recommended, others are recommended for specific occupations (e.g., health care workers) and, in some cases, required by employers. A substantial proportion of the adult population receives influenza vaccine each year (for example, between two-thirds and three-quarters of adults 65 years of age or older received influenza vaccination in 2008; CDC, 2006).

The process of anticipating, detecting, and quantifying the risks of rare adverse events following immunization presents an enormous challenge. Vaccine studies submitted as part of Biological License Applications to FDA's Center for Biologics Evaluation and Research (CBER) have historically included several thousand individuals. Rare but serious adverse events may follow vaccination, sometimes at rates in the range of one in a million vaccine recipients. Even vaccine trials including 100,000 or more participants may not have adequate statistical power to detect such rare adverse events. Delaying licensure after efficacy has been shown in order to amass additional evidence related to rare adverse events associated with a candidate vaccine would result in continuing cases and deaths due to the preventable disease.

After FDA licensure, as knowledge about a vaccine's safety increases when large numbers of individuals are immunized, additional safety assessment becomes possible, complementing pre-licensure data. Vaccine safety researchers both at FDA and outside government have emphasized the equal importance of adequate pre-licensure study and post-licensure surveillance for "signals" of adverse events. It is challenging to detect a true "signal" of a vaccine safety problem amidst the considerable "noise" of coincidental, only temporally related events.

Licensure of second generation rotavirus vaccines offers a clear example in which pre-licensure studies put a special emphasis on vaccine safety because of knowledge about the risk of intussusception acquired after introduction of the first licensed rotavirus vaccine. The large studies undertaken for the second-generation rotavirus vaccines—70,000 subjects for RV5 (bovine-based, RotatTeq) and nearly 75,000 for RV1 (human-based, Rotarix)—reflect a specific safety concern related to the first rotavirus vaccine (Ellenberg et al., 2005; GSK, 2008; Heyse et al., 2008).

The FDA Amendments Act of 2007 has strengthened CBER's authority to require post-licensing studies. FDA may require the manufacturer to conduct post-licensure studies of vaccine safety that meet certain specifica-

tions (e.g., design, size). FDA monitors a wide range of safety data from the systems described below. The Centers for Disease Control and Prevention (CDC), in addition to joint management of the Vaccine Adverse Events Reporting System (VAERS), implements rapid epidemiologic evaluation of possible safety signals, such as the evaluation of intussusception following the use of RRV-TV (rhesus-based, RotaShield).

A CASE STUDY OF VACCINE SAFETY SYSTEM FUNCTIONING

The federal vaccine safety system's response to evaluate reported adverse events following immunization with RRV-TV entailed an extensive effort. The response spanned at least 19 states, involved 40 of CDC's Epidemic Intelligence Service officers, and drew on the capabilities of federal, state, and local public health agencies and health care organizations to locate and verify vaccination histories and outcomes in infants given the rotavirus vaccine and to undertake scientific analysis.[5] A timeline of events culminating in the withdrawal of the ACIP recommendation for rotavirus vaccine is provided in Table 2-1.

The experience with RRV-TV illustrates comprehensively the safety system's components, their capabilities, and their functioning. Subsequent efforts to develop, license, and monitor the safety of RRV5 and RV1 were informed by lessons learned from the first vaccine and led to changes in study design and regulatory expectations for rotavirus vaccines (e.g., a requirement for an unprecedented expansion of the size of the Phase III clinical trials; targeted post-licensure surveillance).

At the time it licensed RV1 in 2008, FDA required a large post-licensure observational safety study in the United States to assess the potential serious risk of intussusception and other serious adverse effects (specifically Kawasaki disease, hospitalizations due to acute lower respiratory tract infections, and convulsions) in vaccine recipients. Requirements included a study sample size of 44,000 vaccinated subjects (to be adjusted based on the background rate of intussusception), and a study design "to detect an increased relative risk of intussusception due to vaccine with a relative risk of 2.5 or greater and with 80 percent power" (FDA, 2008a). The study began June 2009 and is expected to end in 2012.

[5] Personal communication, D. Snider, M. Wharton, T. Murphy, U. Parashar, CDC, August 25-26, 2009.

TABLE 2-1 Rotashield Vaccine Timeline (1999-2001)

Date	Event
Before licensure	In the absence of rotavirus vaccines, there are 3 million cases of rotavirus infection per year (in children under age 5); for 500,000 cases, medical attention is sought, and 60,000 to 70,000 are hospitalized. According to Rennels (2000), rotavirus gastroenteritis caused 25 pediatric deaths per year. There is no known association between wild rotavirus infection and intussusception. The rotavirus vaccine manufacturer sponsors 27 clinical trials in 9 countries involving more than 10,054 children who received the vaccine (Rennels, 2000). Study data are submitted to FDA as part of the Biological License Application process. ACIP forms a rotavirus working group, and the group's review of serious adverse events in the pre-licensure trials finds 5 cases of intussusception in children who received the vaccine and 1 case among 4,633 children receiving placebo (Rennels, 2000; Rennels et al., 1998).
August 31, 1998	Rotavirus vaccine[a] (RRV-TV) is licensed by FDA for use in infants (CDC, 1999). Vaccine package insert includes reference to intussusception as potential adverse event (Rennels, 2000). However, background rates of intussusception are not statistically different from those identified during pre-licensure study (Rennels et al., 1998; see below).

Intussusception in the following groups	**Rate (%)**
Study placebo recipients	0.022
Study vaccine recipients (all doses)	0.05
Study vaccine recipients (dose proposed for licensure)	0.024
Health plan population 1995-1996 (California Kaiser Permanente study)	0.074
General population 1991-1995 (New York State)	0.05

	FDA requires Phase IV (post-licensure study) of adverse events (CDC, 2004). Intussusception search code is added to VAERS database (Rennels, 2000).

continued

TABLE 2-1 Continued

Date	Event
October 1998	Study comparing vaccinated children to unvaccinated children shows no statistically significant difference in intussusception rates between the two groups and "failed to demonstrate an etiologic association between natural or vaccine rotavirus infection and intussusception" (Rennels et al., 1998).
December 1998	FDA-required Phase IV (post-licensure) study by Northern California Kaiser Permanente begins.
December 1998	The first report of intussusception following rotavirus vaccine to VAERS (over the first months of 1999, 1-4 reports of intussusception are received by VAERS) (Zanardi et al., 2001).
March 19, 1999	ACIP recommends use of rotavirus vaccine as a 3-dose series at 2, 4, and 6 months of age (CDC, 1999).
June 2, 1999	Reports of intussusception submitted to VAERS reach 10; most cases occur within 1 week of the first dose of vaccine—"temporal clustering after receipt of RRV-TV suggested a causal relationship" (CDC, 1999). Preliminary findings from the Phase IV study in managed care organizations give additional cause for concern, although "these data did not have adequate power to establish a statistically significant difference in incidence of intussusception among vaccinated and unvaccinated children" (HHS, 2008a).
June 17, 1999	CDC alerts ACIP about emerging epidemiologic information (CDC, 2004). CDC initiates two epidemiologic studies: a 19-state case control study and a population-based retrospective cohort study (Chang et al., 2002; Kramarz et al., 2001; Murphy et al., 2001). CDC investigators review medical records of all VAERS reports of intussusception following rotavirus vaccine (Zanardi et al., 2001).
July 6, 1999	Number of cases of intussusception following rotavirus vaccination reaches 15 (CDC, 2004).
July 16, 1999	CDC recommends that providers suspend use of the rotavirus vaccine (CDC, 2004). The announcement is followed by an increase in reports to VAERS (HHS, 2008a).
October 22, 1999	ACIP withdraws its recommendation for use of rotavirus vaccine at ages 2, 4, and 6 months (CDC, 1999).
December 31, 1999	Number of cases of intussusception following rotavirus vaccination reaches 112 (Verstraeten et al., 2001).
2000-2001	Verstraeten et al. (2001) conduct a capture-recapture analysis of intussusception after rotavirus vaccine between December 1, 1998, and June 30, 1999, and find that VAERS reporting was 47% complete.

[a] Tetravalent Rhesus-based Rotavirus [RRV-TV] RotaShield.

PART I: COMPONENTS OF THE 1986 LEGISLATION

Reporting and Investigating Adverse Events: Assessing Causality

Post-licensure vaccine safety surveillance is an important component of the vaccine safety system that begins operation for a given vaccine at the time it is licensed by FDA and health care providers begin to administer it. Surveillance for adverse events following immunization—based on reporting by the public, health care providers and manufacturers—is conducted by two entities: VAERS and the Vaccine Safety Datalink (VSD). The military also provides vaccination to its personnel, and the Department of Defense operates its own military immunization program and the Vaccine Healthcare Centers Network (2009) that provide "expert consultative services for vaccine adverse events case management and reporting; research in vaccine safety and quality assurance; and healthcare provider/patient education and training programs."

Before the 1986 NCVIA was enacted, reports of adverse events following immunization were captured through two different systems. One was a system administered by FDA and intended to gather spontaneous vaccine adverse event reports from manufacturers, pharmacists, health care providers, and the military. The other system, the Monitoring System for Adverse Events Following Immunization established in 1978, was administered by CDC and intended to collect reports from parents whose children received publicly purchased vaccine. As a result of the law, the two reporting systems were integrated into VAERS, which began operating in November 1990 and currently receives approximately 30,000 reports annually from manufacturers, health care providers, and vaccine recipients or their parents or guardians (CDC, 1990; HHS, 2008b). Approximately 85 percent of reports received by VAERS describe mild events, while 15 percent describe serious adverse events (life-threatening, requiring hospitalization, or resulting in death) (CDC, 2009a). (See Figure 2-1 for an overview of the federal vaccine safety system.)

The VAERS system has strengths and weaknesses. A major strength is that anyone may submit a vaccine adverse event report to VAERS including consumers. Weaknesses of VAERS include incomplete reporting of adverse events, varying quality and completeness of individual reports, and several important biases (Iskander et al., 2006; Varricchio et al., 2004). Although the system is capable of capturing rare and unusual adverse events following immunization, and CDC staff use sophisticated data mining techniques to maximize the usefulness of VAERS data to detect safety signals (Iskander et al., 2006), reports to VAERS may simply indicate a perceived relationship to the vaccine, usually based on a coincidental temporal association between vaccine administration and the adverse event. To assess causality, one needs to compare the expected rate of the reported condition in a comparison

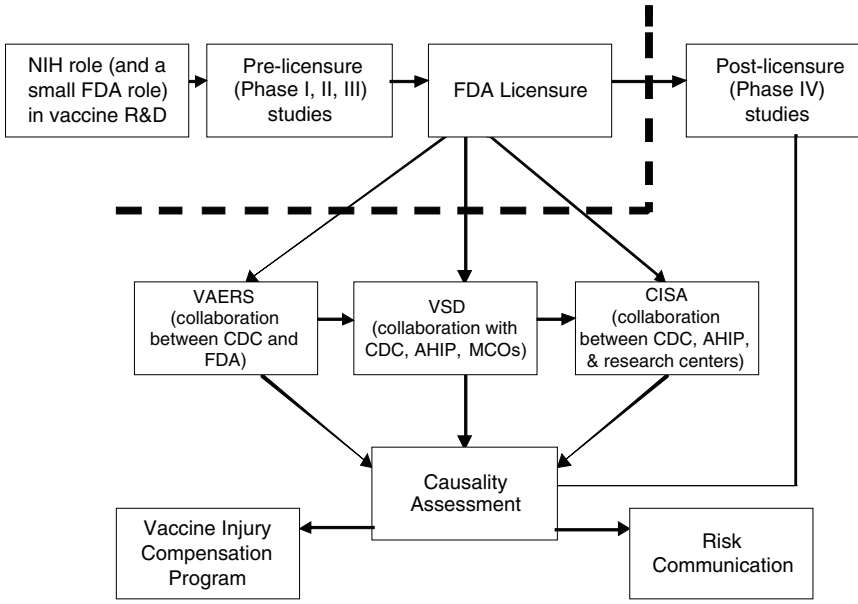

FIGURE 2-1 In December 2008, HHS and NVPO released a detailed overview of the federal vaccine safety system in some detail, with some reference to non-government stakeholders (HHS, 2008). In addition to the federal agencies charged with various components of researching, regulating, monitoring, and communicating about vaccine safety, many other stakeholders, including vaccine manufacturers, academic researchers, health care providers, public health agencies, and the public make important contributions.
NOTE: The thick dotted line represents the point at which vaccines enter the market, become recommended for use, and become increasingly used in the population. Risk communication is discussed in more detail in Chapter 3 of the present report. Adapted from HHS (2008a). For the sake of simplicity, does not reflect Department of Veterans Affairs (VA) and Department of Defense (DoD) contributions to the federal vaccine safety system (see discussion in text). Acronyms: CISA: Clinical Immunization Safety Assessment; MCOs: Managed Care Organizations; NIH: National Institutes of Health.

group. Because there are no comparison groups available for VAERS, data the system collects are almost always only one part of the information needed to assess whether or not there is an association between a vaccine and an adverse event. Due to incomplete reporting and lack of appropriate comparison groups, neither the incidence of an adverse event nor the relative risk of the event in vaccinated individuals can be calculated (Varricchio et al., 2004). Thus, VAERS data cannot ordinarily establish that an epidemio-

logic, much less, a causal, association exists between the suspected adverse event and immunization.

The VSD program represents a model for government-academia-health care delivery system collaboration involving CDC, FDA, AHIP, and university-based researchers. VSD utilizes databases from eight managed care organizations that provide medical care for 8.8 million children and adults. Because VSD has the capability of generating appropriate comparison groups it can also analyze data that establish an epidemiologic association that can provide stronger evidence for causality than that provided by case reports. VSD conducts active surveillance for adverse events of interest and for any adverse event resulting in a health care contact within a time period of interest following vaccination (i.e., VSD data can be searched systematically for specific events or time periods). After the introduction of new vaccines, VSD investigators develop hypotheses, often on the basis of reports to VAERS or data from pre-licensure trials, and the VSD database facilitates their investigation. In the past several years, VSD has developed a new capability—rapid cycle analysis of its database, that enables VSD researchers to conduct near real-time (weekly) active surveillance of vaccine safety.

One of VSD's strengths is the link to electronic medical records and access to medical charts for clinical information and vaccination histories. Limitations of the VSD include its sample size, which, though large, may not be adequate to detect association for extremely rare adverse events, for example those that occur in one in a million individuals. VSD is currently conducting monitoring of adverse events for the following vaccines: meningococcal conjugate vaccine, Tdap, MMRV, seasonal influenza, quadrivalent HPV, combination DTaP-Hepatitis B-IPV, and RRV5. VSD is also preparing for active surveillance using Rapid Cycle Analysis for the vaccine against novel influenza A (H1N1), RRV1, DTaP-IPV, and DTaP/IPV/Hib vaccines.

Another component of the vaccine safety system is the Clinical Immunization Safety Assessment (CISA) network that is a collaborative effort between CDC, AHIP, five academic medical institutions, and one managed care organization. CISA investigators conduct intensive clinical study of cases of adverse events following immunization, in an effort to better understand the complex relationship to vaccines and inform the development of guidance for clinicians on the management of serious adverse events (Halsey et al., 2009). Some of CISA's work leads to publication (Slade, 2009).

One of CISA's collaborators is the Department of Defense's network of Vaccine Healthcare Centers (VHC). CISA's role and expertise are complementary to those of VSD. While VSD takes an epidemiologic approach to assessing causality, CISA's approach is focused on understanding the pathogenesis of adverse events following immunization at the individual level, as the only component of the vaccine safety system that conducts clinical and

basic science research and that provides consultation (via phone and e-mail) to providers managing adverse events following immunization (Halsey et al., 2009; Slade, 2009).

FDA's role in monitoring vaccine safety (together with its effectiveness, as they cannot be considered in isolation from one another [IOM, 2007]) spans a vaccine's entire lifespan. The regulatory role begins when a vaccine developer approaches the agency to discuss preliminary plans for a Biologic License Application and request an Investigational New Drug protocol to allow clinical trials with humans. That role continues during regulatory review, through the point of licensure, which today includes requirements for post-licensure surveillance (i.e., Phase IV) studies, and for as long as the vaccine is manufactured or used. As noted earlier, FDA collaborates with CDC in managing the VAERS system and in overseeing post-licensure safety research. The processes by which the pre-licensure review of a vaccine fully anticipates and informs the post-licensure phase have undergone some strengthening in response to the FDA Amendments Act. For example, FDA has gained authority to require post-licensure studies and specific plans to minimize and manage risks posed by medical products including vaccines.

FDA is in the early stages of establishing the Sentinel Initiative, a system for large-scale surveillance of medical product safety, including vaccines. The initiative is intended "to link and analyze healthcare data from multiple sources" by accessing (and analyzing) data from 25 million patients by July 1, 2010, and from 100 million patients by July 1, 2012 (FDA, 2008b). FDA is supporting researchers to evaluate various methodologic approaches and other dimensions of the use of very large databases to evaluate medical product safety. A national discussion among both federal partners and non-government stakeholders about vaccine safety research priorities could also inform investigations based on the sentinel system. This will require greater coordination between CDC, FDA, and other federal agencies, and the committee hopes, strong coordination with national health information technology efforts. The committee noted that the plans of the Office of the National Coordinator for Health Information Technology (ONCHIT) include objectives on linkage with immunization registries and recognition of immunization status as an important component of electronic health records. Some ONC documents, such as the "Meaningful Use Matrix" (intended to guide the meaningful use of electronic health records to engage patients, provide real-time access to all medical information, and support quality and safety as well as improved access and the elimination of health care disparities [ONCHIT, 2009]) also include references to FDA's Sentinel Initiative. Although there are considerable barriers to the successful development and implementation of health information technology, the committee hopes that what it has noted is an indication that health information technology planning at the highest levels of government is coordinated with the

national medical product safety surveillance effort. At the time of this writing, CDC, FDA, and VSD have developed and are implementing a system to monitor the safety of the H1N1 pandemic influenza vaccine. The network for Post-Licensure Rapid Immunization Safety Monitoring (PRISM) has been established to link immunization registries in a number of states with the databases of large health maintenance organizations. This system considerably expands VSD's sample size and could perhaps provide some idea of how the Sentinel Initiative may function (HHS et al., 2009).

Finally, in addition to its role in VAERS, VSD, and CISA, CDC also is the nation's lead public health agency, able to respond rapidly to the emergence of a vaccine safety question with the expertise needed to assess urgent public health issues such as disease outbreaks or serious vaccine safety concerns. CDC is able to deploy epidemiologists and other experts to conduct case-control interviews, conduct laboratory research, work with state public health personnel and health care providers, and carry out other activities needed to intensively investigate a potential serious adverse event following immunization. The experience with the first rotavirus vaccine, RRV-TV, described above, is an example of the federal and state public health capabilities in quickly responding to and elucidating the meaning of a vaccine safety "signal" captured through VAERS or by other means (e.g., active surveillance through VSD). After a vaccine's licensure, CDC's efforts to ascertain vaccine safety (and effectiveness) complement those carried out by FDA, in addition to activities conducted jointly, such as VAERS and VSD.

Information and Communication

The social context of vaccine safety has changed in the decades since the 1986 act was signed into law. As immunization has resulted in vastly lower rates of some diseases and entirely eliminated other diseases, the direct relationship between vaccine and disease prevention has become less and less visible to the public. Today diseases such as polio, diphtheria, and congenital rubella syndrome no longer top the list of fears parents have for their children's health; polio has been eradicated from the Western Hemisphere, and other diseases may be mere memories or only rare occurrences. A major decrease in the rate of a vaccine-preventable disease may alter the risk-benefit analysis for a vaccine targeting that disease. Other changes in the past two decades include social and cultural transformations that have shaped public attitudes toward vaccination both positively and negatively. These include the emergence of active and engaged patients, and the rapid availability of vast amounts of information via the Internet, and the emergence of organized groups opposed to immunization. The committee believes that one major challenge in communicating about vaccines relates to their dual identity as a medical intervention to protect an individual against

disease and a public health intervention to prevent community-wide outbreaks and protect those in the community who cannot be vaccinated due to age or health status, or those who do not mount an adequate immune response to vaccines.

The committee asserts that this duality—the personal and public benefits of vaccines—has not been clearly conveyed in the process of communicating about immunization. This is a serious omission because it hinders necessary public discussion of the implied conflict between two widely held values: protecting the health of the community and individual freedom of choice. As the incidence of a transmissible vaccine-preventable disease declines questions arise about what is the optimal balance of individual choice and responsibility to the community. Communication on these topics needs to be expanded and strengthened as our nation's public health becomes increasingly dependent on vaccine-induced immunity to diseases still prevalent elsewhere in the world and therefore are only a plane ride away from U.S. communities in addition to diseases that remain endemic in the United States. Also, the many efforts undertaken by the nation's vaccine safety system are frequently invisible to the public and communication about vaccine risk would be strengthened by thorough and clear information about the science of vaccine safety and about the mechanisms that are in place to detect and respond to potential vaccine safety problems. Chapter 3 in this report provides more extensive discussion of communication about vaccines and vaccination.

The Compensation Program

As noted in the Introduction to this report, a central purpose of the 1986 law was compensation of individuals thought to have been injured by vaccines. The rationale underlying the Vaccine Injury Compensation Program (VICP) is that when individuals have been injured by an appropriately manufactured and administered vaccine as part of a public health program they should be compensated. Prior to the creation of the VICP by the passage of the NCVIA in 1986, individuals who believed they had been injured by a vaccine had to seek compensation through litigation in the tort system. Escalating litigation costs related primarily to claims of vaccine-related injuries inadvertently caused by properly manufactured and administered live oral polio virus vaccine and whole cell pertussis vaccines threatened the vaccine industry's economic viability and thereby the supply of vaccine required to continue public health immunization programs. Congress established VICP "[b]ecause society mandates the use of vaccines, through state laws for school enrollment" and therefore "it is reasonable and appropriate that society take responsibility for unavoidable adverse outcomes associated with the use of vaccines" (Evans, 2006:S132).

As described in the Introduction, petitioners to the program who meet basic preconditions (e.g., demonstrating that they received the vaccine they claim caused the injury) may obtain compensation by two pathways, depending on whether the alleged injury is listed on the VICP injury table. If they claim an injury listed on VICP's injury table, they need not demonstrate a causal link between the injury, and the vaccine listing in the table attests that there is accepted scientific evidence of a causal link between the injury and the vaccine. The "off-table" pathway allows individuals who believe they have been injured by a vaccine to be awarded compensation by establishing by only a preponderance of evidence that their injury is related to a vaccine even though the weight of available evidence may fall far short of the scientific standard for establishing a causal link between the vaccine administered and the alleged injury. On-table injuries can be resolved without litigation,[6] since causality has been established. Off-table injuries are more complex to address, and in the absence of scientific consensus about causality U.S. Court of Federal Claims special masters must weigh the evidence. Currently most claims under the Vaccine Injury Act follow the off-table pathway. Because the special masters interpret that the intent of Congress was to compensate all individuals thought to have been injured by ACIP-recommended childhood vaccines, inevitably some individuals will be compensated whose injuries were not in fact caused by a vaccine.

Analysis of the claims relating to off-table injuries may have the potential to generate hypotheses deserving scientific study that could yield evidence of causal associations that would then warrant modification of the vaccine injury table. There have been delays in updating injuries listed in the table and undertaking the necessary research to update the table. This has generated concern that there is a lack of government commitment to understanding the full extent of vaccine risks even as it pursues universal immunization as a public good. Delays also have resulted in the large proportion of off-table awards based only on a preponderance of the often scant evidence available, perhaps heightening public worry about vaccine safety.

NVPO and the Plan

The Introduction to this report provides a history of NVPO and the National Vaccine Plan. NVPO's potential contributions to coordination on vaccine safety are discussed in Part II below.

[6] This refers solely to litigation on the issue of causation. Litigation may be required for other aspects of an on-table case, such as disputes about damages.

PART II: RECOMMENDATIONS ABOUT PRIORITY ACTIONS IN THE PLAN

The committee's process of deliberation identified four priority actions in Goal 2:

1. Development of a coordinated national vaccine safety research agenda;
2. Development of a coordinated, structured process to address vaccine safety signals promptly on detection and track them through until resolution (including a way to consider and address safety concerns raised through the Vaccine Injury Compensation Program);
3. Establishment of a vaccine safety advisory group capable of supporting coordination among federal agencies and with stakeholders, and soliciting and receiving public and stakeholder input on matters related to vaccine safety (the topic of transparency about policy making and other communication issues is discussed in Chapter 3); and
4. Allocating resources adequate to support basic, clinical, and epidemiologic research pertinent to vaccine safety.

A Coordinated and Transparent Process to Address Vaccine Safety Signals from Detection to Resolution

Although there are many effective components of the vaccine safety system (as evident in the detection and investigation of safety concerns related to rotavirus, MMRV,[7] and influenza vaccines, among others), the system can be enhanced through coordination. Coordinating vaccine safety within government agencies (also ideally involving stakeholders) could facilitate application of advances in vaccine safety science, the timely and efficient response to safety concerns, and the best use of resources. As one example, there currently is no formal and coordinated process for referring safety problems to VSD or CISA. The process is largely ad hoc and it appears that CISA, for example, relies on multiple informal mechanisms such as personal contacts with providers in a CISA center's immediate community to generate research questions. Although the committee was not asked to and did not evaluate the functioning or effectiveness of CISA or VSD, the committee believes that these programs play crucial roles in the vaccine safety system, and ensuring their optimal functioning is necessary for an effective vaccine safety system.

Furthermore, the committee understands that there is no organized mechanism to address scientific questions that arise in the course of adju-

[7] Measles, mumps, rubella, and varicella combination vaccine.

dicating cases before the U.S. Court of Federal Claims. Analysis of claims may generate research questions that can both address gaps in vaccine safety science and reduce the complexity of the compensation process. Creating such a mechanism (or expanding the currently limited frequency with which issues are referred from the compensation program to the hypothesis-testing VSD investigators or to the CISA researchers) would "close the loop," incorporating information that emerges from injury cases into the vaccine safety scientific research agenda as an additional source of adverse event detection or hypothesis generation.

In recent years, the public debate about vaccines has extended to vaccine safety research, and questions have arisen about how decisions are made about what research and surveillance activities are undertaken. This is, in part, a communication challenge because the decision-making processes undertaken by CDC together with academic and health care researchers are generally not visible to the public. The approach to assessing causality when a concerning adverse event is temporally associated with a vaccine includes several criteria that evaluate factors such as methodologic rigor, and consistency and frequency of findings.[8] Data obtained from case reports, case series, or court cases are sufficient only for the purpose of hypothesis generation. The possible association with vaccine must then be evaluated in a scientifically rigorous manner to answer the question.

Recommendation 2-1: The National Vaccine Plan should establish a process to identify potential vaccine safety hypotheses for further basic, clinical, or epidemiologic research through annual review of data from VAERS, VSD, CISA and the VICP, and from information available from sources outside the United States.

The compensation program fills a crucial need, and it is important to strengthen its effectiveness. The program needs to preserve its ability to compensate those possibly injured by vaccines, despite a lack of scientific certainty about the etiology of adverse events. The committee believes that scientific hypotheses raised by the compensation program could inform the safety research agenda, help to spur additional research, and potentially

[8] The Global Advisory Committee on Vaccine Safety of the World Health Organization has described a set of widely accepted criteria for assessment of causality with regard to adverse events following immunization (Folb et al., 2004). Criteria may include consistency of findings and methods; strength of the association (dose-response); specificity; temporal association; and biological mechanisms. An association between a vaccine and an adverse event is mostly likely to be considered strong and consistent when based on well-conducted epidemiologic studies in humans, an association demonstrated in more than one human study and showing consistency between studies conducted by different investigators in different settings with consistent results despite different research designs, and in some rare cases, similarity of an adverse event to the disease the live vaccine is intended to prevent, with non-random temporal relationship.

bring resolution to some of the uncertainties encountered in the compensation program. (Decisions in the VICP provide a crucial opportunity [and imperative] to communicate about vaccine safety. This is discussed in more detail in Chapter 3.)

The Research Agenda

The NVAC draft report on the Immunization Safety Office (ISO) agenda (May 28, 2009) stated that "there is a strong need for a federal vaccine safety research agenda that encompasses research undertaken by non-ISO CDC offices, FDA, and National Institutes of Health (NIH) and requires increased collaboration and coordination between all federal agencies with a stake in vaccine safety" (NVAC, 2009b:9).

This statement is similar to comments made at the committee's April 2009 stakeholder meeting on the vaccine safety component of the draft National Vaccine Plan. Stakeholders noted that there are important gaps in basic, clinical, and epidemiologic science relating to vaccine safety at several different levels. The wide range of specific research questions that could be considered includes: safety of concurrently administered and combination vaccines; vaccine safety in special or vulnerable populations; individual susceptibility (urea-cycle defects, other inborn errors of metabolism); and safety of rechallenge (administering another dose in individuals who experienced a serious adverse event following vaccination with a given vaccine).

There is no coordinated national vaccine safety research agenda that includes the combined input of federal agencies and external stakeholders. CDC's ISO has a research agenda, and it has sought the help of NVAC and NVPO to obtain broad public input on updating that agenda. The thorough process of developing guidance for ISO undertaken by NVAC with NVPO support has included a broad level of stakeholder engagement through meetings with the public and expert stakeholders, and solicitation of comments on the agenda through notices in the *Federal Register*. NVPO and NVAC have been reviewing the large volume of material generated by these efforts, and the process has culminated in a report to ISO summarizing the input received and making recommendations on the research agenda (NVAC, 2009b).

ISO is responsible for only a part of the vaccine safety research conducted in the United States, whether by ISO staff or by collaborators, such as VSD and CISA investigators and sites. Although the ISO agenda represents the future work of a considerable proportion of the federal vaccine safety system, a *national* vaccine safety research agenda is needed to help guide and coordinate the efforts of all federal agencies and non-government and industry stakeholders that are responsible for one or more aspects of vaccine safety research. Furthermore, the ISO agenda is largely focused on

epidemiologic and clinical assessments of whether there is a causal connection between adverse events following immunization and the vaccines that were administered, and that agenda includes only a small amount of basic science investigation (conducted by the CISA network).

The NIH website states "vaccine safety is an integral component of all National Institute of Allergy and Infectious Diseases (NIAID) vaccine research and development" but provides no specifics. A review of the list of study sections that conduct peer review of proposals to NIH institutes shows that, although there is one study section on vaccines and another on HIV vaccines, there is no study section on vaccine safety (this confirms an observation made at the committee's April 2009 stakeholder meeting). There clearly is a role for NIH-supported research regarding vaccine safety, but remarkably, given its importance to the nation's public health, vaccine safety research (other than basic, for example, pathophysiology or genomics) does not appear to be included among the many types of research NIH undertakes or supports.

Given the increased interest in and scientific endeavors to support patient-centered medicine, and questions that have arisen about how vaccination may or may not affect certain groups (e.g., children with inborn errors of metabolism), it is important that the U.S. vaccine safety system address these questions. Contributions to vaccine safety science could come from institutes other than NIAID (which has primary responsibilities for vaccine-related research) and could involve the basic science research efforts of the National Institute of Neurological Disorders and Stroke, the National Institute of Arthritis and Musculoskeletal and Skin, the National Institute of Child Health and Human Development, the National Institute of Diabetes and Digestive and Kidney Diseases, National Human Genome Research Institute, and the National Cancer Institute. There has been a high level of public interest in and speculation about potential links between vaccines and certain diseases of the immune and nervous systems, such as Guillain-Barré syndrome, autism, ADHD,[9] and asthma, and the institutes listed above support a variety of studies that might shed some light on biological mechanisms, genetic factors, and other characteristics that may have relevance to vaccine safety.

Recommendation 2-2: The National Vaccine Plan should emphasize the development and publication of a framework for prioritizing a national vaccine safety research agenda that spans all federal agencies and includes all stakeholders, including the public.

[9] Attention deficit hyperactivity disorder.

The scientific criteria of such a framework for prioritization might include, but are not limited to:

(a) Assessment of the nature and extent of existing evidence for a possible association of an adverse event with a vaccine.
(b) Determination of the individual or public health burden of potential adverse events following immunization.
(c) Consideration of the feasibility of scientifically rigorous study of a safety concern.
(d) Assessment of biological plausibility of a causal association between an adverse event and a vaccine.

Coordination and Vaccine Safety

One of the five dimensions of the vaccine safety system outlined by the 1986 act refers to the overarching National Vaccine Program, and by extension, to its operating arm, NVPO. The HHS *Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities* (2008a) states that NVPO coordinates HHS vaccine safety activities and explains that NVAC provides a forum for the exploration of vaccine safety policy issues that arise among HHS agencies (see Box 2-1). Although the legislation was clearly intended to address the need for intra-departmental coordination of

BOX 2-1
Role of the National Vaccine Program Described in the 1986 Act

"[C]oordinate and provide direction for research carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development on means to induce human immunity against naturally occurring infectious diseases and to prevent adverse reactions to vaccines."[a]

[a] And to "coordinate and provide direction for activities carried out in or through the National Institutes of Health, the Office of Biologics Research and of the Food and Drug Administration, the Department of Defense, and the Agency for International Development to develop the techniques needed to produce safe and effective vaccines"; and "coordinate and provide direction for safety and efficacy testing of vaccines carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development."

vaccine safety activities, meaningful, effective coordination to address gaps in the science vaccine safety, as one example, has not been achieved. This may, at least in part, be due to the factors (lack of funding, human resources, authority, and visibility) that have prevented NVPO from functioning as intended by the 1986 law. Additional discussion of NVPO and interagency coordination is provided in Chapter 6.

Multiple government agencies and private sector entities handle aspects of vaccine safety, therefore, developing and implementing a national-level safety research agenda requires coordination among federal agencies, such as NIH and FDA, and with stakeholders (such as health care providers who work with special populations, and vaccine manufacturers) to assume joint responsibility for and work collaboratively on some of the great challenges in vaccine safety research. The committee found evidence that the system can work well to address safety concerns. However, achieving coordination among government agencies, understanding and addressing the public perception of the safety system's competence and transparency, and allocating resources for vaccine safety research that are commensurate with the expanding task (i.e., surveillance and study of the safety of a growing number of licensed vaccines currently in use) all remain major challenges. Factors that may have slowed the pace of progress in vaccine safety include the absence of broader NIH participation in vaccine safety research; NVPO's lack of authority and resources needed to fully perform the coordinating role (with respect to vaccine safety issues, among others) called for by legislation; and the lengthy process over the past several years of finding a permanent home in CDC for ISO, and until recently, lack of stable, permanent ISO leadership.

The absence of interagency coordination on vaccine safety was recognized in a 1998 Task Force on Safer Childhood Vaccines report that recommended that the Interagency Vaccine Group (IAVG) formed in the 1980s take on as a primary responsibility the coordination of vaccine safety activities, and that NVPO function as the secretariat for the IAVG in that area (see Box 2-2). The current IOM committee was struck by the Task Force report's continuing relevance more than a decade later. The committee recognized that the task force was seeking to fill a major gap in the coordination necessary to ensure an effective vaccine safety program. The task force discussed the Interagency Vaccine Group, an internal government entity that is still in operation, and described a potential role for it in strengthening coordination of vaccine safety activities, from communication, to monitoring and surveillance, to safety research. The Task Force report also stated that "[o]verall coordination of programs involving both broad vaccine issues and vaccine safety is the responsibility of the Vaccine Interagency Group [sic]

BOX 2-2
An Example of Coordination Within HHS: Role of the Interagency Vaccine Group

The 1998 Task Force on Safer Childhood Vaccines defined IAVG's role as follows:

A) The IAVG would monitor the vaccine safety activities of the various agencies and work to improve interagency communication. It would also facilitate and monitor progress on the investigation and evaluation of reports of serious or frequent adverse events.

i) Evaluate data relevant to vaccine safety, which may currently be scattered among various agencies and manufacturers.

ii) Ensure periodic reviews of the safety of licensed vaccines and their recommended immunization schedules. If appropriate, propose studies to address areas where additional data may be informative or supportive, such as in special target groups or programs.

iii) Ensure effective communication among existing advisory committees that focus on vaccines and immunization, including specifically the Advisory Commission on Childhood Vaccines, the Advisory Committee on Immunization Practices, the National Vaccine Advisory Committee, and the Vaccines and Related Biological Products Advisory Committee.

B) The IAVG would be expected to seek routine technical consultation from an expert external advisory body. The Task Force is committed to the concept that the public health is best served by the continued pursuit of safer and more effective vaccines and by the safe use of existing vaccines through improvements in the immunization schedule and delivery of vaccines. The recommendations presented in this report are congruent with the Nation's immunization and vaccine goals presented in the U.S. National Vaccine Plan in 1994.[a]

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[a] The task force report added: "Vaccine safety oversight resides among a broad group of advisory committees and government groups. Most notable are the DHHS immunization-related advisory committees including the Advisory Commission on Childhood Vaccines, the Immunization Practices Advisory Committee, the Microbiology and Infectious Diseases Review Advisory Committee (MIDRAC) of NIAID, the National Vaccine Advisory Committee (NVAC), and the Vaccines and Related Biological Products Advisory Committee. The Department of Defense (DoD) is advised on vaccine and other issues by the Armed Forces Epidemiological Board (AFEB). Overall coordination of programs involving both broad vaccine issues and vaccine safety is the responsibility of the Vaccine Interagency Group of the National Vaccine Program Office. Although safety is not the main or only focus of these groups, aspects of vaccine safety coordination and oversight exist within all of them" (p. 276).

of the National Vaccine Program Office" (NIAID, 1998).[10] More recently, the NVAC State of the Program 2008 report, stated that "[f]ederal efforts have suffered from a lack of coordination and oversight of vaccine-related activities, highlighted most recently by the need for the Secretary of HHS to empanel a special interagency vaccine safety working group to better address this growing concern" (NVAC, 2009a).

NVAC's observation raises two related but distinct points about federal vaccine safety activities. Despite some potential overlap, coordination and oversight are somewhat different functions, with different rationales, and likely different solutions. Coordination refers to working together effectively to define priorities, to achieve a shared vision and to resolve strategic issues that exceed one agency or stakeholder's capabilities. Operationally, coordination may mean working to avoid wasteful duplication of effort and inefficient use of funds. Oversight is defined as "watchful care" and typically refers to the function of assuring accountability and propriety. In the realm of vaccine safety, there is a history of dialogue about independent oversight of vaccine safety monitoring and research as a response to concern about a perceived inherent conflict of interest in government in general and CDC specifically, given its responsibility both for preventing disease through the optimal use of vaccines and for monitoring post-licensure vaccine safety in the population (CDC, 2005; Cooper et al., 2008; Salmon et al., 2004).

The committee recognizes the desire to strengthen confidence in the safety system, and is aware of some of the arguments employed. The topic of the placement of an entity conducting vaccine risk management as opposed to risk assessment was discussed at the committee's April 2009 stakeholder meeting. The committee deems only the matter of intragovernmental coordination (HHS, its agencies, and DoD) as directly germane to its task and to the preparation and implementation of the National Vaccine Plan (the primary instrument for effecting coordination in the National Vaccine Program). The matter of independent oversight falls outside this IOM committee's scope of work.

The IAVG's functioning in the area of vaccine safety does not necessarily match the description in the 1998 task force report, and there is no reason why it should. The committee believes that the job description developed by the task force remains relevant, that it calls for a different type of entity (in addition to IAVG in its ongoing role), and that such a role would ideally be performed in a setting that permits meetings that are open to the public.

[10] The IAVG has continued to operate, and the committee has found several references to it in NVAC minutes between 2004 and 2009 (for example, a reference to the group's role in shaping the charge to the former IOM Immunization Safety Review Committee, a reference to a 2008 meeting with the ISO on its draft agenda, and a reference to its role in developing the National Vaccine Plan).

This IOM committee believes that a federal advisory group has the potential to play a crucial role both as a facilitator of coordination (especially with stakeholders, and as a supporter of NVPO's role in coordinating within government), and also as a somewhat independent source of guidance on vaccine safety issues. NVPO provides staff support and works very closely with NVAC, the advisory committee established to advise the Secretary of HHS on matters related to National Vaccine Program. The role played by the NVAC Vaccine Safety Working Group in reviewing policy matters related to vaccine safety appears to have contributed an independent and credible perspective on vaccine safety. With NVPO support, the group also has engaged the public in thoughtful dialogue about challenging matters of vaccine safety policy. While a working group structure provides useful flexibility, its activities may be less transparent than those of a subcommittee, as subcommittees are required to follow the Federal Advisory Committee Act.

Recommendation 2-3: The National Vaccine Plan should include the establishment and scope of work of a permanent NVAC vaccine safety subcommittee to:

(a) provide guidance on the activities described in Recommendations 2-1 and 2-2 in a public and transparent manner;

(b) provide guidance about the identification and evaluation of potential safety signals; and

(c) publish on a biennial basis a review of potential safety hypotheses; current vaccine safety activities including those of pre- and post-licensure studies, VAERS, VSD, and CISA; and planned priorities for research.

The NVAC subcommittee could be informed of potential safety signals and the actions planned to investigate the signal and related public communication. Public representation on the subcommittee is crucial, and the committee notes that NVAC has set strong precedent in including public or consumer representatives (all of its recent committee and working group rosters attest to this; refer to Appendix E for a short history of HHS public engagement activities related to vaccines).

Funding for Vaccine Safety Research

A major theme in the stakeholder comments about Goal 2 of the draft National Vaccine Plan was the inadequacy of funding for vaccine safety research (IOM, 2009). This concern has been voiced elsewhere by other commentators in the field (for example, Cooper et al., 2008). The committee believes that there are two major areas where vaccine safety research

TABLE 2-2 Comparison of Immunization Safety Office and Vaccines for Children Program Funding

Year	ISO Funding	Vaccines for Children Program Funding
2004	$21.8 million	>$1 billion
2005	$22.8 million	$1.2 billion
2006	$21.7 million	$1.7 billion
2007	$21.5 million	$1.9 billion
2008	$21.7 million	~$3 billion

SOURCES: Personal communication, C. Johnson, CDC, July 7, 2009; Shefer, 2008.

warrants additional support. First, the CDC Immunization Safety Office needs more funding and staff to conduct its work. The second area pertains to NIH research and would necessitate a partial reorientation of some of the agency's research priorities to ensure a greater balance between classic investigator-initiated research, which is a crucial engine of vaccine innovation, and research prompted by public health concerns specifically focused on vaccine safety, including some level of directed research, and not simply limited to very basic or early clinical research.

There are strong obstacles to such a reorientation in NIAID (the NIH institute with primary responsibilities for vaccines), especially in the absence of a strong coordinating entity within the National Vaccine Program that can help align program-wide needs (such as vaccine safety research) with solutions. The committee reviewed the lengthy list of NIH-funded vaccine-related research projects and found that a small proportion appear to have some relevance to safety, and an even smaller subset have safety as a primary objective. As a simple illustration, a search of the database of NIH-funded vaccine-related research yielded 24 studies (out of 3,003) that referred to safety in the title (6 from NIAID, 18 funded by other institutes), and the vast majority appear to be pre-licensure Phase I or II studies. This paucity of research on vaccine safety is congruent with stakeholder comments at the committee's April 2009 meeting, where the low level of NIH funding for vaccine safety research was a major theme. The IOM committee contacted NIAID to inquire about the status of the Program Announcement for Research to Advance Vaccine Safety (first introduced in 2008), what and how many proposals had come in, and what proposals were funded. The institute's response was to refer the committee to the RePORTER database to search for the two relevant funding codes.[11] The committee did so in August 2009 but found no information about funded research pertaining to the two program announcements.

[11] Personal communication, K. Callahan, NIH, July 20, 2009.

Funding for vaccine safety research conducted and supported by CDC is also limited. Although the childhood and adolescent immunization schedule has grown between 2004 and 2008 (with the addition of two rotavirus vaccines and two vaccines against human papilloma virus, and new combination vaccines, among others), the budget for CDC's Immunization Safety Office has not. Table 2-2 is provided to illustrate that while funding of vaccine purchases for the Vaccines for Children entitlement program (that may be a reasonable proxy for government expenditures on vaccines) has increased three-fold between 2004 and 2008, the ISO budget has remained unchanged. Funding for vaccine safety monitoring and research has not grown commensurate with the widening task (e.g., a growing list of recommended vaccines) and parallel investment in the vaccine supply. Thus, despite the fact that the universe of potential vaccine safety questions and signals can be expected to expand with the addition of new vaccines, the funds available to support, for example, VSD's Rapid Cycle Analysis and CISA's in-depth clinical studies of vaccine adverse event pathogenesis, have not increased to match the growing responsibilities of ISO.

The committee believes that the current climate of support for science-based policy and for reforming health care offers opportunities not only to enhance coordination and increase the visibility of vaccine safety activities, findings, and policy decisions, but also to strengthen the funding allocated to the crucial tasks of monitoring and studying the safety of licensed vaccines. Stakeholders such as academia, industry, and the public could contribute to the vaccine safety system and are important to include in dialogue about the national vaccine safety research agenda discussed above and in devising innovative mechanisms to fund important research that currently does not have well-established funding mechanisms to address it. With regard to academia and its contributions to the safety research agenda, stakeholder comments identified a need to comprehensively integrate education about vaccines and immunization in professional education, and also to train the next generation of vaccine safety researchers in relevant disciplines.

Recommendation 2-4: The National Vaccine Plan should incorporate concrete steps to expand and strengthen vaccine safety research, including:

- **enhanced funding for CDC's Immunization Safety Office activities, including support of extramural research;**
- **enhanced funding for FDA's safety monitoring activities; and**
- **expansion of NIH vaccine safety activities to include research portfolios, funding through requests for proposals, program announcements, and creation of a study section dedicated to vaccine safety research.**

Funding could be allocated to each federal agency to support activities that implement the identified priorities as appropriate to each agency's research capabilities and strengths.

CONCLUDING OBSERVATIONS

A dearth of vaccine safety research initiatives to address public concern about vaccine safety will not strengthen public confidence in the immunization system. In the legal arena for example, absence of an adequate body of good scientific evidence and a mere preponderance of the scant, often flawed evidence available may result in compensation of off-table injuries that may not be causally related to vaccines, adding to public uncertainty about the safety of vaccines.

As mentioned earlier in this chapter, most discussions about the safety of vaccines raise questions about communication, and one of the important topics in vaccine communication is vaccine safety. The links between Goals 2 and 3 in the National Vaccine Plan were also very evident at the committee's information-gathering meetings with national stakeholders. Communication, or "informed vaccine decision making," as the topic is framed in the draft plan, is discussed in detail in Chapter 3. It is important to recognize that given the current social and cultural climate, many discussions about vaccine safety will have a strong undercurrent of references to public confidence in the system.

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3

Informed Vaccine Decision Making

The desired outcome of the National Vaccine Program and of the National Vaccine Plan is a population protected from vaccine-preventable death and disease through safe and effective vaccines. However, the means to achieve that end must change, just as society itself has changed. In general, it is apparent that long-standing and existing approaches to communicating about vaccination are no longer either sufficient or entirely appropriate. Vaccine communication approaches have been evolving incrementally, but greater and more rapid change is needed. Continuing to use the old approaches (e.g., printed information, material posted on government websites that members of the public may not even know exist or how to access them) does not meet the needs of many groups, and may seem out of touch with a reality characterized by differences in literacy levels, socio-economic disparities that affect access to information, and the needs of families seeking to make informed decisions amidst a maelstrom of conflicting messages (often not based on science) conveyed through social media and online communities. An improved approach is needed to sustain and further the disease prevention achievements of the 20th century. Such an approach requires communication that supports vaccine decision making by the public, providers, and policy makers by conveying detailed information about risks and benefit to both the individual and the community (in an appropriate context and effectively translating scientific uncertainty and other complex but important concepts); valuing individual autonomy and the needs of engaged patients and parents; and increasing the public understanding of vaccine policy making.

Goal 3 of the 1994 version of the National Vaccine Plan (better edu-

cation about the benefits and risks of immunization) was revised in the updated draft plan, and now reads: "support informed vaccine decision-making by the public, providers, and policy-makers" (HHS, 1994, 2008). Communication and risk communication (i.e., two-way communication about threats; Covello, 2008) are implicit in the reframing of the goal, and the language used seems timely and sensitive to public concerns about some aspects of vaccine policy, specifically the contentious area of childhood vaccination.

The goal's pairing of information and decision making also highlights some major contemporary challenges in the national immunization enterprise. On the one hand, the increasing prominence of vocal opposition to vaccines and immunization accompanied by data indicating diminished trust in government public health agencies and vaccine manufacturers causes great concern that these may lead to lower vaccination rates and increased threat of vaccine-preventable diseases. On the other hand, the high-profile of controversies about the safety of vaccines for children may obscure the fact that immunization is important at every age, and unfortunately adult immunization rates in the United States are low for most vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) (NFID, 2008). Among the public, this is due to limitations in the knowledge or misperceptions about the purpose and effects of vaccination (Johnson et al., 2008). Among providers, barriers to immunization include the lack of an adult equivalent of the "well-child visit" in which immunization could be easily incorporated[1] and inadequate insurance coverage (Flowers, 2007; Johnson et al., 2008).

The National Vaccine Plan could be enhanced if the vision seemingly expressed in the title of Goal 3 were described more fully in the plan and traced to its conclusion in the objectives and strategies of that goal. This would mean reconciling the apparent paradox of informed decision making and required vaccination, but more importantly, taking steps to ensure that contemporary communication about vaccines is fully informed by the broad societal context, uses available research and technology effectively, and meets the needs of all age groups and diverse populations. This chapter describes the contemporary societal context of the immunization enterprise, provides a succinct summary of stakeholder input on Goal 3 with references to relevant literature, and communicates two recommendations on priority actions related to this goal.

[1] Medicare Part B covers a one-time preventive physical exam within the first 12 months of enrollment, which includes education and counseling about preventive services such as immunizations. However this one-time service is not widely used (fewer than 3 percent of Medicare enrollees) and does not cover the full adult population in need (HHS, 2009).

THE CHANGING SOCIAL CONTEXT OF VACCINE COMMUNICATION

With the exception of calling for vaccine information on risks and benefits to be provided to parents and patients, the 1986 statute[2] makes no mention of the National Vaccine Program (and thus, the National Vaccine Program Office's [NVPO's]) role in communication about immunization in general and about risks in particular. However, societal trends and the public perception of vaccines over the years since 1986 have made communication a central function and need. These factors clearly contributed to NVPO and its partners' reframing of Goal 3 (compared to the 1994 version) in the draft update of the National Vaccine Plan, and include the following:

- Public complacency about vaccine-preventable diseases driven by the great success of earlier immunization programs and resultant declines in or elimination of such diseases (e.g., polio) as evident in low rates of vaccine-preventable diseases,
- Change in the patient-clinician relationship, including patients who are more engaged participants in health care,[3]
- Greater interest and dialogue in the public arena about the benefits, risks, and areas of scientific uncertainty about vaccines (among other medical interventions),
- Change in how people communicate, and how they access and exchange information about all topics, including health in general and immunization in particular[4] (e.g., tools such as the Internet offer opportunities for both greater knowledge and greater confusion or misinformation), and
- Hesitancy to receive vaccines and skepticism about their safety, much of which may be influenced by some representations of vaccination in the mass media, by the new media-heightened profile of individuals and groups opposed to childhood immunization or to immunization in general[5] and by the social amplification of risk (Fischoff, 1995) fueled by several well-publicized vaccine injury compensation cases.

As discussed in Chapter 2, monitoring and assuring[6] vaccine safety are the responsibility of several government agencies, most notably the Food

[2] National Childhood Vaccine Injury Act, Public Law 99-660, 42 U.S.C. 300aa-1, § 2101 1986.

[3] Examples include the safety and quality movements in health care; the emergence of clinicaltrials.gov; consumer interest in and questions about professional and scientific conduct and conflicts of interest; public awareness of the effects of political processes on the scientific enterprise; and the proliferation of health-related information on the World Wide Web.

[4] This has been substantially documented by the Pew Internet & American Life Project.

[5] Such individuals and groups constitute a diverse array of viewpoints and motivations.

[6] Refers to the assurance function of public health (one of three core functions [IOM, 1988]).

and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). The vaccine safety system has a strong track record and considerable and growing capabilities to detect and respond to vaccine adverse events. However, communicating about vaccines, including vaccine safety, has been a complex and, for government public health agencies and their partners, a largely unsuccessful endeavor. This is in part due to the increasing polarization in the public debate, "which has limited effective dialogue between the contrasting viewpoints. This polarization presents an important challenge to public health officials, who must be careful to ensure that while they reinforce to the public the safety of vaccines, they do not overlook or underplay a potential threat" (Wilson et al., 2006).

One of the five factors described above—changes in the methods or tools of communication—signals an important and growing departure from the traditional sources of vaccine information and loci of vaccine-related communication. The public accesses and receives information about vaccines and immunization from a variety of sources, and individuals do not necessarily turn to government sources or rely on their health care providers as sole sources of information. Sources such as the World Wide Web, blogs, message boards, and organizations both supportive of and opposed to vaccination contribute to the public's decision-making process (Ache and Wallace, 2008; Baker et al., 2003). A 2002 survey supported by the Pew Internet & American Life Project found that 13 percent of Americans reported looking online for "information about immunizations or vaccinations" (Pew, 2003). More recently, a Pew study reported that "79 percent of online young adults 18-29 look for health information," and 18 percent of these look for immunization information (Lenhart, 2009). Keelan et al. (2007) analyzed 153 immunization-related videos on the video-sharing website YouTube. They characterized 48 percent as positive, 32 percent as negative, and 20 percent as ambiguous in their perspective on immunization. Interestingly, they found that negative videos were more likely to receive a rating, had a higher mean star rating,[7] and received more views. Although this descriptive analysis represents one of the early forays in learning about the role of social media in shaping views about immunization, it demonstrates the need for research to inform public health communication and support health care providers in familiarizing themselves with influences on public knowledge about and attitudes toward immunization.

A recent HealthStyles[8] survey by CDC showed that 40 percent of those surveyed turned to Internet sources for health information, and 41 percent of that sample answered yes to CDC's being the information source they

[7] 1 star = poor; 5 stars = awesome.

[8] The HealthStyles survey is one of a pair of linked postal mail surveys sent to a sample of adults 18 years and older, which is drawn to be nationally representative on seven U.S. Census Bureau demographic characteristics.

trust most (43 percent were unsure, and 15 percent said no) (CDC, 2008). In addition, media can play a role in the public's understanding of science (Hargreaves, 2001, 2003), as in the case of the controversy about a link between the measles-mumps-rubella (MMR) vaccine and autism that was posited in an article by Wakefield et al. (1998), which has since been withdrawn and rejected on the basis of the evidence (IOM, 2004; Murch et al., 2004). It is essential that with support from government public health agencies, public health and medical professionals apprise themselves of the nature of information available from the Internet or media sources and become equipped to respond to patients and their family members who ask questions or request clarification.

Challenges and Needs

In its public information-gathering meeting on Goal 3 of the draft plan, the committee heard the views of a variety of stakeholders, ranging from academic researchers to parent groups. The major themes that emerged included patient, provider, and population-level considerations and were for the most part unsurprising. They reflected a concern shared by leaders in the public health and medical communities that there has been a noticeable deterioration of public trust in the immunization system (see also Cooper et al., 2008). Two other themes that describe challenges and needs in the field are provided below:

1. Public health and medical communities' slowness in adapting to the gradual shift in the context of vaccination and fully utilizing existing evidence to improve the communication efforts as evident in the following:

- Decreasing societal consensus about the benefits of immunization
- Gaps in patient and public knowledge about vaccines and immunization
- Gaps in provider knowledge

2. Gaps in the research and evidence needed to inform communication.[9]

[9] The old approach to risk communication complemented the use of child immunization requirements, a successful policy instrument that has helped to dramatically lower rates of vaccine-preventable diseases (Malone and Hinman, 2003). However, there are signs that the general public consensus about childhood immunization once taken for granted has deteriorated (decreased confidence in vaccines; increase in exemptions from immunization requirements in states allowing philosophical exemptions; CDC, 2008; Irving et al., 2007; NCSL, 2009; Omer et al., 2008, 2009; Salmon et al., 1999). Effective communication is essential to explain how policy decisions are made, how benefits and risks are weighed, and both the value and the ethical complexities raised by immunization mandates.

Slowness in Adapting to Change

First, the effects of changes in the social context of communication and in the burden of vaccine-preventable diseases have previously been noted in the 1996 Institute of Medicine (IOM) workshop on *Risk Communication and Vaccination* (IOM, 1997), the 2000 NVPO Workshop on Vaccine Communication, and an article in the 2002 *Jordan Report* (a periodic compendium of current issues in vaccine research) titled "The Evolution of Vaccine Risk Communication in the United States: 1982-2002" (HHS et al., 2002; IOM, 1997; NVPO, 2000). However, while individuals and groups opposed to vaccines have availed themselves of new communication tools and used them to great effect, the response of the public health and medical communities has not been sufficiently swift, sustained, and strategic. This has been especially evident in communication efforts at the population level, as reflected in the general absence of a federal public health voice in the highly publicized controversies about immunization. Sometimes, messages provided by government agencies may have contributed to confusion or misunderstanding of the issues. One example may be found in the news release that followed three high-profile decisions of the U.S. Court of Federal Claims in 2009, which stated: "[h]opefully, the determination by the Special Masters will help reassure parents that vaccines do not cause autism" (HHS Press Office, 2009). This sentence regrettably contributes to the conflation of scientific causality and legal finding, reinforcing the misunderstanding that legal decisions prove scientific facts.

Some of the evidence and the ethical motivation needed to improve communication have been available for some time. For example, it is well understood that communication needs to be informed by social and behavioral science; that providers need to be equipped with information, tools, and time to counsel patients and, where applicable, their families; and that the public must be invited to the table and engaged as an equal partner in the dialogue on immunization (e.g., IOM, 1997; see Box 3-1 and Appendix E for a short history of public engagement activities). However, increased interest in seeking exemptions from immunization requirements, the negative perception of immunization (as reflected by CDC surveys; Sheedy, 2009), the high profile of vaccine controversies in the mass media, and the knowledge gaps among both providers and patients may indicate that not enough is being done to apply what is known to the development of a comprehensive communication strategy.

The committee was informed by stakeholders at its April 2009 meeting on Goal 3 of the plan that some health care providers lack the knowledge, training, and materials to convey information about vaccine risks and benefits to patients. This is consistent with findings in the literature (Davies et al., 2002; Davis et al., 2004). Health care financing is not structured to reimburse providers for communicating with patients about vaccines, let

BOX 3-1
A History of Public Engagement

The committee reviewed the efforts of NVPO and the National Vaccine Advisory Committee (NVAC) to engage the general public in the National Vaccine Plan and the research agenda of the Immunization Safety Office (ISO). The activities conducted in 2008 and 2009 followed an occasional series of notable public engagement activities on vaccine policy issues spearheaded by the Department of Health and Human Services (HHS: CDC and NVPO) over the past decade and a half (e.g., the 2002 Wingspread Public Engagement Planning Group [Keystone Center, 2003], the 2004 CDC Blue Ribbon Panel [CDC, 2005], the 2004 Vaccine Policy Analysis Collaborative [VPACE: Hamlin, 2004], and the 2005 Public Engagement Pilot Project on Pandemic Influenza [PEPPPI] process [Bernier, 2006]). (See Appendix E for more details.)

More recently, beginning in April 2008, NVAC (supported by NVPO) has been involved in two major public engagement activities: (1) a review of the draft ISO research agenda to identify gaps and help set priorities and (2) engagement with the public and other stakeholders to obtain input on the draft National Vaccine Plan. As part of the NVAC-NVPO process for the ISO agenda, one stakeholder and three public engagement workshops (convened in Alabama, Oregon, Indiana) have been held; stakeholder and public comments have been solicited via the *Federal Register* and other outreach; and an NVAC vaccine safety writing group has developed a list of research gaps and criteria for prioritizing items in the ISO research agenda that was used as a basis for discussion at a stakeholder meeting held in March 2009.

For the draft National Vaccine Plan, NVPO has solicited feedback via the *Federal Register*; through vaccine-related meetings in which NVPO staff discussed the plan; and at an NVAC meeting in February 2009 to discuss the plan and comments on the draft plan received by NVPO. NVPO also held three public engagement activities in March and April 2009 in Saint Louis, Missouri; Syracuse, New York; and Columbus, Ohio.

NVAC, with the support of NVPO, is also beginning work on a review of the current federal vaccine safety system and the development of "a White Paper describing the infrastructure needs for a federal vaccine safety system to fully characterize the safety profile of vaccines in a timely manner, reduce adverse events whenever possible, and maintain and improve public confidence in vaccine safety" (NVAC, 2008). The committee praises CDC and ISO for going substantially beyond the recommendation of the 2005 IOM committee that public input be obtained on the Vaccine Safety Datalink research plan. CDC and ISO have opened the entire ISO agenda to public viewing and wide input, facilitated by NVAC and NVPO.

alone to encourage and reward provider performance in this area (Chapter 4 discusses financing challenges in more detail). Davis et al. (2004) found that at in least one type of clinical setting, "[v]accine communication of side effects, risks, benefits, screening for contraindications, and the next visit lasted for an average of 16 s[econds] for all vaccines."

Furthermore, the committee learned from stakeholders that patients and their family members have questions about vaccine risks, benefits, contraindications, and other issues that are not addressed or are inadequately addressed in the public sphere (e.g., mass media, government communication efforts) or in the context of visits with their health care providers (IOM, 2009b). This is supported by the literature (Davis et al., 2001; Gust et al., 2008; NFID, 2008). Among adults, there is a widespread lack of awareness of immunization as a tool for preventing disease and death in all age groups (NFID, 2008). There are also misperceptions about the benefits and risks of vaccines and confusion about the messages available in the public sphere, regarding both vaccine effectiveness and who should be vaccinated (Flowers, 2007; IOM, 2009b). For example, older adults have reported being confused about messages regarding influenza immunization, issues of vaccine availability, such as shortages and availability in one's medical home, and effectiveness (due both to the poor match of vaccine to circulating strains and to the waning of immune response to vaccines due to age) (IOM, 2009b).

In the nationally representative HealthStyles survey, one-third of 4,035 parents of children under 6 years of age believed that they did not have access to enough immunization information (Gust et al., 2005). This lack of knowledge increases the likelihood of confusion when parents and patients are confronted with conflicting messages about vaccine benefits and risks (Downs et al., 2008; Gust et al., 2008). As noted earlier, changes in the risk-benefit profile of vaccines due to decreases in the prevalence of many vaccine-preventable diseases play a role in shaping parents' views about immunization. Kennedy and colleagues (2005) found that the decreased likelihood of contracting a disease contributed to parents' opposition to immunization requirements. The committee also heard that some parents believe their concerns about vaccine safety are not taken seriously and are dismissed by health care providers or by the federal government (CDC, 2008; Cooper et al., 2008; IOM, 2009a).

Gaps in Research

At the committee's April 2009 stakeholder meeting, discussion included communication research needs. There was agreement that more research is needed to help inform vaccine communication messages and efforts. Both quantitative and qualitative research are needed, and given the broad array of factors that contribute to decision making about vaccination, undertaking interdisciplinary research is important.

The committee found limited evidence of efforts to evaluate communication activities undertaken by government public health agencies and their partners (Irving et al., 2007). For example, although there are studies that

have examined providers' use of vaccine information statements, which are required by law but seem to define the lower threshold of the range of possible activities to communicate vaccine risk and benefits, there is little or no evaluation of their effectiveness as a communication tool (Davis et al., 2001, 2004; Irving et al., 2007).

Childhood vaccination is the most visible component of immunization in America, and as a result, research on communication issues pertaining to childhood vaccination and related decision making is more advanced than research on adult vaccination issues.

The National Vaccine Plan cannot address every problem in the vaccine system, but the committee believes it could signal a high-level change of direction in vaccine communication. The language of Goal 3 seems to hint at a new kind of conversation about vaccines. This conversation needs to balance individual choice and patient engagement with responsibility to the community as partners in health care decision making, requiring a fuller dialogue about matters of science, public health practice, and policy (Diekema, 2006).

The committee has identified two priority actions within Goal 3:

1. Development of a national vaccine communication strategy, and
2. A process to develop a communication research agenda.

A NATIONAL VACCINE COMMUNICATION STRATEGY

The communication efforts of most government public health agencies appear to have been slow to adapt to the new environment and the new challenges described in this report. Public confidence in the national vaccine program and awareness of the value of immunization has deteriorated (Cooper et al., 2008; Irving et al., 2007; Sheedy, 2009). By calling for a coordinated national strategy for vaccine communication and its well-resourced implementation, the National Vaccine Plan can help move public health communication about vaccines and immunization toward greater transparency, sophistication, and cohesion.

Although CDC undertakes considerable efforts to communicate about immunization, there is no coordinated government or public health communication presence that addresses the depth and breadth of concerns that the public and other stakeholders have about vaccines. There is not enough coordination of vaccine communication across federal agencies involved in the vaccine enterprise and among federal, state, and local levels of government, sometimes resulting in insufficient and inconsistent messaging to the public.

In the context of considerable gaps in the knowledge of both providers and patients, and active campaigns by individuals and groups to share their

strongly held concerns about the safety of vaccines and immunization, it no longer is sufficient for federal public health agencies to impart information as crises arise, that is, to engage solely in reactive communication. Federal agencies, their state and local counterparts, and relevant partners need to engage in dialogue with the public about vaccines and vaccine safety on an ongoing basis, and to anticipate information needs in their planning. A current example of one area in which this is occurring is CDC's preparations to communicate about background rates of common health events (miscarriages, heart attacks, etc.) in preparation for implementing H1N1 vaccination in the fall of 2009 (McNeil, 2009).

Studies show that health care providers are important influences in patient or parent decision making regarding immunization, but considerable proportions of health care providers lack information about vaccines, may not provide the minimum vaccine information required by the 1986 law, and their immunization practices may not reflect current ACIP guidance about the optimal use of vaccine for children, adolescents, and adults (Daley et al., 2006; Davis et al., 2004; Flowers, 2007; Gust et al., 2008). Health care providers may need both knowledge and tools to help them counsel patients of all ages.

Communication Challenges

There are many gaps in communication and in the knowledge base that informs communication. There are also significant racial and socioeconomic disparities in vaccination rates that are unrelated to vaccine hesitancy or opposition (Roemheld-Hamm et al., 2008; Schwartz, 2009). Hispanic and African-American populations have consistently lower rates of vaccination, particularly among the elderly within these groups (Flowers, 2007). Some of the structural barriers to immunization, such as lack of insurance coverage for preventive health care services and lack of alternate immunization sites, are beyond the scope of a communication strategy.

Implementing a national communication strategy will require attention to the needs of different age groups (including adults); to variations in socioeconomic status, cultural background, and literacy; and to the information needs of groups such as health care workers. There also are inequities in education, access to, and utilization of information technology across different segments of the population that will also have an impact on the vaccine communication strategies that need to be developed. A communication strategy cannot be a one-size-fits-all informed decision making process.

Chapter 2 describes the Vaccine Injury Compensation Program (VICP). Confusion can arise when court decisions and their implications are not made to clear to the public. Although the committee is aware of rules that bar HHS from communicating about legal decisions that emerge from the

VICP, silence in the face of public questions does not advance trust in the immunization enterprise. Also, communicating to the public that awards for off-table events do *not* constitute scientific proof of vaccine risk is a formidable challenge. Failure to distinguish between scientific causality and legal finding may lead to an exaggerated perception of vaccine risks and cast unwarranted doubt on the safety of immunization.

The vaccine system's credibility relies on an open and balanced presentation of benefits and risks, and of what is known and unknown. Confidence in vaccination can be enhanced by transparent communication about all aspects of the system (CDC, 2005). The content of vaccine communication must address its multiple purposes—providing accurate and relevant information, addressing individual and societal concerns, and encouraging vaccination. Those who perceive themselves or their children to be at risk for adverse events may want information related to causality and responsibility in the case of adverse events; health experts and practitioners, however, may want data on vaccine safety and benefits. Not enough is known about common perceptions and understanding, knowledge levels, and points of contention and tension with respect to vaccines and immunization (Bostrom, 1996; Downs et al., 2008). To promote informed consent and informed decision making, the National Vaccine Plan needs to take account of the gaps in current communication and education and to address the complexity of public and stakeholder concerns surrounding vaccines and immunization.

The committee believes that the National Vaccine Plan offers an opportunity to point the way forward or even signal a transformation in how society communicates about immunization. Given the complex challenges inherent in risk communication, solutions would seem to require more than merely a technical fix (e.g., more and better communication) or even a scientific fix (more and better safety science, an area of considerable need discussed in Chapter 2). Rather, addressing the vaccine risk communication needs of a diverse population in the 21st century requires a comprehensive approach that can be outlined in a national plan.

The committee has found no evidence of a national vaccine communication strategy. At the level of CDC itself, there is no strategic plan to guide the work of the communication office that supports the National Center for Immunization and Respiratory Diseases. Instead, communication regarding vaccines has been largely reactive to crises and does not adequately convey information about vaccine risks and benefits. This is not surprising in an office that is understaffed and has limited funds to complete its work. The CDC vaccine communication office has a core budget of $1,868,385 (formerly allocated through the National Center for Health Marketing that was the office's home until recently). It covers items such as staff salaries (nine full-time employees), benefits, travel, equipment and supplies, and contractors. The communication office also receives $1,050,000 in Vaccines

for Children (VFC) and Section 317 funding (discretionary federal funding to support vaccination services for non-VFC eligible underinsured children or children whose parents cannot afford the out-of-pocket costs of vaccination; a smaller proportion may be used for adolescent and adult immunization programs) that supports contracts for child and pre-teen vaccination communication campaigns, and $1.8 million in supplemental pandemic influenza funds for the annual seasonal influenza vaccination campaign.[10] There seem to be limited resources dedicated to communication about adult immunization issues (other than influenza) or to evaluate the effectiveness of current efforts (see discussion below).

The universe of vaccine information, science, safety research, quality control, and policy decisions is large and complex. Both professionals and the public poorly understand many aspects of the system. Pertinent information needs to be communicated in a strategic and comprehensive manner to reach the overarching goal of informed decision making.

There is no coherent effort to apply existing communication science and other evidence (e.g., surveys) to shape a research agenda that could inform the national strategy that is comprehensive and addresses communication needs to support vaccine decision making at all ages.

Recommendation 3-1: The National Vaccine Plan should incorporate the development of a national communication strategy on vaccines and immunization targeting both the public and health care professionals. Such a strategy should:

(a) Reflect current research on communication;[11]

(b) Describe how relevant government agencies will coordinate and delineate primary responsibility for specific components and audiences;

(c) Anticipate, plan, and support rapid response to emerging high-profile scientific, safety, policy, or legal developments;

(d) Provide the right information to the right individual(s) or group(s) in the most appropriate manner, with attention to literacy, linguistics, and culture of the target audience(s); and

(e) Receive adequate support of dedicated human and financial resources.

Communication cannot be an afterthought and requires upfront investment, planning, and implementation. A communication strategy as described above will need to be multi-tiered, with the federal government playing a role in coordinating and directing overall messaging and with

[10] Personal communication, K. Sheedy, CDC, July 2009.

[11] See Recommendation 3-2.

adequately resourced state and local public health agencies and the medical community on the frontlines. Also, all components of a communication strategy will also require evaluation—an activity frequently not undertaken and for which little or no funding is available (see, for example, Irving et al., 2007).

Although different federal agencies have critical roles to play in communication and CDC has the primary role, NVPO seems well positioned (although not adequately staffed or funded), given its interagency coordinating function described by statute, to spearhead certain aspects of communication. For example, communicating the risks and benefits of vaccines to individuals and to society and proactively anticipating and preparing for the likely impact of court decisions in the VICP on how the public perceives the safety of vaccines are areas where NVPO could provide leadership.

A targeted and successful communication infrastructure and strategy is one that is sustained and dynamic over time, results in informed choices (a shift from a focus just on increasing immunization rates), is evidence based, and is supported by adequate resources and good coordination among agencies and stakeholders. It would not be exclusively campaign based or simply reactive to flare-ups of concern. Such a strategy would balance two seemingly but in reality not dichotomous sets of objectives: (1) to increase rates of vaccination to protect individuals and the population from disease and (2) to support informed decision making through honest, frank, and open communication (Bostrom, 1996; Covello, 2008; Slovic, 1987). As recommended in a 2005 IOM report on data sharing, scientific evidence should be put into the appropriate statistical context, with clear characterization of the uncertainties in findings, the strengths and limitations of the data, and the consideration that new data could change interpretations. The strategy would focus on communicating uncertainty, careful tailoring to each audience (e.g., providers, public, employers), choice of appropriate setting to maximize usefulness (e.g., prenatal visits, other "anticipatory" settings), and dissemination channels (e.g., peer-to-peer influence, role of the Internet or mass media). The strategy would ideally be designed to facilitate societal support of immunization informed by changes both in the social environment over the past two to three decades and in the science on vaccine safety.

While health risk communication has benefited from burgeoning research, progress on the science and practice of vaccine risk communication has been minimal as has movement toward rigorously evaluating the effectiveness of risk communication strategies (Irving et al., 2007).[12] Risk communication in the context of vaccines and public and individual health risks

[12] Communication on H1N1 vaccine could be considered a starting point or case study for evaluation.

needs to be further explored. Additional research is needed on perceptions of vaccine risk and individual health decision-making processes. There must be a better understanding of the most effective ways for providers to address patient and parental concerns and questions about immunization. It also is important that government agencies address public concerns while conveying technical information at a level appropriate to the intended audience.

As noted in the 1994 National Vaccine Plan, research is needed on an ongoing basis to assess the public's perception of vaccines and vaccine safety, to provide information about how people make vaccination decisions, and to ascertain how these decision factors may vary among subgroups, in order to ensure that communication efforts are appropriately targeted. Ongoing research is needed to address issues related to the best way to address scientific uncertainty in safety information on vaccines, tailor messages to different groups, and take advantage of emerging technologies and communications strategies (e.g., blogs, social networking sites).

Recommendation 3-2: The National Vaccine Plan should incorporate a process for identifying research needs to inform the national communication strategy, including research on how the public obtains information about vaccines and immunization, perceives risks, and makes decisions concerning vaccination in the contemporary information environment.

Because the research related to vaccine communication spans many disciplines and because of the fragmented nature of vaccine communication across federal agencies and the public, private, and consumer sectors, it would be useful for an agency to serve as an intermediary in shaping vaccine-related information around safety. As noted earlier, CDC's efforts in communication about vaccines are spread out over many areas and its resources are not adequate for all communication needs (e.g., supporting providers with training and information, conducting public communication campaigns for all age groups). It is unclear to what extent FDA and the National Institutes of Health collaborate with CDC on vaccine communication and whether communication efforts at the federal level reach the degree of integration and coordination necessary to use the best current evidence (from communication science, interdisciplinary research, and evaluation of existing communication activities) to inform future communication activities.

A stronger, adequately funded and staffed NVPO could support interagency coordination in the area of communication, in part by helping to identify communication needs that span the entire National Vaccine Program. As noted elsewhere, NVPO could play a convening role (e.g., its 2000 workshop on vaccine risk communication) and could use its resources

to provide support for agency strategic planning on communication and to fund promising research in the area of communication.

Because communication is a cross-cutting activity that is necessary for every other component of the vaccine enterprise and the plan itself, accomplishing the priorities identified by the committee would necessitate a special role for NVPO (owing to its placement in the office of the Assistant Secretary for Health and its presumably panoramic view of federal agencies' functions with regard to vaccines and immunization) as a departmental communicator on critical vaccine and immunization issues. This role will ideally include a continuation of the public engagement tradition advanced by NVPO—serving as a data and best-practices repository to support proactive communication in the department. NVPO also could support department-wide strategic planning of communication activities for specific policy purposes and to complement key ongoing activities.

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4

Vaccine Supply and Use

Goal 4 in the draft National Vaccine Plan—ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability, and death in the United States—covers an extraordinarily broad set of issues. Objectives include topics related to every point along the journey from the manufacturer's production facility to the prospective recipient of the vaccine: supply; purchase, financing, and reimbursement for vaccines; vaccine management and administration; availability of and access to services; compensation for vaccine injuries; and data and information technology needs (from provider-level information technology to disease surveillance, immunization coverage, and safety surveillance capabilities). Also, vaccine supply and use issues are intertwined with safety (covered under Goal 2 of the plan and discussed in Chapter 2), research and development (covered under Goal 1 and discussed in Chapter 1), and communication issues (covered under Goal 3 and discussed in Chapter 3).

Goal 4 illustrates a characteristic of the entire plan: the absence of an explicit vision statement and an extremely broad range of objectives and strategies without explanation of (1) why certain items were included in the plan and what remained on the "cutting room floor," (2) which items represent activities that are budgeted agency strategic priorities and expected to take place regardless of the National Vaccine Plan, and (3) which items represent novel contributions of the plan that are not explicitly part of other existing (agency) plans.

When formulating its recommendations on priority actions in Goal 4, the committee considered the implications of current efforts to reorganize the U.S. health care delivery system to support payment systems and ensure

delivery of vaccines and to make concrete advances in the use of health information technology (HIT) to improve health care performance and effectiveness. Although the fate of health care reform is uncertain at the time of this writing, considerable progress has been made with regard to HIT by building on the foundation set in 2004 by the President's Executive Order 13335, establishing the Office of the National Coordinator for Health Information Technology (ONCHIT) in the Department of Health and Human Services (HHS), whose role is to lead the implementation of a nationwide HIT infrastructure that is interoperable and safeguards privacy (GAO, 2009). Changes in the ways health information is recorded, stored, and used can have enormous implications for the delivery of immunization services.

Vaccination is a cost-effective, high-value component of preventive health care and is a good indicator of how well a health care delivery system functions. Under ideal circumstances, a health information system would indicate a patient's immunization status, remind a provider of needed vaccines for a given patient, record and facilitate the reporting of potential adverse events following immunization, help a provider obtain reimbursement for delivery of immunization services, allow public health officials and researchers to measure vaccine coverage, monitor rates of vaccine-preventable diseases, and facilitate studies of the relationship between vaccines and suspected adverse events. In reality, neither the delivery of health care nor the relevant information technology systems are constituted in ways that optimize the delivery of immunization among other preventive services.

OVERVIEW OF THE NATION'S IMMUNIZATION SERVICES

As noted in the Introduction, the terms vaccination and immunization are sometimes used interchangeably. The committee uses *vaccination* to refer to the delivery of the vaccine to an individual, and *immunization* services to refer to the range of activities (e.g., storage and management of vaccine stocks, communication) that lead to vaccine administration. The Introduction also describes the large network of federal, state, and local public health agencies that play important roles in implementing the use of vaccines routinely to prevent infectious diseases and to respond to public health emergencies such as disease outbreaks and the 2009 H1N1 influenza pandemic. Although the federal government provides advice, support, and funding, most immunization policy is made at the state level, thus stakeholders in this area include organizations such as the Association of State and Territorial Health Officials and National Conference of State Legislatures.

As described in Chapter 2, after vaccines are licensed by the Food and Drug Administration (FDA), they can be used in the population according to the recommendations of the Advisory Committee on Immunization Prac-

tices (ACIP), which is authorized by the Public Health Service Act to provide advice and guidance to the Secretary of Health and Human Services, the Assistant Secretary for Health, and the director of the Centers for Disease Control and Prevention (CDC).

FRAMING OF GOAL 4

The nine objectives (see Box 4-1) in this goal range widely from ensuring consistent and adequate availability of vaccines to maintaining "a strong, science-based process for developing and evaluating immunization recommendations" (see Chapter 3, which discusses the importance of better communication of how immunization policies are made).

This chapter offers discussion and recommendations intended to help focus Goal 4 on addressing a narrower set of challenges and on a priority action pertaining to each major challenge to the effective use of vaccines for children, adolescents, and adults. Major types of challenges are described below.

Some barriers to effective use of vaccines stem from the lack of affordability of certain newer vaccines (e.g., HPV [human papilloma virus] vaccines recommended for young women, varicella zoster vaccine recommended for older adults) for significant numbers of patients. Not all private insurers cover such vaccines, and patients may be unwilling or unable to incur an out-of-pocket cost.

There are challenges that stem from the failure of health care financing (whether via public and private insurance or through direct grant financing by the federal government) to ensure that health care providers are adequately reimbursed for the purchase and provision of vaccines (Freed et al., 2008a,b). Related to these challenges are problems associated with vaccine production and interruption of the supply of vaccines available (Hinman et al., 2006; IOM, 2003). Another Institute of Medicine (IOM) committee has described the "tensions [that] exist between the need to control public and private expenditures on vaccines and the need to encourage investment in their development" (IOM, 2003). In other words, inadequate financing for vaccines and related costs have played a role in decreasing the attractiveness of the vaccine market to companies and investors.

Another category of challenges relates to system performance in the delivery of immunization services. Health plans have had some success using pay-for-performance approaches to incentivize provider practices that led to increased immunization rates (AHIP, 2009). However, incentives for high performance in immunization within the health care system are lacking (Berman, 2005), as is clear evidence about what works to motivate high performance. The Centers for Medicare & Medicaid Services (CMS) require managed care organizations to submit Healthcare Effectiveness Data

BOX 4-1
Goal 4 Objectives in the 2008 Draft National Vaccine Plan

- Objective 4.1: Ensure consistent and adequate availability of vaccines for the United States.
- Objective 4.2: Reduce financial and non-financial barriers to vaccination.
- Objective 4.3: Maintain and enhance the capacity to monitor immunization coverage for vaccines routinely administered to infants, children, adolescents, and adults.
- Objective 4.4: Enhance tracking of vaccine-preventable diseases and monitoring of the effectiveness of licensed vaccines.
- Objective 4.5: Educate about, and support, healthcare and other vaccination providers in vaccination counseling and delivery.
- Objective 4.6: Maintain a strong, science-based, transparent process for developing and evaluating immunization recommendations.
- Objective 4.7: Strengthen the Vaccine Injury Compensation Program (VICP) and Public Readiness and Emergency Preparedness (PREP) Act compensation fund.
- Objective 4.8: Enhance the effectiveness of state and federal immunization programs.
- Objective 4.9: Enhance immunization coverage of international travelers who are at risk of acquiring vaccine-preventable diseases.

SOURCE: HHS, 2008.

and Information Set (HEDIS)[1] data for Medicare enrollees (i.e., Medicare Advantage). HEDIS contains several measures of immunization status.

Challenges pertaining to health information systems affect immunization. Local public health agencies cannot adequately measure local-level immunization[2] patterns to guide appropriate targeted supplemental population interventions. Gaps in local-level data are currently due to incompleteness of immunization registries and the expense of sample surveys; in the future widespread use of electronic health records and adequate national health information network infrastructure should facilitate monitoring coverage of immunization services. Exceptions that point the way forward may be found in the Veterans' Health Administration health information system and

[1] A tool used by more than 90 percent of America's health plans to measure performance on important dimensions of care and service.

[2] High-quality national and state-level data are available, but local-level data has been a challenge in part due to high cost and lack of electronic health record infrastructure.

Louisiana state immunization information systems that survived Hurricane Katrina and facilitated the delivery of care including enabling providers to determine a patient's immunization status and provide needed vaccinations (Bristol, 2005; Urquhart et al., 2007).

There are challenges stemming from gaps in knowledge regarding the balance of vaccine risks and benefits for individuals and for society. These challenges affect the behavior of both providers and patients (or parents) within the system, and include failure to provide immunizations in clinical practice settings, and avoiding age-appropriate vaccinations. These challenges are exacerbated by a health care delivery system that not only lacks incentives for providers but also in fact does not even reimburse providers for conversations with patients or parents on the topic of immunization and vaccines.

Finally, there are challenges having to do with preparedness for naturally occurring or deliberately introduced infectious disease threats. In a public health emergency, such as a disease outbreak, the capabilities of public health agencies at all levels are tested, including all aspects of their ability to mount mass vaccination efforts, such as the availability of vaccine, distribution of vaccine, identification of unvaccinated individuals, administration to appropriate populations, and monitoring potential adverse events and the spread of disease. Not only are vaccine shortages a concern in a response to an outbreak, but a shortage may itself precipitate a potential public health crisis. A recent example may be found in the response to the 2004-2005 influenza vaccine shortage, and the decision making at different levels of government and in the private sector regarding allocation of scarce vaccine. This is also an area in which coordination among all public health agencies is essential, and the influenza vaccine shortage highlighted both positive aspects and areas in need of improvement.

It is important that Goal 4 address these challenges faced by our nation's immunization system with a clear and coherent vision of what is needed to ensure the effective use of vaccines to prevent and control infectious diseases. A comprehensive reframing of Goal 4 to focus on priority areas germane to the range of challenges presented above would strengthen the plan. Such clarity is necessary to develop measurable performance standards that can be translated into action. The committee suggests key elements (shown in Figure 4-1) needed to achieve the vision of enabling effective use of vaccines.

This suggested reframing endeavors to address all dimensions of the problems relating to the effective use of vaccines, refers to the evidence presented to this committee as well as the findings of previous IOM studies (2000, 2003), and reflects the modernization of health information technology as applied to immunization services and the integration of immunization into broad health care reforms currently in progress.

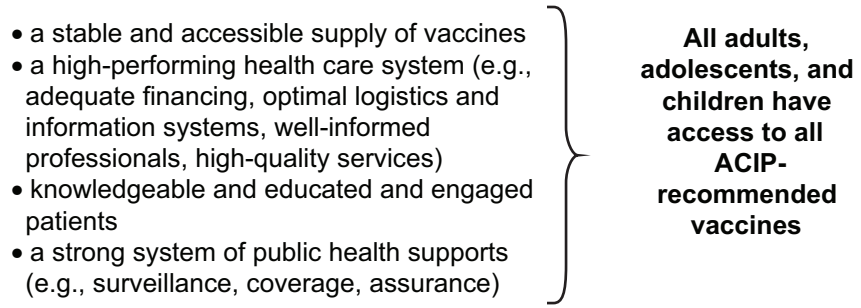

FIGURE 4-1 Prerequisites to achieve a vision for vaccine use.

To set strategic direction in Goal 4 of the National Vaccine Plan and ensure translation into effective action over time, the goal could be restructured into a smaller set of broad sub-goals, each of which would have its own set of objectives. The following five sub-goals are based on the committee's information-gathering activities and a review of the literature, including past IOM reports.

Sub-goal 1. Assure a stable and adequate vaccine **supply** for public health preparedness and for recommended routine use purposes.

Sub-goal 2. Eliminate **financial** barriers to vaccination.

Sub-goal 3. Eliminate barriers related to **access** (for consumers) and to medical **practice** and delivery system functioning (for health professionals). Note that one specific non-financial[3] barrier, knowledge regarding the safety and effectiveness of vaccination, is discussed in Chapter 3.

Sub-goal 4. Develop and adopt **health information technology** systems that can advance clinical and public health immunization practice, measure clinical and system performance, advance knowledge about immunization status and system effectiveness in achieving high immunization rates and reducing immunization disparities, and support research on alleged adverse events and the potential link to immunization (see discussion of vaccine safety in Chapter 2). This sub-goal aims to assure better alignment between the National

[3] Because "non-financial" may be used to describe a range of issues, thus overlapping with knowledge, communication, informed decision making, and with information system challenges, the committee has found it more useful to be specific about the two types of non-financial barriers that pertain to consumers and to providers, respectively.

Vaccine Plan and existing planning efforts within HHS regarding HIT adoption, stemming from the American Reinvestment and Recovery Act (ARRA).

Sub-goal 5. Strengthen the **public health infrastructure** to measure system performance, support high quality clinical practice that maintains or improves rates of disease and vaccine coverage, facilitate study of alleged adverse events (discussed in Chapter 2) and intervene to address disparities in health and health care, as well as emerging naturally occurring and intentional public health threats.

SUB-GOAL 1: SUPPLY

Vaccine shortages are, surprisingly, a predictably perennial problem of the U.S. immunization program. As an example, Coleman et al. (2005) found that "between 2000 and 2004 there were nationwide shortages of six recommended, childhood vaccines that prevent nine diseases, and the supply of adult influenza vaccine was interrupted three times." More recently, the 2004-2005 influenza season coincided with a much-publicized serious shortage of influenza vaccine that required close public-private collaboration and coordination to ensure the best allocation of limited vaccine. Despite that coordination, there were problems with allocating available vaccine, and the season ended with 5 million doses of unused vaccine. In 2007, a recall of certain lots of *Haemophilus influenzae* b (Hib) conjugate vaccines (both as a single antigen and as a combination vaccine with meningitis and hepatitis B vaccines) led to a shortage, and CDC recommended deferral of a booster dose of Hib vaccine in most children who had already received the three-dose primary series (CDC, 2007b). The recommendation for a fourth (booster) dose was reinstated in June 2009, although supply was still not back to normal levels (AAFP, 2009).

Shortages occur for a complex set of reasons, such as the nature of the product and market (e.g., single manufacturers for some vaccines); manufacturing challenges with regulatory implications (e.g., contamination of vaccine lots); demand for a newly ACIP-recommended vaccine outstripping supply; and uncertain demand for seasonal influenza vaccine. Each shortage may have a somewhat different etiology (Hinman et al., 2006; Santoli et al., 2003) but all present communication and practice challenges for providers, confuse consumers, complicate the work of public health agencies at all levels, and place people at risk for contracting and spreading disease.

The committee recognizes that the draft plan contains an objective that addresses supply issues, and the recommendation below represents the committee's agreement that this is an area that rises to the level of a priority.

Recommendation 4-1: The National Vaccine Plan should include the development and implementation of strategies to assure a stable and adequate vaccine supply for public health preparedness and recommended routine use purposes.

SUB-GOAL 2: FINANCING BARRIERS IN THE UNITED STATES

There is a high level of consensus among stakeholders on the financial barriers to immunization (e.g., failure by payers and others to acknowledge the full range of costs associated with securing, stocking, managing, and administering vaccines at the practice level) and about plausible solutions. In 2005, Partnership for Prevention issued *Strengthening Adult Immunization: A Call to Action,* which was widely endorsed by medical and public health organizations (including the American Medical Association and the American Public Health Association) and called for the purchase and distribution of influenza vaccine for uninsured adults, first-dollar coverage for influenza and pneumococcal vaccines in the Federal Employee Health Benefit Program, expansion of Section 317 of the Public Health Service Act to cover adult immunization needs, and the launch of a national education campaign on the value of adult immunization (Hinman and Orenstein, 2007).

Evidence suggests that pediatricians and family practitioners are not adequately reimbursed for providing vaccines to children (Freed et al., 2008a; National Immunization Congress, 2007). As newer, more costly vaccines such as HPV and meningococcal vaccines are recommended for use in children, providers have encountered significant financial barriers including large cash outlays with hundreds of thousands of dollars spent on the purchase of vaccines, potential delays in timely reimbursement by some insurers, and in some cases lower reimbursement for vaccine purchase than the price paid. In a study by Freed et al. (2008b), 11 percent of providers reported they had considered no longer purchasing and providing vaccines for their primary care practice due to these financial barriers. Furthermore, reimbursement of vaccine administration fees has remained extremely low and has not kept pace with the growing financial and administrative burden of practices that provide immunization services, such as the need for providers to carefully monitor vaccine inventories, ensure that vaccines are stored and transported at the correct temperature, purchase immunization supplies (e.g., syringes, needles, alcohol pads), pay for insurance or maintain backup generators in case of power outages, ensure competent administration of vaccines by trained professionals, counsel patients about the risks and benefits of vaccination, and record information in medical records and in many cases with duplicate data entry of information for electronic immunization information systems. For example, vaccine administration costs may range from $5 in public health clinics to $20 in private sector clinics

or according to another source from $20-$40 (NVAC Vaccine Financing Working Group, 2009; Shepard et al., 2005), but some payers reimburse providers far less than the cost incurred by providers. For example, one state Medicaid program reimbursed private sector providers as little as $2 per dose for administration of vaccines given (Freed et al., 2008b). Vaccines for Children (VFC) does not reimburse providers for costs associated with administering the vaccine, but most VFC vaccinations are given to children on Medicaid, which reimburses for vaccine administration. VFC providers can charge an administrative fee to patients without insurance; it is hoped they would not withhold vaccination due to inability to pay.[4] Although Section 317 funding may be used for provider reimbursement, there currently is no mechanism for doing so (CDC, 2009c).

Adult health care providers also receive inadequate reimbursement for immunizations. Adults 65 years of age and older are typically covered for vaccines by Medicare, although there are barriers (e.g., the complicated process for receiving Zostavax vaccine, described in this committee's 2008 letter report in Appendix D). Adults younger than 65 years who are uninsured or underinsured generally do not have an alternative way to finance vaccines other than to pay for them out of pocket.

Rationale for Removing Financial Barriers

Removing financial barriers to immunization could have a considerable impact on access to services, as shown by the 2008 update to the *Guide to Community Preventive Services*, which found that reducing out-of-pocket costs for immunization services is an effective intervention in increasing access to immunization services (Briss et al., 2000).[5] Research also shows that children's health insurance coverage determines whether they are up-to-date on recommended vaccinations, but gaps in private insurance allow some children to fall through the cracks (Blewett et al., 2008; Santoli et al., 2004). State immunization requirements for school and child care entry also raise an ethical argument for ensuring that children have no financial barriers to receiving needed vaccines.[6]

[4] Providers may charge eligible but uninsured children "up to but not more than the maximum regional administration charge."

[5] The intervention was "recommended," meaning that "the systematic review of available studies provides strong or sufficient evidence that the intervention is effective."

[6] One example of policies that could lead to improved equity in the delivery of immunization services may be found in the World Health Organization's Reaching Every District Strategy, which aims "to ensure the full immunization of children under one year of age at 90 percent nationally, with at least 80 percent coverage in every district or equivalent administrative unit by 2010." By focusing on increasing coverage in every district in addition to a national goal (and in order to make the national goal achievable), it increases the likelihood that disadvantaged communities will not be left out.

Proposed Solutions to Financing Barriers

In April 2008, the National Vaccine Advisory Committee (NVAC) finance workgroup convened a workshop and published a paper on a childhood and adolescent immunization that involved stakeholder input from manufacturers, distributors, insurers (e.g., private, Medicaid), employer groups, providers, state and local public health agencies, and others. While there was general agreement at the workshop that primary care providers are inadequately reimbursed for their role of providing vaccines to children, consensus was not achieved by the NVAC finance work group on the best solutions to the problem at hand. Possible solutions discussed at the NVAC meeting included legal mandates for employers and insurers to provide first-dollar coverage of vaccines; increasing the amount of reimbursement paid for administrative fees to VFC providers by Medicaid programs; and revising the VFC legislation to ensure the purchase and provision of vaccines to underinsured children. These solutions were all challenged by several stakeholder groups at the NVAC vaccine financing meeting. Other potential approaches, such as providing assistance and training to primary care providers on better business practices; facilitating timely reimbursement by insurers; and allowing providers to purchase vaccines on a delayed payment schedule to minimize a practice's cash outlay, were considered tenable solutions. While many of the solutions put forward by the NVAC financing committee are clearly needed to ensure that children can continue to be vaccinated in their medical home, these solutions should be part of a larger comprehensive approach to solving the overarching problem of how to provide better incentives and remove disincentives for a preventive intervention that is clearly a public health good.

The NVAC finance work group made final recommendations on vaccine purchase and administration reimbursement in the public and private sectors. Recommendations included expanding funding to the Section 317 and Vaccines for Children programs to cover vaccine administration and reimbursement; broadening access to VFC through public health clinics (access is currently allowed only at federally qualified health centers and rural health centers); and expanding VFC to include all underinsured children and adolescents. NVAC also recommended that all states reimburse for Medicaid vaccine administration and fund Medicaid- and SCHIP (State Children's Health Insurance Program)-managed care plans at a level that provides vaccine administration reimbursement at the CMS-established maximum allowable amount. Another recommendation called for CMS to "update the maximum allowable Medicaid administration reimbursement amounts for each state and include all appropriate non-vaccine related costs as determined by current studies" (NVAC, 2009b).

Although much effort has been devoted to ensuring the gaps in financing

are minimized for children and adolescents, attention to gaps in financing vaccination for adults has lagged (NFID, 2008; NVAC, 2009a). However, the committee is aware of the ongoing activity of the NVAC Adult Immunization Working Group, including draft recommendations (NVAC, 2009b). The financing issues for adults are even more complex than for children. For example, primary care services for the two populations differ considerably—immunization is not a major part of services provided to adults, and there is no adult equivalent of "well child visits" (Orenstein et al., 2007). Although reimbursement for adult vaccination has improved in recent years (compared to data cited in the 2003 IOM report), a majority of providers consider lack of reimbursement a barrier to zoster vaccination, and some providers remain concerned about reimbursement for other vaccines, including influenza, pneumococcal, and hepatitis B.[7] In the public sector, there is no VFC-like program for adults who are uninsured. Gaps in funding in the public sector for adult immunization further exacerbate the disparities in access to recommended vaccines for adults.

Committee Recommendation for Financing Immunization

The committee believes that Objective 4.2 in the National Vaccine Plan on reducing the financial barriers to immunization is insufficient. The target that is needed is elimination, not reduction of such barriers. No individual should be denied the opportunity to receive ACIP-recommended vaccines due to inability to pay. Innovations in insurance and direct financing arrangements to assure affordability at point of delivery, coupled with system supports that enable efficient practice, such as changes in how practices are supplied with vaccines, are needed.

A gap in the draft Goal 4 is the lack of an objective or strategy on performance measures related to the use of financing to induce and enable providers to seek out, stock, and administer ACIP-recommended vaccines. The committee would like to draw attention to the following matters, which must be addressed in the plan with clear objectives and performance measures:

- Adoption by public and private insurers and by payers of provider payment mechanisms aimed at assuring that there are incentives for selecting and providing the right care (in this case, ACIP-recommended immunizations) at the right time and in the right setting

[7] See for example the following studies about provider-reported barriers (including lack of reimbursement) to zoster, influenza, pneumococcal, and hepatitis B vaccination: Daley et al., 2009; Hurley et al., 2008; Kempe et al., 2008; and Szilagyi et al., 2005.

- Acknowledgment of the range of health care providers (e.g., obstetrician-gynecologists and infectious disease specialists) are able to provide vaccination but may not be included in payment systems
- Integration of immunization in national systems of continuing performance measurement, with data collected by population characteristic, care setting, type of vaccine, and provider type
- Sufficient funding to cover lapse in public and private coverage
- The adoption of supply-chain mechanisms across insurer and third-party payer type, similar to the VFC program, so that the cost of stocking and storing vaccines is directly addressed and providers are not discouraged by the cost of carrying fragile and costly inventory that may or may not be used before it expires (this issue is obliquely referenced in strategy 4.2.5 of the draft plan—develop, implement, and evaluate strategies to reduce the financial burden on vaccination providers for purchase of initial and ongoing vaccine inventories).

To realize the full potential of vaccines to prevent costly disease and disability, the committee recommends:

> **Recommendation 4-2: The National Vaccine Plan should include the development of strategies to eliminate financial barriers such as unreasonable cost-sharing by patients who are unable to afford out-of-pocket costs for vaccines and provider payment mechanisms that discourage full and meaningful participation in the delivery of immunization services.**

Strategies could include identifying ways of maximizing the use of public insurance options for the uninsured, as well as efficient use of available funds to aid uninsured and underinsured adult populations, and comparative-effectiveness research of various payment and reimbursement mechanisms for providers.

SUB-GOAL 3: ACCESS AND PRACTICE

Objective 4.2 in the draft plan is extremely broad, combining financial and non-financial barriers to immunization. The term non-financial barriers is used to refer to a vast array of barriers to both patients (e.g., inconvenient hours of operation, long waits for appointments, limited transportation, knowledge and communication challenges) and barriers to providers (e.g., incomplete information about or failure to review or assess a child's immunization status) and gaps in provider knowledge that lead to missed opportunities to vaccinate (e.g., not vaccinating when a patient has a mild illness). Some examples of non-financial barriers, such as communication

and information, would seem to fit more appropriately in Goal 3. Aside from organizational matters, the committee has focused on two remaining major non-financial barriers: access to immunization and healthcare provider practice concerns.

In the past decade, non-traditional sites for the delivery of vaccination have become more prominent. These include retail- and other community-based sites (including pharmacies). School-based health centers and senior centers have been part of the immunization delivery landscape for some time, but have also garnered more attention as awareness of adolescent and adult immunization need has increased, owing both to the introduction of new vaccines for these groups and a recognition of poor vaccine uptake, due in part to gaps in access. The dialogue about the optimal sites for delivery of immunization services includes references to the importance of immunizing in the context of a medical home,[8] but that may or may not be an appropriate model, depending on the population. Although the emergence of complementary sites for the delivery of health care has been regarded both negatively and positively by health care professionals (CHCF, 2008; Scott, 2007), they offer some advantages for the delivery of immunization services, such as increased access. However, for quality alternative sites to be a useful mechanism to increase access to immunization, they must include financial coverage. The Infectious Diseases Society of America has recommended quality standards for complementary sites of immunization, including "ability to appropriately manage vaccine-related adverse events, proper storage and handling of vaccines, appropriate record keeping, regulatory issues, and provision of education regarding both risks and benefits of immunizations" (Pickering et al., 2009).

Over the past several years, the concept of comparative effectiveness research has been explicitly expanded to include comparisons not only of medical interventions, but also of the ways and settings in which health care is delivered (Brookings Institute, 2009; National Journal Online, 2009; NEHI, 2009). The committee believes that comparative effectiveness research could build on and strengthen the evidence base concerning immunization practices. For example, there are questions about the best settings to deliver immunization services to different populations and age groups, but little research has been done examining the strengths and weaknesses of each delivery setting (e.g., primary care setting versus retail based) for various populations and age groups. For example, how do various settings handle communication about vaccine risks and benefits?

Efforts to improve the delivery and quality of health care include a growing recognition of the value of immunization as a cost-saving and

[8] The medical home concept is described in *Joint Principles of the Patient-Centered Medical Home*, and practices that meet medical home standards can receive National Committee on Quality Assurance recognition (AAP et al., 2007).

cost-effective preventive service. Public health and disease prevention objectives are hallmarks of the contemporary policy effort to reform health care. Research indicates that geographic areas with high rates of high-cost health care often have low rates of low-cost preventive services such as influenza and pneumococcal immunization (Fisher and Wennberg, 2003; Fisher et al., 2003). It is possible that the low rates of reimbursement for immunization services are partly to blame, but this example illustrates some of the perverse incentives and disincentives that exist within the U.S. health care system.

In another example of efforts to link immunization with quality measures, the National Committee for Quality Assurance has developed a measure referring to the percentage of Medicare members 65 years of age and older who have received an influenza vaccination. There is increasing recognition that all age groups need access to ACIP-recommended vaccines and that health plans ought to include immunization coverage rates among measures of quality of health systems and communities.

Studies of provider knowledge and practices have indicated both knowledge gaps and systems challenges that range from major hurdles (inadequate or no reimbursement for counseling patients about needed vaccinations) to administrative issues such as lack of effective reminder systems (Davis et al., 2001; Flowers, 2007).

Comparative effectiveness, cost-effectiveness, and other types of research could contribute to determining the best ways to organize immunization services to ensure optimal access in various communities, the best ways to measure quality of services, and the best ways to structure incentives and pay for services (at both the insurer and the provider levels, and to promote the advance purchase and allocation of supply to the point of service).

Recommendation 4-3: The National Vaccine Plan should emphasize the application of research and best practices in the organization and delivery of immunization services to improve patient access (such as location and hours) and service efficiency and quality (such as improved provider knowledge and decrease in missed opportunities for vaccination).

SUB-GOAL 4: INFORMATION SYSTEMS

There are five purposes for information systems used in immunization services:

1. To track vaccine supply,
2. To assess vaccination coverage at the individual level through immunization information systems or registries,

3. To assess vaccine coverage at the population level through tools such as the National Immunization Survey (NIS) and the Behavioral Risk Factor Surveillance System (BRFSS),
4. To conduct surveillance of disease, and
5. To conduct surveillance of vaccine adverse events.

Tracking Supply

A stable vaccine supply (and distribution of that supply) for ACIP-recommended vaccines is a high priority, and a variety of information systems can provide added intelligence about the movement of vaccine supplies and support decision making. At the national level, CDC is developing a vaccine tracking system (VTrckS) that will be a "fully functional on-line ordering system that supports centralized distribution" and that may help explain some causes of vaccine shortages or excess supply of various vaccines (in both the private and public sector) (CDC, 2009a). If health information technology goals came to fruition, HIT could be used to track data on where vaccines are used and therefore track supply (health care providers, hospitals, retail stores) and identify area's where certain vaccines have not been administered or if there are pockets of need to determine where excess supply should be sent.

Assessing Vaccination Coverage at the Individual Level

Immunization information systems (IIS) or registries that collect individual-level vaccination coverage data are operated by individual providers, health care organizations, public health agencies, and school systems. Immunization information systems are confidential, computerized systems operated at the state and local level that are intended to record every vaccination given to children; some have additional functions, such as vaccine inventory management and adverse events reporting (CDC, 2007a). In 2006, 64 (70 percent) CDC grantees (i.e., states, territories, several metropolitan areas) reported that their IIS had the ability to track immunizations of people of all ages (CDC, 2008). In 2006, 65 percent of U.S. children under age six were included in an IIS, although the definition of participation is two or more doses recorded, and many records are incomplete (CDC, 2008). IIS permit providers to determine vaccination status of a child seen in their practice and generate the immunization records needed, for example, for school entry or childcare.

Electronic health records (EHRs) are records of "health-related information on an individual that conforms to nationally recognized interoperability standards and that can be created, managed and consulted by authorized clinicians and staff across more than one health care organization" (National

Alliance for Health Information Technology, 2008).[9] Ideally, electronic health records would be interoperable with immunization information systems so that the record of immunizations received in a health care setting would automatically be submitted to IIS; practitioners should also be able to search IIS and import a history of previous immunizations received by a specific patient into the EHR at their practice. However, a study conducted in 2007 and 2008 found that only 4 percent of physicians reported having "an extensive, fully functional electronic-records system and 13 percent reported having a basic system" (DesRoches et al., 2008). The 2008 National Ambulatory Medical Care Survey (NAMCS), "an annual nationally representative survey of patient visits to office-based physicians" conducted by the National Center for Health Statistics (NCHS), similarly found that 4 percent of providers use fully functioning electronic medical records systems and 17 percent use basic systems (Hsiao et al., 2008). Denmark is a good example of successful implementation of electronic health records. Denmark has a centralized computer database to which primary care physicians (98 percent), all hospital physicians, and all pharmacists have access to medical records. Patients can also access their own personal records though a secure website. Although it does not have one overarching system, the Danish system is able to link networks established by regional health agencies (Harrell, 2009).

HIT is important in informing providers about patient immunization history. Providers need to be able to obtain information on the vaccination status of their patients quickly and easily (to avoid missed opportunities or duplicate vaccination) both in their practice and remotely; it is also crucial that alternative immunization sites such as schools, workplaces, and pharmacies are able to document vaccinations received and share these data with public health agencies.

Assessing Vaccination Coverage at the Population Level

National, state, and large-city data about vaccination coverage are obtained from the NIS, an annual list-assisted random-digit-dialing telephone survey followed by a mailed survey to children's immunization providers. The NIS is conducted jointly by the CDC National Center for Immunizations and Respiratory Diseases and NCHS. Levels of coverage in children, and recently adolescents, are assessed through the NIS and for adults through the BRFSS. Since NIS is a phone-based survey with verification through medical records it has small study samples. Local-level data is dif-

[9] The Agency for Healthcare Research and Quality defined electronic medical records (EMRs) as "the set of databases (or repositories) that contains the health information for patients within a given institution or organization." The EHR concept takes the EMR one step further, to institutional exchange (Hinman and Davidson, 2009).

ficult to obtain through national surveys such as the NIS and BRFSS, but attempting to expand NIS or similar mechanisms to gather local data for much larger sample sizes would be costly and extremely difficult.

Surveillance of Infectious Diseases

One striking illustration of the complexity of the public health network of information systems is found in the influenza surveillance system (CDC, 2009b), which

> . . . consists of nine complementary surveillance components in five categories. These components include reports from more than 150 laboratories, 2,400 outpatient care sites, vital statistics offices in 122 cities, research and health-care personnel at the NVSN[10] and EIP[11] sites, and influenza surveillance coordinators and state epidemiologists from all 50 state health departments, and the District of Columbia health department.

Interoperable electronic health records could facilitate surveillance of vaccine-preventable diseases by automating the reporting of notifiable conditions. It would also allow public health workers to measure the impact of vaccines and identify pockets of under-vaccination (and therefore an increased risk of an outbreak) and more effectively distribute resources.

Surveillance of Adverse Events

Surveillance of adverse events is fairly limited at the local and state level. Currently the Vaccine Adverse Events Reporting System, the Vaccine Safety Datalink, and the Clinical Immunization Safety Assessment network described in Chapter 2 are used to identify potential adverse events, but an integrated interoperable system would increase the population studied and would increase the likelihood for a study of an adverse event to have statistical power. Such systems could also be searched systematically for a putative adverse event related to immunization which could accelerate the detection and evaluation of a post-licensure safety problem. Interoperable electronic health records can build on these existing systems to increase the power of studies and evaluation of adverse events following immunization and facilitate research studies (e.g., linkage studies, control groups; see Chapter 2 for a detailed discussion).

In addition to efforts to obtain safety data described in Chapter 2, government agencies and other institutions are looking at additional opportunities to collect data—for example, FDA's Sentinel Initiative (intended

[10] NVSN is the New Vaccine Surveillance Network that gathers information about viral strains to inform vaccine development.

[11] Emerging Infections Program Surveillance.

to link multiple large databases to enable widespread surveillance of adverse events) and the 2009 Post-Licensure Rapid Immunization Safety Monitoring constructed to conduct active surveillance of adverse events following influenza immunization with the monovalent H1N1 vaccine. However, as programs such as the Sentinel Initiative move forward it will be important for planners to think strategically about what information can be obtained from current systems and what will be the most useful investment of resources. Planners also need to look toward the future (interoperable health records), which will likely obviate the need for these interim solutions. What is learned from working with these interim systems will create a core of analytic and information technology expertise, which will be important to tie into the future HIT activities. State, local, and to a certain extent federal public health agencies must be prepared to participate effectively in HIT by having the technical expertise and the HIT systems to support interfacing with EHRs and the National Health Information Network. Current immunization systems need to be developed using evolving national standards for interoperable HIT to the maximum extent possible. Since many IIS originated in the 1990s and were not based on national standards, it will be necessary to develop strategic approaches to support IIS functions in the evolving NHIN—some functions may be incorporated into clinical EHRs, while some functions will be the responsibility of public health agencies.

Recommendation 4-4: The National Vaccine Plan should encourage the exploration of non-traditional approaches to disease surveillance, monitoring vaccine safety, and assessing vaccine coverage. Such approaches might leverage the increasing ubiquity of the Internet and wireless data services, personal communications devices, and social networking facilities.

The committee believes that the health information technology investments spurred by the American Recovery and Reinvestment Act (ARRA) of 2009 are an extremely important new development, and their implications for immunization deserve careful consideration in the National Vaccine Plan.

Recommendation 4-5: Given the importance placed on the national adoption of certified, interoperable health information technology and electronic health records, the National Vaccine Plan should ensure active involvement of NVPO and relevant partners in the planning and implementation of the national health information initiative.[12]

[12] Currently called the National Health Information Network (NHIN).

This involvement should include:

- Ensuring the development and adoption of standards necessary for effective immunization clinical practice and population surveillance systems,
- Ensuring that the definition of "meaningful use" considers immunization practice and reporting,[13]
- Facilitating use of vaccine-related data by all public health partners (e.g., state and local health departments),[14] and
- Ensuring that all public health partners have the expertise and resources to participate in the initiative.

SUB-GOAL 5: PUBLIC HEALTH INFRASTRUCTURE

Public health agencies at all levels play a central role in assuring the best use of vaccines to achieve prevention of infectious diseases. Strengthening and clarifying the draft plan's strategies for public health agencies would help to reflect the ideal of integrated measurement, monitoring, assurance, and standard setting of public health functions. Specific activities could include assuring that all states have the resources to support immunization services in communities and for populations with inadequate access to immunizations. For example, although ethnic disparities in receipt of recommended vaccines among children have decreased, disparities in receipt of pneumococcal vaccination have increased among Black and Asian adults 65 years or older (AHRQ, 2009). The ability to conduct disease surveillance and registry capacity in all states to ultimately enable identification of underimmunized populations in real time is also important (see earlier discussion about local area monitoring). Review and modernization of health professions licensure statutes to assure that all states have the maximum capacity to deploy all health professionals for immunization practice within their scope of competence is an additional area that warrants attention. For example, only a small number of states have made clear the legal authority of nursing professionals to immunize under standing orders (Smith et al., 2006; Stewart et al., 2005). This could lead to missed opportunities to provide recommended vaccinations. Although standing orders have been shown to

[13] The ARRA has targeted funding for both Medicaid and Medicare to incentivize implementation of EHR systems in physician offices and acute care facilities, which meet "meaningful use" criteria defined by federal statute. The key characteristics for implementation are yet to be determined but will likely involve an operating governance structure; a defined technical plan; defined clinical use cases; and statewide policy guidance for privacy and security.

[14] Public health departments are authorized by law (Health Insurance Portability and Accountability Act) to access data needed for "public health activities and purposes" such as immunization (45 CFR § 164.512(b)(i)).

help prevent missed opportunities (CDC, 2000; Daniels et al., 2006) communicating with patients about recommended vaccines and responding to their questions and concerns is an important contributor to decisions about vaccination. Communication is discussed in detail in Chapter 3.

Recommendation 4-6: The National Vaccine Plan should include strengthening the public health infrastructure to support vaccine delivery, measure immunization practice and performance, intervene to address disparities in access to immunization, and respond to emerging infectious disease threats.

Efforts to strengthen the public health infrastructure could include:

(a) Development of capacity in all health departments to assure the delivery of immunization services to underserved populations in all communities or during an emergency;[15]
(b) Development of greater public health capacity to identify deficits in access to immunization services;[16] and
(c) Assistance to states to eliminate barriers to the full use of all appropriate personnel in vaccine administration due to restrictions on licensure and scope of practice.

The final outcome of health care reform efforts will have implications for the delivery of immunization services, and the committee hopes the changes that result will be conducive to improved access and information. Health care reform legislation will ideally include monitoring immunization coverage and achieving targets as a measure of success. At the practice level, measures of health care quality would ideally include the provision of immunization services to adults, adolescents, and children.

Recommendation 4-7: The National Vaccine Plan should incorporate rapid and comprehensive assessment of the outcomes of national health reform and their implications for the nation's vaccine and immunization priorities.

Specifically, NVPO, as "owner" of the plan, could contribute by:

- Tracking House and Senate reform proposals and forwarding comments to the Secretary when appropriate;

[15] See Recommendation 4-7 on the implications of health care reform.
[16] See Recommendation 4-5 on health information technology.

- Participating as early as possible in implementation efforts related to the expanded health insurance access for the population;
- Participating as early as possible in implementation efforts related to the design of health insurance coverage and cost-sharing features, administrative matters affecting the actual provision of vaccines, and standards and procedures governing the measurement and reporting of health plan performance; and
- Promoting the integration of health plan performance and operations with community public health policy and practice in order to assure (a) the availability of community-wide information about population immunization status, disparities in access, and areas of need; (b) access to immunization services; (c) public health agency analytical, management, and other needed capabilities; and (d) the ability of public health workers, health insurers, and health care providers to mount a joint response to emerging public health threats.

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5

Vaccines and Global Health

Goal 5 in the draft National Vaccine Plan states: Increase global prevention of death and disease through safe and effective vaccination (HHS, 2008). The plan would likely benefit from a clear explanation of the relevance to the United States of global immunization as it may seem unusual that an American national vaccine plan would include objectives and strategies related to implementation and financing of vaccination programs in other countries.

Several developments justify the inclusion of global vaccine issues in the plan. The world is not as it was when smallpox was declared eradicated in 1980; air travel and global trade have grown exponentially, and the scientific and commercial entities that develop, manufacture, and market vaccines span the globe. The American infectious disease landscape includes emerging infections (e.g., severe acute respiratory syndrome), re-emerging infections (e.g., tuberculosis [TB]), and even the occurrence of vaccine-preventable childhood diseases through international travel (e.g., of unvaccinated American children or unvaccinated foreign visitors). Infectious diseases, especially vaccine-preventable diarrheal and respiratory infections in children, are responsible for millions of deaths (one-fifth of global mortality) (Kieny and Girard, 2005). Pneumococcal disease and rotavirus diarrhea alone cause approximately 1.3 million deaths among infants and young children (WHO, 2006b).

Many diseases that are potentially preventable by vaccines cause considerable social burden including chronic disabilities (such as deafness and brain damage) in low- and middle-income countries. Improved health and resultant reduced morbidity and mortality in developing countries contrib-

utes to economic development, reduction of poverty, and greater political stability. Reduction and eradication of infectious diseases overseas (e.g., polio, measles) also decreases the likelihood they will affect Americans traveling or working overseas and reduce the risk of importation into the United States by returning travelers, refugees, and immigrants. The U.S. interest in global health in general[1] and in immunization in particular is motivated by many factors, including the interconnectedness of the world and a "humanitarian obligation to enable healthy individuals, families, and communities everywhere to live more productive and fulfilling lives" (IOM, 2009b:1).

Since the completion of the 1994 plan (HHS, 1994), the landscape of global immunization has changed dramatically. Low- and middle-income country manufacturers have gained increased prominence in manufacturing and furnishing affordable vaccines in these countries. In fact, most of the world's supply of certain vaccines is manufactured by these companies. Philanthropic organizations and the public-private partnerships (such as product development partnerships [PDPs]) they support have emerged as major actors in vaccine research and development specifically for the developing world. Global funding, from both private philanthropy and government aid, has markedly increased to support the purchase of newer and costlier vaccines, such as pneumococcal conjugate vaccines.

The stakeholders for Goal 5 in the National Vaccine Plan include an array of public, private, and not-for-profit entities. The federal agencies with responsibilities for developing country vaccine issues (e.g., development, regulation, and use of vaccines for diseases not endemic to the United States) include the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), the U.S. Agency for International Development (USAID) in the Department of State, and the Department of Defense. USAID represents the United States in most global organizations that provide governance, develop policy, or coordinate financing for immunization. USAID also supports the ImmunizationBASICS program that supports lower income countries in policy development and aspects of capacity building. The United Nations Children's Fund (UNICEF), the World Health Organization (WHO), the Pan American Health Organization (PAHO), and WHO's expert committees play central roles in developing international vaccine policy and programs, and in advising and supporting developing countries' own immunization policies and activities. In the past decade, foundations such as the Bill and Melinda Gates Foundation have emerged as major contributors to financing and innovation in the realm of immunization for low- and middle-income countries. The Global Alliance for Vaccines and Immunisation (GAVI) is a relatively new

[1] As exemplified in the Administration's Global Health Initiative (White House, 2009).

global entity with a governing board that includes representatives of WHO, UNICEF, and various nations (such as USAID for the United States). GAVI has been a coordinating mechanism for a number of major immunization initiatives such as the Vaccine Fund, the International Financing Facility for Immunization (IFFIm), and Advanced Market Commitments (AMCs). Finally, there are several disease-specific vaccine initiatives, including the Meningitis Vaccine Project, the Malaria Vaccine Initiative, and the AERAS Global TB Vaccine Foundation.

In June 2009 the committee held a meeting with stakeholders on Goal 5 in the National Vaccine Plan. Several themes surfaced during the meeting, reflecting areas of agreement about major challenges and opportunities in the field. These themes include the following:

- Programmatic and infrastructure challenges, including most prominently surveillance and epidemiologic research to provide burden of disease data needed to inform vaccine research on and the development of new vaccines and to assess rates of vaccine-related adverse events,
- The promise of PDPs and the U.S. government role,
- Competing priorities: program-specific versus broader health infrastructure objectives and investment; periodic intensification of immunization (e.g., polio campaigns) versus routine immunization programs, and
- Creating a viable market for vaccines using both innovative and well-established financing mechanisms (e.g., IFFIm, differential pricing).

CHALLENGES AND OPPORTUNITIES IN A CHANGING LANDSCAPE

In Chapter 1, the committee cites a 1997 paper prepared by the U.S. National Vaccine Advisory Committee on the "delicate fabric" of the public-private vaccine development enterprise (NVAC, 1997). A contemporary update of that paper would reflect greater complexity and a similar level of fragility. Also, it is no longer applicable to speak of the American enterprise without reference to the fact that it is part of a global network of national and international governmental, commercial, academic, and civil society actors. The makers of vaccines licensed for the United States are largely multinational corporations.

There are multiple barriers to ensuring that developing countries can immunize against major vaccine-preventable diseases. These include market-related factors (lack of incentive to develop vaccines for neglected diseases that affect low- and middle-income countries), financing (for both vaccine development and purchase), operational problems (lack of immunization infrastructure, health care workforce), managerial expertise, scientific and technical issues (such as the challenges encountered in developing HIV and

malaria vaccines), and lack of political will (Mahmoud, 2005). Despite the array of challenges described above immunization is the most consistently delivered health service in most of the world, and coverage remains reasonably good. Efforts by global partners to increase the availability of vaccines in low- and middle-income countries have led to significant increases in immunization rates and lower rates of disease in the past few decades. Nearly three-fourths of children around the world complete their series of DTP (diphtheria, tetanus, pertussis) vaccinations.[2] Moreover, the uptake of additional vaccines (e.g., hepatitis B, *Haemophilus influenzae* b [Hib]) into the routine Expanded Program on Immunization in developing countries has greatly increased. By 2009, 61 of 72 countries eligible for GAVI funding were expected to have introduced Hib vaccine into their routine immunization programs (PneumoADIP, 2009).

Vaccine manufacturers make products that have historically offered minimal or modest returns on investment in high-income countries in part due to uncertain demand and in part because vaccines are one-time or limited-use products (Milstien et al., 2006). Although the vaccine market in developed nations has experienced a kind of renaissance (Gapper, 2009), concerns about profitability remain strong in the context of the vaccine needs of lower income countries (Batson, 2005; Danzon et al., 2005). Consequently, the development of new vaccines for diseases that primarily affect poor counties has been slow. Innovative solutions have been devised to provide incentives for vaccine makers or to find alternate ways and partners to develop a needed vaccine. Manufacturers in developing countries supply an increasing proportion of vaccines purchased by or on behalf of developing countries. One concern is that as this segment of the global vaccine industry grows, its growing capacity for research and development paired with a potential shift from its current humanitarian focus could lead manufacturers away from a focus on traditional, low-cost childhood vaccines (Frew et al., 2008).

The story of meningococcal conjugate vaccine for Africa's meningitis belt offers one case study of a novel kind of partnership to facilitate vaccine development for a market with limited financial potential. The collaboration has involved WHO, Program for Appropriate Technology in Health (PATH), U.S. government agencies, and a developing country manufacturer (Serum Institute of India, Limited) to develop a new vaccine against meningococcal meningitis with technological support from the public and nonprofit sectors (see the meningitis vaccine timeline in Table 5-1).

The areas of need in the field of global immunization include the following:

[2] Tetanus, diphtheria, acellular pertussis vaccine is used in the United States, but diphtheria, tetanus, whole cell pertussis remains in use in most low- and middle-income countries.

- Development of novel vaccines against diseases and strains not targeted by currently licensed vaccines,
- Infrastructure and capacity,
- Financing vaccine development and purchase, and
- Surveillance infrastructure and operational or programmatic capacity.

TABLE 5-1 Developing Meningococcal Conjugate Vaccine for Africa's Meningitis Belt

Date	Event
1986	Polysaccharide vaccines available in developed countries show limited duration of protection in Africa (Reingold et al., 1985).
	Vaccine protects individuals for a short time, but does not prevent spread to others, so useful primarily to control epidemics.
1996	Epidemic of meningococcal meningitis in sub-Saharan meningitis belt results in 250,000 cases and 25,000 deaths; generally, 10% of those infected die within days, and 10-20% of survivors suffer neurological sequelae (WHO, 2006a).
1990s	WHO decides that a conjugate vaccine for Africa is a high priority; Pasteur Merieux develops conjugate vaccines against meningitis that contain both serotypes A and C; WHO supports evaluation in Niger (Campagne et al., 2000).
2001	Gates Foundation awards WHO and the non-governmental organization PATH $70 million for the Meningitis Vaccine Project (PATH, 2009).
2003	CDC and a British public health laboratory are selected to implement serologic studies.
	Serum Institute of India is selected to develop the vaccine (PATH, 2009).
	Meningitis Vaccine Project contracts with a European research group to develop the conjugation technology to be transferred to the Serum Institute of India and used in making the new vaccine (Roberts, 2008).
2003-2004	The European research group refuses to transfer the new technology to the Serum Institute so FDA transfers its recently developed conjugation technology to the Serum Institute (Roberts, 2008).
2009	An epidemic in the meningitis belt causes more than 25,000 cases and more than 1,500 deaths (WHO, 2009a).
	In the 2008-2009 epidemic season 73,398 cases and 3,869 deaths are reported (UNICEF, 2009).
2010	The new vaccine is expected to be introduced starting 2009-2010 in Burkina Faso and will be phased into an additional 24 countries between 2010 and 2015, with GAVI support (LaForce and Perea, 2008).

DEVELOPING NOVEL VACCINES

In Chapter 1 of this report, the committee discussed the first goal in the National Vaccine Plan, which pertains to developing new and improved vaccines. As noted above, the United States is part of an increasingly global vaccine enterprise (i.e., vaccines for the U.S. market are largely produced by multinational companies) thus, the discussion in Chapter 1 also applies to vaccines for so-called neglected diseases that disproportionately affect developing countries.

In Chapter 1, the committee recommended two priority actions pertaining to the development of new and improved vaccines for both domestic and global use. The first action would be to prioritize new and improved vaccine candidates, and the committee has recommended that separate but similar information-gathering and decision-making processes be undertaken to set vaccine priorities for domestic and global health objectives. Storability and ease of delivery are related issues of crucial importance to vaccines for the developing world. Vaccines that do not need refrigeration and vaccines that may be administered orally or intranasally could dramatically transform the immunization landscape, removing or considerably lessening the logistical challenges, training requirements, and potential safety challenges related to vaccine management and administration.

The committee recognizes that prioritization of new and improved vaccines described in Chapter 1 would have no effect unless it is paired with a coordinated, outcome-focused process for facilitating action to implement the priorities. The domestic and global challenges in this area differ somewhat, but there are lessons that may be shared. For example, the PDP model, although insufficiently evaluated to determine its overall effectiveness and specific aspects most likely to contribute to effectiveness, represents an innovative tool that could be adapted to accelerate vaccine development for U.S. use as well as for global purposes.

Effective surveillance systems can monitor the impact of vaccine use and inform research and development. The basis of priority setting for new and improved vaccines for global health can be strengthened when information is available on diseases to target based on (1) the burden of disease, and (2) which strains, serotypes, or antigens to include in vaccines developed for low- and middle-income countries (e.g., rotavirus, *Neisseria meningiditis*). Ascertaining the impact of vaccine use can inform governments, health care workers, and funders of successes of and gaps in the immunization infrastructure (WHO, 2009b).

Four models of vaccine research and development have been defined (Wilson, 2007). These include (1) predominantly private sector development; (2) public sector vaccine design, and transfer to the private sector for clinical trials and production; (3) predominantly public sector development; and (4) coordination by a non-profit entity. The model still common in the

United States is the second: government-supported academic research at the early stage of discovery and design, followed by transfer to industry for product development (IAVI, 2009). The model used to develop vaccines for low- and middle-income countries is an increasingly hybrid model, or rather, an array of hybrid arrangements. A main example is the PDP, a public-private entity designed to manage the entire process, from discovery through selection of the most viable candidates, clinical trials, and production.

Other novel mechanisms intended to spur innovation have emerged in recent years. As an example, a recent Institute of Medicine (IOM) workshop summary on Drug Development for Rare and Neglected Diseases and Individualized Therapies (IOM, 2009a) described the approach of the Collaboration for AIDS Vaccine Discovery (CAVD), a program of the Bill and Melinda Gates Foundation consisting of a network of centers and consortia. The network adopted a process for exchanging "essential research materials and information to accelerate research" that includes participant agreement and compliance with "certain principles for the sharing of materials and data, as well as to use a master MTA [material transfer agreement] and a confidential disclosure agreement for exchanges of materials and information among the various CAVD awardees and collaborators" (IOM, 2009a).

INFRASTRUCTURE AND CAPACITY TO PROVIDE IMMUNIZATION

Low- and middle-income countries have limited health care infrastructures that are unable or only partially able to support the delivery of needed vaccines, although each country's needs and circumstances may differ. Infrastructure limitations include obstacles in obtaining and maintaining cold-chain equipment, lack of sufficient and appropriately trained health care personnel to administer vaccines safely and manage all aspects of immunization programs, and lack of systems to monitor vaccine use and potential adverse events (in addition to disease surveillance). Without strengthened infrastructure, funding for vaccines alone will not get vaccines to those who need them. The efforts of low-income countries to recruit and retain health care workers have been complicated by structural adjustment programs, recruitment of health care workers by program-specific activities such as HIV treatment and research, and by emigration to developed countries. Furthermore, developing nations are facing increases in chronic diseases, such as diabetes, and this may place additional requirements on the limited health care funds available. In both developed and developing nations, immunization may be an indicator of health care delivery system status and its contemporary challenges. For example, in low- and middle-income countries, a high vaccination rate in children may be indicative of

the overall strength or quality of the health care infrastructure (German et al., 2001). In the United States, the fact that some populations do not have access to immunization services is reflective of the health care system's challenges in the area of access and payment.

Strategies for introducing human papilloma virus (HPV) vaccine, not currently supported by any of the global vaccine purchasing arrangements (UNICEF, PAHO), are under consideration by GAVI and others. HPV vaccine provides a forward-looking example of the utility of disease burden information to determine the cost-effectiveness of a vaccine in the global context. The introduction of HPV vaccines offers an opportunity to address a cause of substantial mortality, because women in developing countries typically do not have access to screening, detection, and treatment and could potentially benefit enormously from a vaccine that prevents the majority of cervical cancers. However, this will require a new immunization infrastructure targeting adolescents, which will make demands on the systems and capacity.

Recommendation 5-1: The National Vaccine Plan should call for the engagement of U.S. federal agencies and partners to support immunization capacity-building to implement new vaccines in low- to middle-income countries through the provision of expertise and financial resources necessary to incorporate new vaccines, strengthen immunization infrastructure, and achieve higher levels of vaccination. One infrastructure component requiring specific attention is the development and implementation of surveillance systems for vaccination, disease burden, and vaccine safety that are innovative and appropriate for developing countries.

FINANCING VACCINE DEVELOPMENT AND PURCHASE

Vaccines are a cost-effective global public health strategy, and they are a good and in some cases excellent investment. For example, the World Bank's 1993 World Development Report described interventions costing less than $100 per disability-adjusted life year (DALY) as "highly cost effective." Glennerster and Kremer (2000) calculated the savings made possible by a malaria vaccine and found that over a 10-year horizon, $13 per DALY would be saved, including the cost of vaccine administration and of the U.S. tax incentive. Despite their cost-effectiveness, investment in the development of vaccines for low-to-moderate income countries is limited (WHO, 2003).

Just 10 percent of global investment in biomedical research and development targets the needs of the world's poorest 90 percent—the so-called 10/90 gap, and this also applies to vaccine research and development (Flory

and Kitcher, 2004; Oxfam, 2008). The vaccine industry may not have sufficient incentives, such as an ability to recoup high research and development costs and a reasonable return on investment, to develop vaccines solely for low-income countries (Batson and Milstien, 2008). A consequence of these factors for the global immunization enterprise has been an enormous lag in the development of vaccines needed to combat malaria, tuberculosis, and other diseases responsible for the great burden of illness and death in low-income countries.

Funding for vaccine research and development for low- and middle-income countries has utilized two types of approaches called "push" and "pull" strategies.[3] The former refers to direct support for technological and scientific research that turns an idea into a product, such as through tax credits and funding for investigator-initiated research (Grabowski, 2005). The latter refers to enhancing the demand or creating a market for a given vaccine, for example, through an AMC—a recent example is the U.S. government's purchases (through Project Bioshield) of vaccines needed to meet biodefense or pandemic preparedness goals (Milstien et al., 2006).

Partnerships between foundations and the public sector are supporting some progress (Lieu et al., 2005). Changing this situation requires a creative blend of "push" and "pull" strategies, and over the past decade, novel partnerships between foundations, governments, and international organizations have led to some progress in addressing vaccine gaps for developing world needs. Several financing mechanisms have emerged. Advance-purchase agreements (also known as AMCs) have been proposed to increase incentives for the development and production of needed vaccines. The first pilot AMC to accelerate the development, production, and introduction of pneumococcal vaccines was developed by GAVI and became operational in June 2009 (Frew et al., 2008; GAVI, 2007; World Bank and GAVI, 2006). In such agreements purchasers commit in advance of product development to the purchase of specific vaccines meeting appropriate criteria for low-income countries, at a fixed price specified in advance (Berndt and Hurvitz, 2005). Such arrangements are intended to reduce uncertainty about return on investment for pharmaceutical companies and give investors confidence (Berndt and Hurvitz, 2005).

Another policy model that has been used successfully in the United States is the 1983 Orphan Drug Act that provides tax credits for research

[3] As noted in Chapter 1, the terms "push" and "pull" refer to strategies to spur vaccine research and development from the supply side and from the demand side, respectively. "Push" mechanisms include tax credits for research and development, as well as the traditional strategy of funding investigator-initiated research. "Pull" mechanisms include mandates and incentives such as the AMCs for diseases in the developing world and Biomedical Advance Research and Development Authority requests for proposals for bioterrorism countermeasures (Grabowski, 2005).

and development of products for neglected diseases as well as priority review and a "guaranteed seven-year market exclusivity that runs concurrently with any patent-exclusivity terms" (Grabowski, 2005). This strategy was further strengthened by the 2007 FDA Amendments Act that offered sponsors of a New Drug Application (NDA) or Biological License Application (BLA) for a product targeting a tropical disease a priority review voucher[4] could be redeemed on a subsequent NDA or BLA or could be transferred and sold to another sponsor, generating income for the sponsor of an "orphan" vaccine (IOM, 2009a).

PDPs are another mechanism to spur research and development (first initiated by the Bill & Melinda Gates Foundation and The Rockefeller Foundation). PDPs have emerged specifically to address neglected diseases that affect low-income countries and novel "social technology" that has the potential to transform research and development to meet global health needs. PDPs bring together foundations, pharmaceutical companies, academia, and the public sector to support research and development of drugs and vaccines for neglected diseases, while reducing the risk and uncertainty inherent in pharmaceutical product development (Freire, 2007; Frew et al., 2008; IAVI, 2009; Oxfam, 2008; Sorenson, 2009). While AMCs are intended to pay only for successful vaccine development, PDPs pay at every step of the development process. PDPs have been substantially funded by foundations with generally modest support from governments (IOM, 2009c; Oxfam, 2008). However, some PDP products are nearing the end of the pipeline and would benefit from an influx of funding to support them through the costly Phase III clinical trial and regulatory processes (Batson and Milstien, 2008). The unique operational strength of the PDP approach is that it generally entails building a portfolio of products against a single disease. This has the following advantages: vaccine design occurs across a variety of technologies using standard methods to compare them, there is an inherent incentive to terminate projects that are not promising and simply redirect resources, and PDPs can more easily mix and match technologies. The crucial decisions for PDPs include: how early to start along the development pipeline (earlier projects may carry more risk but also greater promise), what minimum standards a product must meet before it can be included in the portfolio, what the target product profile is, and finally, how to structure and manage the portfolio (how many projects, at which stages, what criteria to use in advancing projects between stages).[5]

One of GAVI's objectives has been to support countries' move toward sustainability of their vaccine needs. From 2000 to 2005, the GAVI Financing Task Force helped 50 countries examine their key financial concerns

[4] The voucher ensures review and action by the agency within six months of submission of that application.

[5] Personal communication, M. Moree, Global Health Services, September 2009.

with regard to immunization and to develop financial sustainability plans. Although GAVI found some signs of success, "huge funding gaps remain for these countries due to the initial underlying assumptions of the GAVI and financial sustainability plan model" (Kamara et al., 2008). Given current economic pressure on national health budgets, the fiscal sustainability of immunization will remain a great challenge (Lydon et al., 2007).

Many vaccines are used in both high- and low-income countries. Historically, once vaccines are developed, they become available in high-income countries first and in low-income countries much later, at lower prices. During this lag, mortality and morbidity from certain diseases continue to grow (Batson and Milstien, 2008). Thus, the challenge has been to find a way to facilitate timely access to new vaccines at a price low-income countries can afford. Differential pricing strategies involve charging different prices for the same vaccines, whereby "prices in affluent (and, to a lesser extent, middle income countries) exceed the marginal cost of production and distribution in these countries by enough, in aggregate, to cover the joint costs of R&D, while prices in [developing countries] cover only their marginal cost" (Danzon and Towse, 2003).

Bulk procurement systems, such as those used by UNICEF and PAHO (the Revolving Fund) set the greatly reduced prices they will pay for specified member countries. A uniform price would bar low-income countries from having access to a vaccine. Differential pricing serves as an incentive to multinational manufacturers to develop and continue to produce needed vaccines, it enables producers to expand revenues and profits by having a larger market for their product, and it also makes possible slightly lower prices for higher income countries (Plahte, 2005). Differential pricing is important to facilitate ongoing availability and use of the vaccines at affordable prices (often paid for out of U.S. assistance funds) for the lowest income countries (i.e., GAVI-eligible).

The committee finds that ways vaccines are priced have the potential to simultaneously achieve two different objectives: increase affordability of vaccines in lower income countries and increase incentives for manufacturers to innovate. The committee also finds that vaccine pricing is not always congruent with a country's ability to pay. There is a difference between what a high-income country and a low-income country can afford, and pricing is generally consistent with that difference. However, certain international pricing mechanisms set the same price for low- and middle-income countries. This may keep certain vaccine prices unnecessarily low and thus limit the manufacturer's ability to recoup research and development costs for vaccines for diseases endemic to low- and middle-income countries.

TABLE 5-2 The Complexity of Financing Global Vaccines and Immunization

On the One Hand	On the Other Hand
Investment in vaccine financing is humanitarian aid	Investment in vaccine financing is enabling nations to stand on their own feet
Investment in vaccine financing is an investment in targeting help where it is needed most now (putting out fires)	Investment in vaccine financing is an investment in sustainable infrastructure (helping to prevent fires)
Vaccines are about improving health	Vaccines are about economic development
It is critical to use the vaccines that exist today	It is critical to develop the better vaccines that may be used tomorrow
Need to leverage the risk management benefits of long-term partnerships	Need to leverage the innovation and efficiency benefits of competition
Differential pricing: expanded access, justice	Differential pricing: anti-efficiency, hard to enforce, unfair to middle-income nations

Recommendation 5-2: The National Vaccine Plan should endorse active U.S. engagement in the development of global policy frameworks to further global adherence to differential pricing in order to ensure access to needed vaccines in all countries.

Table 5-2 illustrates the extraordinary balancing act required of the global vaccine enterprise and the myriad governmental, multilateral and bilateral, industry, and non-governmental actors that are involved.

SURVEILLANCE

> Surveillance systems in industrialized and developing countries suffer from a number of common constraints, including a lack of human and material resources, weak infrastructure, poor coordination, and uncertain linkages between surveillance and response. However, these constraints are more pronounced in developing countries, which bear the greatest burden of disease and are where new pathogens are more likely to emerge, old ones to reemerge, and drug-resistant strains to propagate. (GAO, 2001:16)

CDC defines public health surveillance as "the ongoing, systematic collection, analysis, interpretation, and dissemination of data about a health-related event for use in public health action to reduce morbidity and mortality and to improve health" (German et al., 2001). Establishing and maintaining effective surveillance for diseases and vaccine adverse events in low-resource environments presents considerable challenges. (Disease surveillance at or across international borders is particularly challenging.) Like the delivery of immunization services in general, surveillance relies on the existence of an adequate public health and health care infrastructure, the political will to support it, and many other resources. Many developing

countries have limited capacity to conduct surveillance of any kind, including the surveillance of basic health indicators such as death rates, causes of death, or general burden of disease, let alone surveillance for specific diseases and vaccine adverse events (GAO, 2004; IOM, 2007; WHO, 2009b). The World Health Organization operates an adverse event database—the Program for International Drug Monitoring—but reporting by most low- and middle-income countries has been extremely limited and in many cases non-existent (Letourneau et al., 2008).

Traditionally, surveillance consists of a chain of reporting that begins at the level of an "astute clinician" who detects an adverse event or disease and ends at the level of national public health authorities. In settings where health care providers may be limited in number and overburdened by the volume of patients to be seen, disease surveillance may not be a high priority, and the very first link in the chain may be missing. For this and other reasons, surveillance in developing countries requires creative uses of appropriate technology and cannot necessarily rely on the methods and tools used to conduct surveillance in developed countries. One example may be found in the use of cell phones to report adverse events by individuals who receive a modest amount of training. Cell phones are a modern technology widely available in some of the farthest reaches of developing countries (IOM, 2007). (Box 5-1 describes the purpose of Vaccine Adverse Event Surveillance.)

CDC supports two programs intended to strengthen surveillance in developing countries: the International Emerging Infection Program and the Field Epidemiology Training Program/Field Epidemiology and Laboratory Training Program (FE[L]TP) (CDC, 2009a,b; GAO, 2004). CDC also has described several important criteria for decision making when developing surveillance systems: usefulness, flexibility, acceptability, portability,

BOX 5-1
Purpose of Vaccine Adverse Event Surveillance

Adverse event surveillance serves several different purposes that are of varying importance to immunization programs. These include "(1) detection, correction and prevention of programmatic errors; (2) identification of problems with a specific vaccine lot or brand; (3) prevention of false blame from coincidental events; (4) maintenance of confidence by properly responding to parent/community concerns while increasing awareness; (5) generate new hypothesis (signal generation); (6) estimation of rates of adverse events following immunization (AEFI) in local populations; and (7) adjust informed consent, contraindications and benefit/risk analysis" (Duclos, 2004).

stability, and cost. The same criteria apply to surveillance in developing countries, although some criteria may require additional consideration in that context (Buehler et al., 2004). At the committee's June 2009 meeting with stakeholders for Goal 5 in the draft National Vaccine Plan, the committee heard that when surveillance data are not used, or findings are not communicated to the workers who gather and report data, the willingness to conduct surveillance may be adversely affected. This remark echoed comments at a past IOM (2007) workshop that when pathways for use of surveillance data are unclear, there is a decreased likelihood that countries will be willing to collect such data in the future because they cannot see a return on their investment.

> The best mix of surveillance interventions will vary from community to community. A challenge now is to do the operations research to adapt academic surveillance concepts to unique community circumstances. This is important not only in communities with strong health systems, but also in developing countries, where nontraditional approaches may be more essential and affordable than in places with a relative abundance of astute clinicians, laboratories, and hospitals, such as the United States. (IOM, 2007:50)

The capacity for surveillance (of disease, vaccine use, and adverse events) in low- and middle-income countries is variable, depending on the perceived importance of surveillance, available resources, infrastructure, regulation, and available expertise. Both in the 2007 IOM workshop and at the committee's information-gathering meeting there was agreement that the U.S. government could contribute valuable expertise to countries developing innovative and appropriate surveillance systems to meet local needs. This may mean employing currently available techniques or may require innovative techniques (Curioso et al., 2005, 2007).

Laboratory capacity is also a critical component of effective vaccine-preventable disease surveillance. For example, laboratory diagnosis of yellow fever is invaluable because the clinical presentation can be non-specific and confused with other conditions. Also, determining the serogroup and type of an appropriate sample of meningococci has been useful for assessing the potential and actual impact of vaccines. Improved and rapid agent-specific laboratory and field diagnostics to support surveillance objectives could be useful tools. Whatever the type of surveillance and new technologies employed, they need to be used in a thoughtful, well-planned manner that does not burden the system.

The history of global polio immunization programs raises some important questions about the future of immunization infrastructure and capacity, including surveillance, in a polio-free world. Polio eradication programs have served as a model for other programs, such as measles, and have led to the creation and mobilization of a variety of resources, including expertise. U.S. plans for technical assistance and resources to support capacity building

need to consider the transition away from polio to other diseases once polio is eradicated. This would help to ensure that the decades of good work on polio eradication serve as a foundation for more widespread strengthening of all components of the immunization and public health infrastructure in developing countries.

There are several interesting case studies in global disease surveillance. One comes from GAVI's Pneumococcal Vaccines Accelerated Development and Introduction Plan surveillance initiative, which aimed to "strengthen and expand surveillance of bacterial meningitis and pneumonia in developing countries" (Levine et al., 2009). The initiative included approximately 90 sites in 15 countries, and a March 2009 supplement to the journal *Clinical Infectious Diseases* included overviews of some of these activities (Levine et al., 2009). The initiative conducted surveillance through networks of sites that were created and sustained through annual meetings for sharing of data, best practices, and experiences. The initiative was primarily a collection of specifically-funded applied research studies, but it facilitated collaborations between national government decision makers and researchers, and may provide some interesting lessons that could be applied to more routine surveillance systems.

Global surveillance for avian influenza (H5N1) provides another case study of surveillance needs. The Wildlife Conservation Society has worked with individual governments to conduct surveillance of avian flu in wild birds (basic epidemiology and viral sample collection and characterization) in Mongolia. That surveillance program provided a candidate virus for the development of a human H5N1 influenza vaccine. These efforts have recently been integrated and combined with the global avian influenza network for surveillance to expand international surveillance for influenza in wild birds and promote the dissemination of surveillance information to governments, international organizations, and the private and public sectors. A key strategy has been training individuals and organizations to collect samples for analysis, and results are provided in an open access database.

Although surveillance of adverse events following immunization in low- and middle-income countries is extremely limited and the underlying infrastructure is also limited, some targeted efforts have shown that adverse event surveillance is possible, especially in areas that have a basic public health infrastructure, such as health districts and personnel who can take reports and, in turn, convey them to central authorities.

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6

Coordination

Effectiveness in achieving the goals of the National Vaccine Plan requires (1) agreement on a shared purpose and vision among all relevant government entities and stakeholders, and (2) coordination of the complex network of actors and activities needed to achieve this goal.

As the committee noted in its June 2008 letter report,[1] it is impossible to evaluate the effect of the 1994 plan (HHS, 1994) because it had few measurable objectives and was largely a collection of short-term activities that were part of agency strategic plans and were scheduled to occur regardless of the National Vaccine Plan. Also, by many accounts, the 1994 plan developed by the National Vaccine Program Office (NVPO) with input from other agencies in the Department of Health and Human Services (HHS) was shelved (IOM, 2008). It was neither designed to be nor played the role of a "living" strategic document, and was not updated or evaluated as required by the 1986 law[2] that called for a National Vaccine Plan.

The committee's charge did not explicitly mention the matter of coordination. However, coordination is at the heart of the National Vaccine Plan purpose, which is "to promote achievement of the National Vaccine Program mission by providing strategic direction and promoting coordinated action by vaccine and immunization enterprise stakeholders" (HHS, 2008:8). For this reason the committee found it difficult to separate the goals and the priorities identified for the plan from the question of how coordination on these matters could be accomplished. Additionally, in a letter to the Institute

[1] Full letter report available in Appendix D.

[2] National Childhood Vaccine Injury Act, Public Law 99-660, 42 U.S.C. 300aa-1, § 2101 1986.

of Medicine (IOM) committee (provided in Appendix B) the National Vaccine Advisory Committee (NVAC) urged the IOM committee to comment on NVPO's coordinating role with regard to the National Vaccine Plan, including interagency and interdepartmental coordination and coordination with external stakeholders.

In this chapter, the committee examines what it considers the inextricable link between NVPO's effectiveness to coordinate and the plan's success, and develops the rationale for strengthening NVPO to ensure successful implementation and maintenance of the National Vaccine Plan as a tool for coordination on critical issues in the national vaccine program.[3] This chapter also discusses several case studies that illustrate the effects of a lack of coordination: unmet challenges and unmet statutory responsibilities.

COORDINATION: ESSENTIAL TO PLAN SUCCESS

The IOM committee received input from multiple stakeholders on NVPO's role, authority, and resources and its ability to coordinate on communication and research prioritization (IOM, 2009a,b,c). NVPO's role and effectiveness also have been reviewed and discussed by Cooper et al. (2008), and were the subject of an evaluation conducted by RAND Corporation. RAND found that NVAC's role and effectiveness have suffered as a result of the fact that NVPO is underfunded and understaffed (Ringel et al., 2009).

The committee believes that coordination will not occur in areas where it is needed in the absence of a federal entity that can support it, and that the 1986 National Childhood Vaccine Injury Act (NCVIA) defined such an entity and outlined its responsibilities. NVPO was established to comply with the act but has not been given the opportunity to play the crucial role described in the statute (i.e., "coordinate and provide direction" to relevant government agencies in several areas of the National Vaccine Program).[4] It was not given the resources described in the act or the authority needed to motivate and facilitate coordination on major challenges facing the U.S. immunization effort in the past two decades.

Public administration literature on interorganizational coordination

[3] In this report, the committee uses *national vaccine program* in lower case to denote the vast and complex network of actors and actions related to vaccines and immunization, and uses *National Vaccine Program* (per the 1986 act) when referring to the governmental agencies that have responsibilities related to vaccines and immunization.

[4] The 1986 act charged the National Vaccine Program (whose operational arm is NVPO) with coordinating and providing direction in the areas of vaccine research, vaccine development, safety and efficacy testing of vaccines, licensing of vaccine manufacturers and vaccines, distribution and use of vaccines, evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities; with coordinating governmental and nongovernmental activities; and with funding of federal agencies in implementing the National Vaccine Plan.

offers several concepts that may be useful to understanding the role and potential of NVPO. The National Vaccine Program is an interorganizational network—a set of federal organizations linked by common purpose in relationships that vary in strength and complexity (Provan et al., 2007). The literature describes entities such as NVPO as *network administration organizations* (Provan et al., 2007) or as *coordinating units* (Alexander, 1993). These terms refer to entities created expressly to support and facilitate coordination and collaboration among the organizations in a network; these entities generally do not have any "line" functions and are not responsible for implementing any of the tasks they are charged with coordinating (Alexander, 1993). However, entities charged with facilitating interorganizational coordination have the potential to be powerful and effective under certain conditions. Notably, a balance of authority and resources is needed to enable such entities to be effective—"If it has decision-making power but lacks implementation resources, the coordinating unit may suffer a 'crisis of competence;' if it controls resources but lacks authority, it may encounter a 'crisis of legitimacy'" (Alexander, 1993:337). As discussed in this chapter and elsewhere in the report, NVPO has neither sufficient authority to "coordinate and provide direction"[5] nor resources to accomplish its statutory responsibilities and optimally support the various roles it plays as a coordinator both within government and with stakeholders.

Interorganizational networks use a variety of formal and informal tools to facilitate coordination, including agreements, contracts, and plans (Alexander, 1993; Graddy, 2008; Provan et al., 2007). The coordinating tool for the National Vaccine Program is the National Vaccine Plan, but as noted in this report, it has been underused.

The need for high-level coordination in important areas of the National Vaccine Program has been noted by a Congressional Research Service report that described the large group of federal agencies with roles in vaccines and immunization but noted that "[t]here is no central federal authority for vaccine policy" (Thaul, 2005),[6] and has been noted repeatedly by NVAC (NVAC, 2009; Appendix B). Over the years, there have been efforts at different levels to coordinate the actions of government agencies responsible for vaccine and immunization policies and programs. The large and complex network of government agencies and diverse stakeholders understandably requires a variety of mechanisms, processes, and groups to achieve some shared goals. Examples of prior or existing entities created within the National Vaccine Program include the Interagency Vaccine Group, an ongoing activity, and the Task Force on Safety of Childhood Vaccines, a temporary group that produced an important report on vaccine safety (NIAID, 1998).

[5] National Childhood Vaccine Injury Act, Public Law 99-660.

[6] Similarly, a 1993 report of the HHS Office of the Inspector General described NVPO's mission as "bring[ing] coherence to a fragmented immunization system" (OIG, 1993).

Similarly, each government agency undertakes its own internal efforts to coordinate activities and ensure efficient and satisfactory achievement of its own strategic plans, budgetary imperatives, and commitments to constituencies.

It is apparent that the responsibilities of the National Vaccine Program described in the 1986 statute do not refer merely to ad hoc interorganizational committees or other informal and often temporary structures for coordination (called *interorganizational groups* in the public administration literature [Alexander, 1993]). The law clearly describes a central coordinating unit with its own budget, staff, and scope of work separate from those of federal agencies concerned with vaccines and immunization, and NVPO was clearly established to be that entity. Below, the committee summarizes some of the differences between interorganizational groups (in this case, the Interagency Vaccine Group) that arise within networks such as the National Vaccine Program, and coordinating units, such as NVPO, that are created, resourced, and empowered specifically to facilitate coordination (see Table 6-1).

Why Authority and Resources Are Needed

> What then is the nature of structural arrangements that are likely to be associated with inter-organizational effectiveness? First, a clear delineation of roles and responsibilities is critical for effective collective action. Transaction costs decline and uncertainty is reduced when the roles of constituent parties are clearly delineated. In addition, some mechanism must direct resources to collective activities, rather than individual organizational goals. (Graddy, 2008)

NVPO's authority to facilitate and even compel coordination in areas of great importance to the success of the National Vaccine Program was never clarified, and the office has struggled to reach its full potential. NVPO is located in the Office of Public Health and Science, which is led by the Assistant Secretary for Health. It seems that soon after the act was signed into law by an administration that had "grave reservations" about it (Reagan, 1986), the National Vaccine Plan and the statutory requirement for a process of implementing, assessing effectiveness of, and periodically updating the plan ceased to be a priority for HHS leadership. Over the following two decades, NVPO's budget to support coordination never reached even the baseline established by the 1986 act (see Introduction for additional information).

In 1986, the Assistant Secretary for Health had line and budgetary authority over the agencies of the Public Health Service (PHS). Following major changes in the composition of the department in the 1980s and 1990s, authority over the PHS agencies was transferred to the Secretary of HHS and the Assistant Secretary for Health was named primary advisor to the Secretary on public health matters (HHS, 2009). Some attribute the

TABLE 6-1 Comparison of Two Types of Coordinating Mechanisms at HHS

Coordinating Structure	Interorganizational Group	Coordinating Unit
Example	• The Interagency Vaccine Group and similar entities	• National Vaccine Program Office
Resources	• No separate resources for the group • No staff to support the group • Representatives of different agencies (e.g., CDC,[a] NIH,[b] FDA),[c] each with its own authority, agenda and priorities, responsibilities, budgets, expectations, etc.	• A separate budget, authority (derived from statute and endorsed by Secretary and Assistant Secretary of Health) • Dedicated staff charged with facilitating interagency coordination and other related duties (NVPO serves as secretariat of NVAC)
Purpose	• Confer, share information, work on issues of mutual interest through regular meetings and calls	• Coordinate and provide direction on longer term strategic issues described in the National Vaccine Plan
Public interface	• None[d]	• National Vaccine Advisory Committee

[a] Centers for Disease Control and Prevention.
[b] National Institutes of Health.
[c] Food and Drug Administration.
[d] However, some of the agencies represented have their own federal advisory committee.

challenges faced by NVPO to the shift in the role of the Assistant Secretary for Health, but it is unclear whether that is the case. The committee believes that a structural change is not necessarily an appropriate solution for an operational problem. The Assistant Secretary for Health represents the Secretary. Therefore, a strong secretarial endorsement of NVPO and the National Vaccine Plan, conveyed through the Assistant Secretary as a departmental policy and priority, and a forceful call for the full participation of relevant HHS agencies would be sufficient to clarify NVPO's authority and the plan's relevance.

Information gathered for a 2009 review of the effectiveness of NVAC

in fulfilling its role as advisors to the National Vaccine Program and its Director (the Assistant Secretary for Health) included input from former and current members of NVAC, and NVPO's lack of resources and adequate staffing was a frequent theme of key informant interviews (Ringel et al., 2009). The review also included references to areas where NVPO expertise could be strengthened, such as communication.

Effects of the Gap in Coordination

Evidence of the need for a higher level of coordination and an effective coordinating entity may be found in two areas: (1) unmet challenges and (2) unmet statutory responsibilities described by the 1986 act.

Unmet Challenges

First, the need for alternate production methods for influenza vaccine (such as cell culture) has been recognized for decades, but manufacturers continue to rely on egg-based vaccine production nearly seven decades after development of the first influenza vaccine. Significant progress in the direction of cell-based vaccine was not made until the emergence of the 2009 influenza pandemic and the critical need to increase vaccine production capacity. Although many factors contributed to maintenance of the status quo, one can postulate that a coherent effort led by NVPO could have encouraged targeted research funded by the National Institute of Allergy and Infectious Diseases (NIAID) to undertake the necessary initial studies. Strategic approaches to licensing alternate production methods would need to engage the Food and Drug Administration (FDA), but would also need to consider financial incentives. As an example, companies currently have little or no incentive to invest the very substantial financial and personnel resources needed to apply for licensure of a new production method when the current method is viable.

Pandemic influenza also provides a positive example regarding the utility of NVPO coordination. The emergence of H1N1 has occasioned a newly heightened profile for NVPO that has filled the gap of limited coordination among the various government agencies, including FDA, CMS (Centers for Medicare & Medicaid Services), CDC (Centers for Disease Control and Prevention), and the Department of Defense, responsible for managing some aspect of H1N1 vaccine safety. NVPO convened an interagency working group to ensure coordination and collaboration on safety protocols related to the 2009 H1N1 pandemic influenza vaccine and is providing a crucial convening function and serving as a clearinghouse for all safety information

related to the new vaccine.[7] With regard to the H1N1 pandemic influenza vaccine effort, NVPO's potential as a coordinating entity has blossomed. The Assistant Secretary for Health and the Assistant Secretary for Preparedness and Response have shown support for NVPO in letters to NVAC and comments made at meetings. It is important to ensure that this example of NVPO's potential does not remain a rare exception and that it is not dependent on the support or goodwill of specific individuals or officials. The full support and imprimatur of the Secretary of HHS is needed to clarify NVPO's authority.

Second, communication about vaccine safety issues—clarity and transparency about the safety system, including areas of uncertainty—has been a consistent challenge that has not been appropriately met. By calling for a coordinated national strategy for vaccine communication and its well-resourced implementation, the National Vaccine Plan and coordination by NVPO can help guide public health communication about vaccines and immunization toward greater transparency, sophistication, and cohesion. The public engagement efforts conducted by CDC and increasingly, by NVPO, illustrate one positive area of vaccine communication, where efforts are made to bring together the public health and medical communities with groups opposed to vaccines (and others whose concerns about vaccine safety inform their refusal of some or all vaccinations).

Third, in Chapter 1 the committee discussed the need for a periodic, systematic process for prioritizing candidate vaccines and recommended more coordinated research and development of priority vaccines. The committee asserts that enhanced coordination by a stronger and better resourced NVPO may have supported the establishment and maintenance of such a process sooner. Such an action could have led to better alignment of basic research with public health and other needs for specific vaccines. As further discussed in Chapter 1, pharmaceutical research has made advances in identifying compounds that may enhance immune response to a vaccine. These compounds, called adjuvants, may be added to a vaccine or may be administered concurrently with a vaccine, and effects of their use may include needing less antigen in the vaccine and better immune response in the elderly and newborns (Aguilar and Rodríguez, 2007). Due to several regulatory and scientific obstacles, the United States has been slower to evaluate and license vaccines containing adjuvants other than alum. Novel adjuvants may pose novel safety concerns, but they also may hold great promise with their potential to lessen the amount of antigen needed and to strengthen immune reaction and therefore, vaccine effectiveness, in older adults. The committee asserts that enhanced coordination by a stronger and better resourced NVPO might have contributed to more rapid resolution of

[7] Personal communication, G. Lee and S. Black, September 9, 2009.

scientific and regulatory questions (including concerns about the safety of adjuvants) and integration of adjuvants into U.S. vaccines. As an example, one of NVPO's responsibilities is a convening role. Through the membership of NVAC, NVPO is uniquely able to engage industry representatives with other stakeholders. NVPO and NVAC have convened meetings and developed proceedings and reports on several matters of relevance to the future of the vaccine industry. These included the 2000 Workshop on Aluminum in Vaccines, which included a call for research on new adjuvants (Eickhoff and Myers, 2002).

Statutory Responsibilities That Have Not Been Met

The 1986 NCVIA charged the National Vaccine Program, and thus NVPO, to provide supplementary funding to government agencies (e.g., CDC, NIH [National Institutes of Health], FDA) to implement the National Vaccine Plan.

> The Director of the Program shall make available to Federal agencies involved in the implementation of the plan[8] issued under section 2103 funds appropriated under section 2106 to supplement the funds otherwise available to such agencies for activities under the plan. (Public Law 99-660, Title XXI, Subtitle 1, Section 2102:3757)

Section 2106 of the act authorized the appropriation of $20 million dollars in the first year of the program's existence (projected to be 1987, but NVPO did not come into existence until 1991), with annual increases of $2.5 million. This level of funding was never allocated to NVPO, and as described in the introductory chapter, NVPO's funding decreased sharply for several years, and then increased to its current, modest level of just under $7 million (House of Representatives, 1995). As a result of its limited funding and staffing, NVPO's ability to "coordinate and provide direction" in the areas outlined by the act has been hampered, resulting in the missed opportunities described above.

FACTORS CONTRIBUTING TO THE PROBLEM

There are several factors that contribute to the problem of an inadequately supported NVPO, a National Vaccine Plan that was not updated, and a series of major and persistent systemic challenges (including the unmet challenges described above) that have not been addressed sufficiently. Factors include (1) statutory limitations, (2) inadequate funding and staff resources for NVPO, (3) vaguely defined responsibilities for NVPO, and (4) resistance from other agencies and inertia.

[8] Section 2103 calls for the National Vaccine Plan.

First, the 1986 act is limited in two ways. Its existence alone will not ensure that the activities described will be accomplished. Attention and support at the departmental level is necessary. Further the act itself lacks any built-in incentives for the department to support the formal structure for coordination it describes, to attract the relevant agencies to work with NVPO as the coordinator, and to actively participate in developing an actionable and measureable (in terms of outcomes in disease prevention, innovation, and efficiency and effectiveness in the delivery of immunization services) plan, which is needed to ensure the plan's success.

Second, NVPO's funding and staff resources are not adequate to support its coordinating role. At the time this report was written, NVPO had a staff of five and a budget of $6.9 million for FY2009. The budget covers the FTEs (full-time employees) and program activities, including the Strategic Issues in Vaccine Research Program (SIVR, known before 2007 as the "unmet needs fund") that has provided competitive, peer-reviewed grants to HHS agencies and academic researchers. According to NVAC meeting materials from 2005 and 2006 (the most recent information about the program that is publicly available), the research fund supported projects totaling approximately $4-5 million dollars (NVAC, 2006; Schwartz, 2005, 2006). The minutes from a 2007 NVAC meeting include the following description of 2007 funding disbursed by the program:

> A total of 31 projects were funded from a pool of over $4 million, with an average award of $129,000. Of these projects, 19 were continuation projects in one of the previous year's priority topic areas, and 12 projects are new proposals in one of the 5 priority areas for 2007 established with NVAC input: Vaccine safety, adolescent vaccination, vaccine economics and financing, public engagement, and improved diagnostic tests for vaccine-preventable diseases (VPDs). Notably, nine of the new projects included interagency collaborations, a real success of the program. (NVAC, 2007)

The SIVR program is a unique mechanism for dispersing funding to conduct research that may not be supported by other federal agencies to advance vaccine research. (This is consistent with provisions in the 1986 act that called for specific funds to "supplement the funds otherwise available to such agencies for activities under the plan" [Public Law 99-660, 42 U.S.C. 300aa-6].) It is also noteworthy that collaborative interagency projects funded by the program constitute a concrete and potentially fruitful way to facilitate collaboration on critical issues.

Third, NVPO's role is vaguely defined. On NVPO's website, its role is described as "coordinating and ensuring collaboration among the many federal agencies involved in vaccine and immunization activities. The NVPO provides leadership and coordination among Federal agencies, as they work together to carry out the goals of the National Vaccine Plan" (NVPO, 2009). The website lists the following NVPO functions:

- Coordinate and integrate activities of all federal agencies involved in immunization efforts,
- Ensure that these agencies collaborate, so that immunization activities are carried out in an efficient, consistent, and timely manner,
- Develop and implement strategies for achieving the highest possible level of prevention of human diseases through immunization and the highest possible level of prevention of adverse reactions to vaccines, and
- Ensure that minimal gaps occur in federal planning of vaccine and immunization activities.

The committee believes that NVPO is capable of playing several very specific roles in fulfilling its statutory responsibilities, some in conjunction with and in support of NVAC. Some of these roles are currently part of NVPO's scope of work but can be considerably strengthened and expanded. Others are consistent with statutory framework provided by the 1986 law and denote areas of potential NVPO activity. These roles include

1. Facilitating expert guidance on emerging issues characterized by high level of uncertainty, unfolding in real-time, and requiring rapid response,
2. Public engagement on major topics in vaccines and immunization,
3. Convening a diverse range of stakeholders to discuss complex challenges in the field,
4. Funding certain types of research through its fund for the SIVR program (proposals are peer-reviewed by NVAC),
5. Assisting in the formation of communication strategy and coordinating department-level/interagency messages to the public about vaccine issues,
6. Through NVAC, providing a unique forum in which industry representatives can fully participate, and
7. Spotlight special critical issues (examples include the measles White Paper that represented an analysis of system failures leading to the measles epidemic of 1989-1990 [NVAC, 1991], influenza vaccine shortages, and topics in vaccine research and development) and effectively communicate them to diverse audiences including the public.

NVPO's functions would not involve micromanaging or second-guessing specific aspects of vaccine regulation or research spearheaded by other agencies. PHS agencies (e.g., CDC, FDA, NIH) have their own strategic plans, agendas, priorities, and budgets. NVPO's coordinating role would be limited to issues of a high (policy) level and great importance that require joint action and input or assistance from the stakeholders.

Finally, as it is frequently noted, everyone likes coordination but no one

wants to be coordinated. Given NVPO's lack of authority and resources that could serve as incentives for agencies to work together on specific issues, it seemed apparent to the committee that there has been some understandable resistance by various agencies to become fully involved in the type of coordination described in the 1986 act. For example, the committee heard at its first meeting in March 2008 that because agencies' primary commitments are to their mission and their own strategic plans, that will inevitably affect how they will view a call to interagency coordination (IOM, 2008). The committee also heard statements suggesting that government collaboration may be most effective and productive:

- in response to a crisis (e.g., SARS, H5N1, and current H1N1 experience); and
- when there is a congressional mandate, as was the case with the successful effort to accelerate acellular pertussis vaccine development that involved NIH/NIAID, FDA, and support from NVPO (Klein, 1995).

Although sympathetic to the intense challenges and demanding agendas that face federal agencies, the committee believes that NVPO can and should be more proactive in assuming responsibility for implementation of the National Vaccine Plan, and the agencies more receptive to NVPO's coordination than has been the case in the past. The committee asserts that a fundamental contribution of an effective strategic plan for coordination is that it positions partners (e.g., agencies and stakeholders) both to be proactive and to be strategically and synergistically reactive. The challenging contemporary environment on matters related to vaccine communication and vaccine safety is something akin to a crisis that in the committee's view warrants collaboration and coordination. Also, limited high-level support for NVPO and the plan as evident in inadequate funding of the office and in the 14 years that passed between the first and second plans, the lack of clarity about NVPO's functions and relationships with agencies, and the lack of a clear vision in the draft plan may all contribute to agency reluctance to fully participate in the plan.

FIXING THE COORDINATION GAP

Although coordination is not always possible, or even necessary, there are areas where it is critical. For example, using a vaccine research agenda to spur the efficient development of priority vaccines requires coordination at a high level. Building a structured way of identifying and addressing emerging safety information, where appropriate, useful, and realistic, requires input from multiple agencies and external stakeholders. Each agency has its own fairly distinct responsibilities in the area of vaccines and vaccination, but

there are areas where it is important to ensure cost-effective use of finite funds available to the federal government and to address redundancy and duplication of effort. There also are areas where one agency's efforts are not enough to reach an important goal, and where coordination between the federal government and stakeholders is necessary.

Based on its information-gathering, including input from national stakeholders, and on its review of the evidence, the committee believes that the absence or gap at the heart of the nation's vaccine program is at least a partial hindrance to addressing some of the most important challenges facing the program, including addressing public concern about the safety of vaccines, taking full advantage of the national health information technology effort (to support the data and scientific needs of the immunization program), and ensuring that the national effort to transform health care strengthens the availability, quality, and access to immunization services.

The committee asserts that because vaccines and immunization constitute a major public health matter that involves multiple government agencies and has great importance to the public's health, an effective coordinating entity is needed, and effectiveness is dependent on authority and funding commensurate with the task at hand. A strengthened NVPO could play the role intended by the 1986 statute in coordinating the nation's actions related to vaccines and immunization. As described in this and previous chapters, coordination could occur in several ways and may involve NVPO in extending, amplifying, or complementing the functions of other HHS agencies with vaccine-related responsibilities by serving as a convener of effective, action-oriented[9] meetings; a resource for strategic planning and evaluation; a funding source for strategic topics in vaccine research (i.e., the SIVR program); and as a better resourced secretariat to support the activities of NVAC. Because it is not part of CDC, NIH, FDA, CMS, or the Health Resources and Services Administration, NVPO occupies a somewhat independent place in the program and has a unique vantage point. Given adequate authority, staff, and funding, it could cultivate its ability to develop the potential afforded to it by that vantage point. An example of NVPO's potential as promoter of interagency coordination may be found early in its history. In 1991, 3 years before its funding and staff were sharply reduced, NVPO provided 8 FTEs and almost $1.9 million to FDA, and that support resulted in development of a safer pertussis vaccine and other vaccine-related activities (IOM, 1993). A contemporary example of NVPO's potential may be found in the assignment to and evolving responsibility of NVPO to coordinate a national response in the monitoring of H1N1 vaccine safety.

[9] Meetings that are more than just a forum for discussion.

Recommendation 6-1: The Secretary of HHS should actively demonstrate the Department's support for the National Vaccine Plan by:

(1) clarifying its primacy as the strategic planning tool applicable to all federal agencies with roles in the National Vaccine Program, and

(2) allocating the resources necessary to assure robust planning and implementation, with coordination by the National Vaccine Program Office.

CONCLUDING OBSERVATIONS

It is important to note here that a plan is a paper document that cannot mobilize action or facilitate coordination by simply being. A stronger, well-resourced NVPO is needed to breathe life into the plan, facilitating initial coordination necessary to bring agencies and stakeholders to the table to finalize and implement the plan, and overseeing the periodic updating of the plan and evaluation of what is achieved.

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Appendix A

Draft Strategic National Vaccine Plan

Draft Strategic National Vaccine Plan

November 26, 2008

Draft Strategic National Vaccine Plan

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Preface: Letter from the Assistant Secretary for Health

Given the importance of vaccines and immunizations in the prevention of an expanding number of infectious diseases, it is important that we – as a Department and as a Nation -- clearly articulate our vision for the vaccine and immunization enterprise. In my role as the Assistant Secretary for Health and the Director of the National Vaccine Program, I have directed and monitored the efforts to update the 1994 National Vaccine Plan

The accompanying draft strategic National Vaccine Plan reflects current priorities and potential future directions for the next decade. This draft Plan offers a clear signal about our goals for vaccines and immunizations to our domestic and international partners in the United States vaccine and immunization enterprise and abroad, both public and private in the United States and abroad. It is a strong beginning, but requires extensive consultation with and input from many partners, including the public. This input will also enable us to develop an implementation plan with discrete activities and measurable milestones. With release of this draft Plan, consultations with stakeholders will begin, led by the National Vaccine Program Office and the National Vaccine Advisory Committee. We all look forward to the final products of these efforts in late 2009.

This draft strategic National Vaccine Plan responds to the mandate of Congress contained in P.L. 99-660, in which the vision of the National Vaccine Program was first outlined. The first National Vaccine Plan had fourteen expected outcomes, most of which have been achieved at least in part. However, the world of vaccines has changed dramatically since 1994, with more diseases for which vaccines could be available, multiple new research tools, many available new vaccines, heightened interest in vaccine safety, new communications tools, and many more people for whom vaccines are routinely recommended.

This draft Plan describes proposed strategies for ways in which the United States can promote immunization to protect the health of all people. Subsequent work with our many partners will enhance and improve this draft, so the final plan can implement strategies to assure all people can benefit from the prevention of infectious diseases.

Joxel Garcia, M.D., M.B.A.
Assistant Secretary for Health
And Director, National Vaccine Program

Acronyms and Abbreviations

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
AEFI	adverse events following immunization
ASPA	Assistant Secretary for Public Affairs (Department of Health and Human Services)
ASPR	Assistant Secretary for Preparedness and Response (Department of Health and Human Services)
BARDA	Biomedical Advanced Research and Development Authority
BLA	Biologics License Application
CDC	Centers for Disease Control and Prevention
CBER	Center for Biologics Evaluation and Research
CMS	Centers for Medicare and Medicaid Services
DARPA	Defense Advanced Research Projects Agency
DoD	Department of Defense
DHS	Department of Homeland Security
DoJ	Department of Justice
DTP	diphtheria, tetanus toxoids, and pertussis vaccine
DTaP	diphtheria, tetanus toxoids, and acellular pertussis vaccine
DTRA	Defense Threat Reduction Agency
DVIC	Division of Vaccine Injury Compensation
FDA	Food and Drug Administration
FY	fiscal year
GAVI	Global Alliance for Vaccines and Immunization, now formally known as the GAVI Alliance
GMP	Good Manufacturing Practices
HBV	Hepatitis B virus
HEDIS	Healthcare Effectiveness Data and Information Set
HHS	U.S. Department of Health and Human Services
Hib	*Haemophilus influenzae* type b
HIV	human immunodeficiency virus
HP2010	Healthy People 2010
HRSA	Health Resources and Services Administration
IDSA	Infectious Diseases Society of America
IHS	Indian Health Service
IOM	Institute of Medicine
IPV	inactivated polio vaccine

MCOs	managed care organizations
MMR	measles, mumps, and rubella virus vaccine (combined)
NCIRD	National Center for Immunization and Respiratory Diseases
NCPDCID	National Center for Preparedness, Detection, and Control of Infectious Diseases
NGO	Non-governmental organization
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NVAC	National Vaccine Advisory Committee
NVP	National Vaccine Program
NVPO	National Vaccine Program Office
OD	Office of the Director
OMHHD	Office of Minority Health and Health Disparities
OPDIV	Operating Division of the Department of Health and Human Services (e.g., CDC)
OPV	oral polio vaccine
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS	Public Health Service
P.L.	public law
STAFFDIV	Staff Division of the Department of Health and Human Services (e.g., Office of Public Health and Science, of which NVPO is included)
TB	tuberculosis
Td	tetanus and diphtheria toxoids (adult formulation)
Tdap	tetanus and diphtheria toxoids, and acellular pertussis vaccine (adult formulation)
UNICEF	United Nations International Children's Emergency Fund (now United Nation's Children's Fund)
USAID	U.S. Agency for International Development
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
VA	Department of Veterans Affairs
VAERS	Vaccine Adverse Event Reporting System
VFC	Vaccines for Children program
VHA	Veterans Health Administration
VICP	National Vaccine Injury Compensation Program
VPD	vaccine-preventable disease
VRC	Vaccine Research Center
VSD	Vaccine Safety Datalink project

WHO World Health Organization

Executive Summary

The National Vaccine Program was established in 1986 to achieve optimal prevention of infectious diseases through immunization and optimal prevention of adverse reactions to vaccines. The purpose of the National Vaccine Plan is to promote achievement of the National Vaccine Program mission by providing strategic direction and promoting coordinated action by vaccine and immunization enterprise stakeholders.

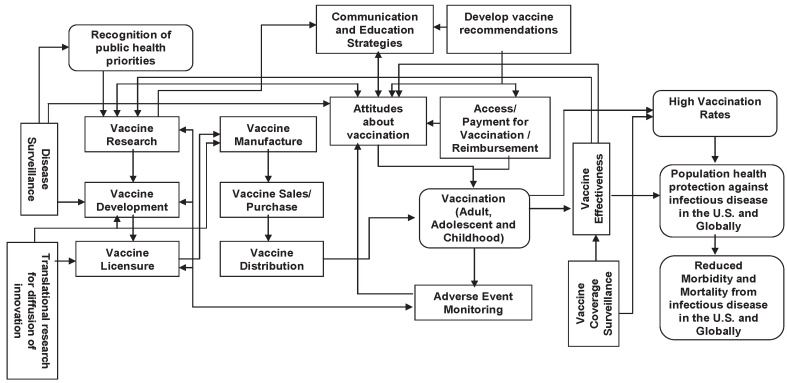
Federal involvement in civilian and military vaccination programs is longstanding, including in research and development, regulation, vaccine delivery and the evaluation of the impacts of immunizations. This draft strategic National Vaccine Plan builds on the many achievements of the vaccine and immunization enterprise prior to and since the establishment of the National Vaccine Program in 1986 and the completion of the first National Vaccine Plan in 1994. New vaccine preventable disease targets have been identified and new vaccines have been developed and licensed; many of these new vaccines are now recommended for children, adolescents and adults. These new vaccines have expanded the number of infections that can be prevented, and more effectively and safely prevent some diseases for which earlier generation vaccines already existed. In addition, federal immunization financing programs have reduced or eliminated many financial barriers to immunizations, particularly for children. The number of infections that are preventable by vaccination has decreased significantly while vaccination coverage in the United States has increased, and coverage for many vaccines has reached record levels. More robust systems have been developed to identify adverse events following immunization and to assess potential associations of those events with vaccination. Globally, the United States has worked with multilateral and bilateral partners and non-governmental organizations in contributing to improvements in child health status and the prevention of hundreds of thousands of child deaths each year through improved vaccine coverage and introduction of new vaccines. Of the fourteen anticipated outcomes included in the 1994 National Vaccine Plan, most were substantially or fully realized (see Appendix 1).

Despite these successes, however, many of the challenges that stimulated establishment of the National Vaccine Program and the development of the 1994 National Vaccine Plan remain relevant today. Vaccine shortages have frequently been experienced for many routinely recommended vaccines. Despite improved vaccination coverage among children, the occurrence of several recent vaccine preventable disease outbreaks serves as a reminder that these diseases still occur. Among older adults both vaccination coverage and the effectiveness of some routinely recommended vaccines remain sub-optimal. As the number of vaccines has increased and vaccine preventable diseases have declined, vaccine safety concerns are expressed more prominently today and may be more widely shared. Enhancing the current vaccine safety system is important to keep pace with several factors influencing it: an increasing number of vaccines and vaccine combinations, expanding target populations, and a better understanding of human biology, especially the human immune system. As the cost of vaccination has increased, financial barriers to vaccination have emerged for health departments, healthcare providers, and the public. Significant scientific challenges remain in the development of

safe and effective vaccines against existing global health threats, such as HIV, TB and malaria. Vaccines that have been developed and are in use in industrialized countries have the potential to make major contributions to health in developing countries, but are being underused. Additionally, emerging and pandemic infections and bioterrorist threats pose new challenges for vaccine development and regulation, manufacturing, vaccine delivery and access in the US and abroad.

In the context of the many challenges and opportunities that exist, updating the 1994 National Vaccine Plan is an opportunity to provide a strategic focus for the nation's efforts to improve disease prevention and enhance vaccine safety. This draft strategic National Vaccine Plan is primarily the result of deliberation, analysis, and input from multiple Federal agencies under the coordination of the National Vaccine Program Office (NVPO). A committee empanelled by the National Academy of Sciences' Institute of Medicine (IOM) reviewed the 1994 National Vaccine Plan and provided guidance on the development of the updated Plan (see Appendix 2). Because successfully preventing infectious diseases and enhancing vaccine safety are outcomes of a complex process, identifying objectives and strategies that lead to and sustain these outcomes is facilitated by understanding the many interconnected determinants of these outcomes. A framework that identifies components of the vaccine and immunization enterprise and illustrates their interrelationships is shown in Figure 1. While a simplification of a complex system, this framework provides an overview of key processes from beginning to end (critical components are shown as rectangular boxes and intermediate and long term outcomes as rounded boxes). The intermediate and long term inputs and outcomes of the vaccine and immunization enterprise include the Recognition of public health priorities, Vaccination (adult, adolescent and childhood), High vaccination rates, Population health protection against infectious disease in the U.S. and globally, and Reduced morbidity and mortality from infectious diseases in the U.S. and globally. The critical components of the vaccine and immunization enterprise that contribute to achieving the desired outcomes include Translational research for diffusion of innovation, Disease surveillance, Vaccine research, Vaccine development, Vaccine licensure, Vaccine manufacture, Vaccine sales/purchase, Vaccine distribution, Communications and education strategies, Attitudes about vaccination, Develop vaccine recommendations, Access/payment for vaccination reimbursement, Adverse event monitoring, Vaccine effectiveness, and Vaccine coverage surveillance.

Figure 1. Overview of the vaccine and immunization enterprise



The goals, objectives, and strategies included in this plan were drafted by Federal departments and agencies for which vaccines and immunization are a significant part of their mission and provide a comprehensive approach to reach these outcomes through coordinated efforts of Federal, State, local, multinational and non-governmental stakeholders. Recognizing that success is facilitated by careful planning that includes defining specific activities, milestones and measurable outcomes, an implementation plan will be developed based on this draft plan. With a ten-year horizon, the framework balances a strategic vision, which requires development and implementation of new initiatives, with the recognition that changing circumstances and new opportunities and challenges will occur over the next decade. The ten-year horizon also allows incorporation of the HealthyPeople 2020 objectives once those are established. Annual monitoring of progress and a mid-course review will promote both accountability and flexibility.

The Plan is built around the achievement of five broad goals:

Goal 1: Develop new and improved vaccines

Goal 2: Enhance the safety of vaccines and vaccination practices

Goal 3: Support informed vaccine decision-making by the public, providers, and policy-makers

Goal 4: Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability and death in the United States

Goal 5: Increase global prevention of death and disease through safe and effective vaccination

These goals will be achieved by pursuing objectives and strategies that address each of the key determinants of those outcomes. Success in achieving these goals will be assessed by tracking progress in achieving measurable outcomes ("indicators") associated with each goal. Final definition of the indicators and the development of specific numeric targets will occur through further consultation with stakeholders and the IOM Committee.

The indicators for each of the goals are listed below (Table 1):

Table 1. Measurable Indicators by Goal in the draft strategic National Vaccine Plan

Goal 1: Develop new and improved vaccines	• Within one year, create an evidence-based list of new vaccine targets to prevent infectious diseases that are high priorities for development. • Identify X candidate vaccines (*e.g.*, for HIV, malaria, TB, and a cross-protective vaccine for influenza) and advance Y priority vaccine candidates along the research and development pipeline including Z candidates into advanced clinical trials. • Advance X new delivery strategies that will improve effectiveness, feasibility, acceptability, safety, or ease of administration of new or improved vaccines into clinical trials. • In X years, have the capability to test potential vaccine candidates in clinical trials developed in response to an emerging infectious disease health threat within six months of the identification of the need for a vaccine.
Goal 2: Enhance the safety of vaccines and vaccination practices	• Conduct and disseminate the results of active and passive surveillance-based safety assessments for newly recommended vaccines or for vaccines with expanded recommendations: ○ Within 1 year of publication in CDC's Morbidity and Mortality Weekly Report of new or revised ACIP recommendations. ○ Within 1 year after X million doses have been distributed • Develop and disseminate plans for further investigation, if any, of newly detected AEFI signals

	and the rationale for those plans within X months of signal detection. • By X year, X % of infants, children, adolescents, adults, and pregnant women will be under active surveillance for AEFIs • Conduct research to explore host factors and biological mechanisms associated with serious AEFIs and annually report results to the Assistant Secretary for Health, vaccine advisory committees, vaccine policy makers and other stakeholders
Goal 3: Support informed vaccine decision-making by the public, providers, and policy-makers	• Enhance communication with stakeholders and the public to more rapidly inform them (within _X_ days) about urgent and high-priority vaccine and vaccine-preventable disease issues (e.g., outbreaks, supply shortages, vaccine safety concerns). • __X__ % of the public will report that they are satisfied with how their health care provider answers their questions about the benefits and risks of vaccines by Y (year). • __X__% of the public will report they have access to information which allows them to make informed vaccination decisions for themselves or their children by Y (year). • __X__% of health care providers will report that they have access to accurate and complete information about vaccine benefits and risks and are able to adequately answer questions of parents and patients by Y (year). • __X__ % of key decision- and policy-makers will report they have access to vaccine benefits, risks, and costs to make informed decisions about vaccine policy by Y (year). • By Y (year) all health professional schools and training programs will include vaccine and vaccine-preventable disease content in their curricula, and assess students' and trainees' knowledge. • By Y (year) all relevant health professional certifying examinations will include vaccine and vaccine-preventable disease questions.
Goal 4: Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability and death in the United States	• The United States will have 6 months' supply of all vaccines appropriate to stockpile. • Reduce financial and nonfinancial access barriers, such as cost, availability, and language, to immunization by 2020 so that: ○ _X_% of parents of infants and children report no barriers to immunization;

	○ _X_% of parents of adolescents report no barriers to immunization; and ○ _X_% of adults report no barriers to immunization. • Reach or exceed HealthyPeople 2020 vaccine coverage levels once established, through incrementally increasing coverage rates for pediatric, adolescent and adult populations using coverage levels in 2010 as a baseline. • X% of electronic health record systems and Y% of immunization information systems will include reminder and recall systems for vaccination by Y (year). • Within Y years after its ACIP recommendation, surveillance for at least one major disease outcome for each routinely recommended vaccine will be implemented in X% of states. • The Vaccine Injury Table is updated as needed (at least every X years).
Goal 5: Increase global prevention of death and disease through safe and effective vaccination	• Transmission of wild polio virus will be eradicated by Y (year). • Mortality from measles will be reduced by X% by Y (year) compared with an X (year) baseline. • X% of countries will achieve DTP3 vaccination coverage of 90% or greater nationally (and 80% or greater in each country's district) by Y (year). • Support introduction of new vaccines as part of national vaccination programs: ○ Meningococcal vaccine in all African countries in the "meningitis belt" by Y (year); ○ Rotavirus vaccine in X countries by Y (year); and ○ Pneumococcal conjugate vaccine in Z countries by Y (year). • X countries establish immunization advisory committees by Y (year) that make evidence-based decisions on adding new vaccines to the routine program and monitor program quality, vaccination coverage, and vaccine safety. • X countries enhance injection safety by Y (year) through the use of auto-disable syringes or other safe injection devices (e.g., needle free delivery) for all immunizations.

The current draft strategic National Vaccine Plan is based largely on input received from Federal Departments and agencies. Recognizing that success can best be achieved through a national plan that includes coordinated action by public and private sector stakeholders in pursuit of the Plan's goals, extensive outreach and consultation will be implemented as the Plan is finalized. An IOM committee is holding a series of national meetings focused around each of the goals in which perspectives from many of the stakeholders will be obtained. Following these meetings, the IOM committee will prepare a report that includes conclusions and recommendations about priority actions within major components of the Plan. The National Vaccine Advisory Committee, a Federal advisory committee that includes representatives from many of the key vaccine and immunization enterprise stakeholders, also will implement a process to obtain input from a wide range of stakeholder groups. This input will include comments on this draft Plan and additional strategies that they can contribute to achieve Plan goals. In addition, input from the public will also be solicited to identify priority areas from their perspective. This draft will serve as the basis for the development of the updated National Vaccine Plan and based on this range of input, indicators of measurable outcomes will be determined and priorities will be presented. In addition, an implementation plan will be drafted that identifies specific actions that will be undertaken by government and other vaccine and immunization enterprise stakeholders to achieve the objectives and strategies in the plan and milestones will be established that will allow progress to be measured.. The updated National Vaccine Plan and an accompanying implementation plan is expected to be completed by fall 2009.

Introduction

Federal involvement in civilian and military vaccination programs is longstanding including research and development, regulation, vaccine delivery and the evaluation of the impacts of immunizations. The National Vaccine Program was established by Congress (Title XXI of the Public Health Service Act [Public Law 99-660]) in 1986 to achieve optimal prevention of infectious diseases through immunization and optimal prevention of adverse reactions to vaccines. The Act called for the development of a National Vaccine Plan to guide activities in pursuit of program goals. This initial plan, completed in 1994, defined goals, objectives and strategies to achieve the Program's mission through coordinated action by Federal agencies, State and local governments, and private sector partners including manufacturers and healthcare providers. The four goals of the 1994 National Vaccine Plan were: 1) Develop new and improved vaccines; 2) Ensure the optimal safety and effectiveness of vaccines and immunization; 3) Better educate the public and members of the health professions on the benefits and risks of immunizations; and 4) Achieve better use of existing vaccines to prevent disease, disability, and death.

The National Vaccine Program was established in an environment characterized by U.S. outbreaks of several vaccine preventable diseases, increased public concern regarding vaccine safety, and liability concerns among vaccine manufacturers that had led some companies to stop producing vaccines for the U.S. market. Since 1986, there have been substantial changes in the nation's vaccine program aimed at addressing these issues. The National Vaccine Injury Compensation Program, created through the same legislation as the National Vaccine Program, established a Federal claims process for persons experiencing adverse events following immunization. New vaccine recommendations and increased vaccination coverage among infants and children have reduced the risk of vaccine preventable disease outbreaks and reduced morbidity and mortality from infectious diseases that are now effectively prevented by vaccination. New vaccines have also been licensed by the U.S. Food and Drug Administration (FDA) that result in fewer adverse events compared with previously recommended vaccines (e.g., DTaP), improve effectiveness (e.g., conjugate Hib and pneumococcal vaccines), and expand the number of diseases that can be prevented in children, adolescents, and adults (e.g., rotavirus, varicella, human papillomavirus, zoster). Release of the 1994 National Vaccine Plan[1] coincided with passage of the Vaccines for Children (VFC) amendments to Medicaid (Public Law 103-66), which provides for Federal vaccine purchase for children enrolled in Medicaid, uninsured children, American Indians and Alaska Natives, and underinsured children served through Federally Qualified Health Centers. Through these and other achievements, substantial progress has been made in addressing National Vaccine Program objectives and National Vaccine Plan goals (see Appendix 1).

Despite the successes that have been achieved in disease prevention and enhancement of vaccine safety, many of the challenges that stimulated establishment of the National Vaccine Program and led to the goals defined in the 1994 National Vaccine Plan remain relevant today. Although the specific issues are different, many have concerns about

[1] See http://www.hhs.gov/nvpo/vacc_plan/ for the 1994 National Vaccine Plan

vaccination and vaccine safety, and new communications channels such as the internet have resulted in widespread dissemination of these concerns. Despite an increased number of vaccine manufacturers, several routinely recommended vaccines are produced by single manufacturers and intermittent supply shortages continue to occur. Recent mumps and measles outbreaks and continued circulation of pertussis are reminders that despite changes in vaccine recommendations and higher coverage, vaccine preventable diseases still occur. The pace of development of new vaccines is much slower than advances in our understanding of immunology and several significant infectious diseases remain leading causes of death globally. In the U.S., the success in achieving high vaccination coverage among children has not been replicated for routinely recommended vaccinations among adolescents or adults. And as the cost of vaccination has increased, financial barriers to optimal program implementation have emerged for health departments, healthcare providers, and the public.

Development of an updated National Vaccine Plan to address current challenges and continue progress toward prevention of disease and enhanced safety is informed by an evaluation of the 1994 Plan and its implementation, conducted by a committee empanelled by the Institute of Medicine (IOM). The committee reviewed the goals, objectives, and strategies of the plan; assessed vaccination program progress; heard presentations from Department of Health and Human Services (HHS) agencies; met with government officials and others who were involved or familiar with development of the plan; and reviewed relevant literature. While the committee noted "many remarkable achievements" of Federal agencies working in collaboration with other stakeholders in the U.S. vaccine and immunization enterprise, they also noted that there was little evidence that the 1994 plan guided or motivated activities and it was difficult to attribute the changes that occurred to the plan.[2]

Based on its evaluation, the IOM committee made several recommendations to consider in developing and implementing an updated National Vaccine Plan (see Appendix 2 for the complete IOM recommendations). The committee emphasized the importance of a national rather than Federal plan, recognizing the important roles of many stakeholders in achieving program goals and objectives (see Appendix 3 for a list of key stakeholders in the vaccine and immunization enterprise). Non-Federal stakeholders should be involved in the development of the plan and approaches should be developed to motivate stakeholders to implement activities that achieve plan objectives. The committee also suggested that an updated plan include specific milestones, assignments of responsibility, objective measures, and evaluation mechanisms to increase the likelihood and success of implementation. Recognizing that a strategic plan will not include every activity that should be undertaken, the committee recommended describing the rationale for decisions on what was included.

With respect to the specific content of an updated plan, the committee highlighted several issues. They recommended that the plan include the following:

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[2] See http://www.iom.edu/CMS/3793/55143.aspx for the IOM letter report, Initial Guidance for an Update of the National Vaccine Plan.

- Mechanisms to assess the potential ("horizon") for innovation and new developments in vaccines and promote timely decision-making in response to opportunities and challenges;
- Consideration of vaccine financing issues;
- Focus on disparities in access to vaccines;
- A comprehensive framework for communications with the public and other stakeholders;
- Creative solutions to vaccine supply problems;
- Increased attention to global immunization issues.

IOM committee guidance on process and content has contributed to the development of this draft Plan and each of the issues that have been highlighted is addressed in the Plan or the approach to its implementation.

Purpose, Perspective, and Scope

The purpose of the updated National Vaccine Plan is to promote achievement of the National Vaccine Program mission to prevent infectious diseases and reduce adverse reactions to vaccines by providing strategic direction and promoting coordinated implementation by vaccine and immunization enterprise stakeholders.

Consistent with this purpose, this draft Plan is ***strategic***, defining goals, objectives, and strategies. The Plan is ***national***, defining goals and objectives to pursue through coordinated actions by a broad range of governmental and non-governmental stakeholders. The National Vaccine Advisory Committee, a Federal advisory committee that includes representatives from many of the key vaccine and immunization enterprise stakeholders, will implement a process to obtain input from a wide range of stakeholder groups. This input will include comments on this draft Plan and additional strategies that they can contribute to achieve Plan goals. In addition, input from the public will also be solicited to identify priority areas from their perspective. This draft will serve as the basis for the development of the updated National Vaccine Plan and based on this range of input, indicators of measurable outcomes will be determined and priorities will be presented. Recognizing, however, that success is facilitated by defining and monitoring specific activities, milestones and measurable outcomes, an implementation plan will also be developed. A ***ten-year horizon*** was chosen, balancing strategic vision which requires development and implementation of new initiatives with the recognition that changing circumstances and new opportunities and challenges are likely and may require adjustments to strategies and measurable outcomes.

The scope of the plan is broad, including vaccines and vaccine-related issues for the U.S. and globally. While several currently recommended vaccines prevent non-infectious outcomes – hepatitis B vaccine preventing hepatocellular carcinoma and HPV vaccine preventing cervical cancer – and future vaccines may prevent other cancers, autoimmune diseases, or other non-infectious conditions, based on the statute that established the National Vaccine Program, the focus for this plan is ***prevention of infectious diseases and adverse reactions to vaccines***. Nevertheless, it is clear that progress made for

vaccines that prevent infections will also lead to progress more broadly. In addition, whereas emergency preparedness and vaccines and vaccination for pandemic or bioterrorist threats are important issues and are included in this draft Plan, they are considered more completely in other HHS strategic plans.[3]

Vaccine development, regulation, and program implementation are major components of HHS agency activities and those of other federal departments and agencies (see Appendix 4 for a description of relevant federal agency roles and responsibilities with respect to vaccines and the immunization enterprise). Strategic plans developed by these agencies identify vaccine-related objectives that are consistent with those included in this plan. Appendix 5 lists the agency and department strategic plans relevant to this plan**.** The HealthyPeople 2020 objectives will also be addressed in the Plans once those are established.

Approach to Developing the Draft Plan

This draft strategic National Vaccine Plan is primarily the result of deliberation, analysis, and input from multiple Federal agencies under the coordination of NVPO. Development of the draft Plan proceeded through a series of steps, with additional actions proposed that will lead to its completion (Table 2).

Table 2. Steps in developing and finalizing the draft strategic National Vaccine Plan

- Collection of information from Federal agencies regarding priority issues to address in the Plan.
- Consideration of outcomes and lessons learned from the 1994 National Vaccine Plan and its implementation
- Establishment of the Plan's guiding perspective, structure, and overarching goals
- Development of objectives and strategies that will lead to achievement of the Plan's goals

Next Steps:

- Review and revision, as needed, of objectives and strategies based on input from vaccine and immunization enterprise stakeholders and an IOM committee [ongoing]

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[3] For example, see BARDA strategic plan http://www.hhs.gov/aspr/barda/phemce/enterprise/strategy/index.html

- Public engagement to define values, perspectives, and priorities for the vaccine and immunization enterprise [pending]

- Finalization of the National Vaccine Plan and development of implementation plans that will lead to achievement of Plan goals and strategies [pending]

Analysis and recommendations from the IOM committee, based on its review of the 1994 National Vaccine Plan, provided useful perspectives that contributed to defining the scope of the plan (e.g., as a national rather than Federal plan), the process of development and implementation, and some of the key issues to include. A framework identifying key activities and pathways to achieve vaccine and immunization enterprise outcomes (see Framework) also was developed[4] to facilitate a systematic approach to identifying objectives and strategies whose implementation will lead to achievement of Plan goals.

Objectives, strategies, and indicators by which success could be measured were drafted by lead Federal agencies for each of the five goals. In an iterative process, input was received from other agencies that will contribute to reaching the specific goal and all Federal agencies with a stake in the vaccine and immunization enterprise. Concurrent with this process, the IOM committee held an open meeting at which it reviewed the proposed objectives and strategies for the Plan goal to "Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability and death in the United States." Comments from this meeting also contributed to revision of the draft for this goal.

Stakeholder review is a critical component of finalizing the draft Plan. Because stakeholder activities in pursuit of its goals and objectives will be essential to success, such input will contribute to buy-in, implementation planning, and coordination as activities are implemented. Stakeholder input will be obtained in four primary ways:

- By input gathered by the IOM committee at four scheduled public meetings that will focus on different goals in the plan and will take place before June 2009. These meetings will include participation by stakeholders in medicine, public health, industry, and vaccinology and will include review of the draft Plan and other HHS planning documents[5];
- From interviews of Federal vaccine advisory committee members[6] conducted by NVPO;
- Through a process to engage domestic and international stakeholders coordinated by the National Vaccine Advisory Committee; and
- From input by the public and others in response to a notice in the Federal Register.

[4] RAND Corporation assisted in the development of the framework, under a contract from NVPO .
[5] More about this committee's work can be found at http://www.iom.edu/CMS/3793/51325.aspx.
[6] Committees include the National Vaccine Advisory Committee (NVAC), the Advisory Committee on Immunization Practices (ACIP), the Vaccine and Related Biological Products Advisory Committee (VRBPAC), and the Advisory Commission on Childhood Vaccines (ACCV).

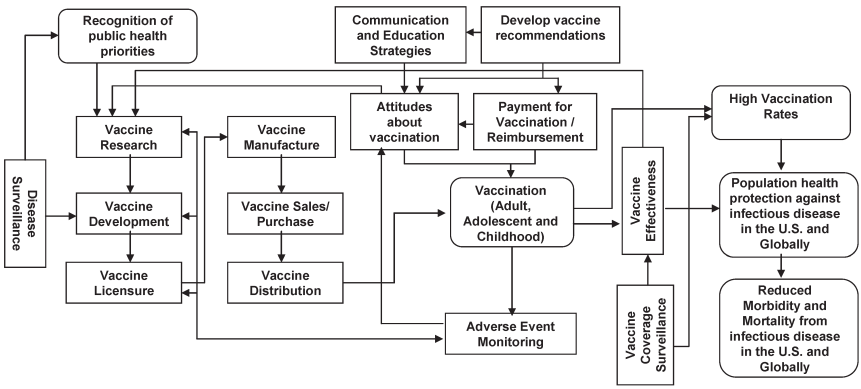
Public input also will contribute to finalization of the Plan. Public values and perspectives can contribute to identifying the most important priorities for achieving and sustaining an effective and safe vaccination program. NVPO will seek input from the general public to assess their expectations and priorities about the Nation's vaccine and immunization activities and programs.

Input and comments from stakeholders, the public, and recommendations from the IOM committee all will contribute to the final Plan to be released in the fall 2009. This plan, in turn, will serve as the basis for implementation planning by Federal agencies that will define specific actions and timelines and measurable outcomes to assess progress in accomplishing each of the strategies in the Plan. Non-Federal stakeholders also will be engaged in this process in order to develop specific actions that they will contribute to achieving the vision and goals of the National Vaccine Plan.

Framework

Disease prevention and enhanced vaccine safety are ultimate outcomes of a successful vaccination program. Identifying objectives and strategies that lead to and sustain these outcomes is facilitated by understanding the many processes or determinants of these outcomes. Figure 2 provides a simplified overview of these complex processes from beginning to end. It shows the key components (the rectangular boxes in Figure 2), the intermediate and long term outcomes (rounded boxes), how they relate to each other, and how they fit together to support the overall mission of the plan.

Figure 2. Overview of the vaccine and immunization enterprise



This complex process of preventing infectious diseases safely and effectively by vaccination begins with the identification of public health priorities informed by disease

surveillance data, which in turn, can guide vaccine research and development priorities. Following the licensure of a vaccine and recommendations for its use, receipt of vaccination requires manufacturing (with ongoing monitoring of product safety and quality) and sales, distribution, storage and handling of vaccines, vaccine payment and reimbursement policy, and communications and education to support decision making about vaccination. Attitudes, vaccination coverage and the effectiveness of disease prevention also are influenced by issues related to vaccine safety and effectiveness. Ultimately, attitudes, safety and effectiveness inform the development of the next generation of new vaccines. The desired outcomes of this process include high vaccination rates which lead to reduced morbidity and mortality from infectious disease in the U.S. and globally, and improved population health. The complex pattern of connections between these components suggests that to achieve the goals of the Plan, the objectives and strategies need to be comprehensive, addressing the vaccine and immunization enterprise as a whole rather than focusing on specific activities in isolation.

Toward that end, the components relevant to each goal were identified. A graphical representation and description of those components is provided for each goal. Then, in an effort to identify the factors critical to the achievement of each goal, a more detailed schematic was developed and analyzed. Objectives were developed to comprehensively address the critical factors for each goal along with the strategies needed to accomplish them. Finally, for each objective, relevant stakeholders were identified.

This approach to the development of the Plan provides a systematic process for identifying objectives and strategies and a rationale for their inclusion in the Plan. Moreover, it helps to ensure that the Plan is comprehensive in its approach to achieving the stated goals. The graphical representation of each component of the Plan, and the identification of key stakeholders involved, form the foundation for accountability in achieving each goal.

As is evident from a review of the figure, some vaccine-related activities are crucial to achieving more than one goal. To simplify the presentation of the plan, objectives and strategies were assigned to a single primary goal area. However, overlap between the goals is identified in the introduction to each goal area and are reflected in the figures showing the key components related to each goal.

A similar approach is being used to develop the corresponding Implementation Plan; that is, mapping the key activities associated with each objective and strategy. Identifying the sequence of steps in this manner facilitates the identification of milestones, for both Federal and nonfederal stakeholders, which can be monitored and reported to ensure that the plan is being implemented.

National Vaccine Plan Structure

The Plan is built around the achievement of five broad goals:

Goal 1: Develop new and improved vaccines

Goal 2: Enhance the safety of vaccines and vaccination practices

Goal 3: Support informed vaccine decision-making by the public, providers, and policy-makers

Goal 4: Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability and death in the United States

Goal 5: Increase global prevention of death and disease through safe and effective vaccination

Vaccine development, safety, and improved vaccine use goals also were included in the 1994 plan. Supporting informed decision-making expands the 1994 plan goal to better educate the public and healthcare professionals on the benefits and risks of immunization. Inclusion of a global immunization goal in this plan emphasizes the key role that U.S. governmental and non-governmental stakeholders can play in enhancing prevention of disease and death throughout the world

Each goal is realized by achieving several objectives that are pursued through defined strategies. Strategies can be mapped back to the key components of the vaccine and immunization enterprise diagram and each of the key determinants of an outcome is addressed by one or more strategies. Reaching goals and objectives generally requires action by many stakeholders in the vaccine and immunization enterprise, while individual strategies may require action by one or a small number of stakeholders.

Success in reaching the goals defined in the final Plan will be monitored by assessing progress in achieving measurable outcomes for each goal. The proposed indicators are measurable outcomes related to this draft strategic Plan's objectives and are directly in a path toward, and critical to, realizing the Plan's goals. Revision and definition of specific numeric targets (milestones) will occur through further consultation with stakeholders and the IOM. Approaches currently exist or can feasibly be established to provide dependable information on progress in reaching these quantitative outcomes. In contrast to milestones or measurable outcomes of individual action steps, indicators are broader and quantify outcomes rather than processes. Indicators in this plan also differ from the fourteen "predicted outcomes" in the 1994 plan which generally were not quantitative and often defined aspirations rather than specific targets.

Monitoring and Evaluation

Monitoring progress toward achievement of the indicators included in this Plan and the milestones in the ensuing implementation plan will contribute to success: both because monitoring stimulates action ("what gets monitored gets done") and because measuring

progress can help identify problems and barriers that require the development and implementation of new approaches.

The National Vaccine Program Office (NVPO) is the principal coordinating office for the National Vaccine Program and reports to the Assistant Secretary for Health, who is the Director of that program. NVPO is responsible for providing leadership, facilitating coordination, and monitoring progress as the National Vaccine Plan is implemented. NVPO interacts directly with each of the HHS agencies and other federal Departments with vaccine and immunization portfolios.

The National Vaccine Advisory Committee (NVAC) is a federally chartered advisory committee which reports to the Assistant Secretary for Health (http://www.hhs.gov/nvpo/nvac) . The Committee includes non-governmental members with expertise in vaccine development, public health and healthcare, and representatives from the vaccine industry and consumers. Liaison members represent Federal agencies with interests in vaccines and vaccination, including the Veterans Administration, Department of Defense and U.S. Agency for International Development; representatives from other vaccine-related advisory committees; and representatives from major stakeholder organizations. NVPO supports NVAC and the NVPO Director is the Executive Secretary for the committee. Given the broad participation in NVAC – either as members or liaisons – of public and private sector vaccine and immunization enterprise stakeholders, the Committee also will have an important role in monitoring progress in achieving National Vaccine Plan goals.

NVPO will be responsible for assuring coordination and for monitoring federal actions and accomplishments on an ongoing basis and NVPO and NVAC will report their findings to the Assistant Secretary for Health annually. This report will include a summary of progress, identify areas where progress is lagging, and propose corrective action where needed. The report also will be presented at an NVAC meeting, which is open to the public and is attended by many stakeholders not represented directly on the Committee.

Key federal stakeholders in global immunization include CDC and USAID . Many of the global immunization targets included in the Plan were established by international organizations (e.g., the World Health Organization) in consultation with U.S. stakeholders. However, the role of those stakeholders in achieving these targets most often involves providing technical assistance and support rather than direct implementation

Many factors may affect the ability to achieve National Vaccine Plan indicators and implementation plan milestones. Existing challenges and barriers may be more difficult to overcome than anticipated and new challenges may emerge. For example, a range of scientific and technical issues may delay development and licensure of new vaccines; safety concerns may affect vaccine uptake; financial constraints may affect vaccination delivery. One of the biggest challenges to success is the availability of resources to implement activities pursuing Plan strategies and objectives. Conversely, opportunities

may emerge that facilitate more rapid progress such that strategies and objectives are reached sooner than anticipated. Recognizing these uncertainties, NVPO will coordinate a mid-course review of the Plan after five years allowing changes to be made which respond to the reality of the environment. Modified indicators, strategies, actions, and milestones will guide subsequent annual evaluation through the overall ten-year horizon of the Plan.

Goal 1: Develop new and improved vaccines
Introduction

Vaccines have changed humanity. In the United States and around the world vaccines (along with clean water and sanitation) are responsible for the most significant impacts on the health of the public. Not only has the investment in vaccine research and development and the implementation of effective vaccine delivery programs led to the eradication and elimination of several serious infectious diseases that were once common, but by preventing diseases from occurring, vaccines can reduce the emergence of antimicrobial resistance, reduce health care costs and pressure on health care systems.

At the core of this progress is the vaccine research and development enterprise that brings scientific ideas forward and, if successful, into the clinic. Vaccine development in the US is comprised of networks of public and private stakeholders that have been successful at bringing many candidates to licensure for commercial use in the US and globally. These stakeholders support various segments of the vaccine research and development process through collaborative and cooperative relationships. Today hundreds of vaccine candidates are in public and private sector vaccine development pipelines. These candidates address a myriad of diseases and utilize an arsenal of new and existing tools to design safe and effective vaccines that can aim at disease targets of public health and biodefense importance. Target populations for these candidate vaccines include routine use in healthy pediatric and adult populations, travelers, the military, and potentially among many sectors in the event of an emerging biological threat.

Understanding the priorities for development and encouraging collaboration between stakeholders (including researchers, manufacturers, funders, and policy makers) is essential to addressing the challenges of making new and improved vaccines for the future. Vaccine development is time and resource intensive. In addition to the technical and scientific challenges that face vaccine researchers and developers, gaps in funding also exist particularly between early phases of pre-clinical and clinical development and the later stages of advanced development (Phase II or III). Fostering continued investment from all sectors ill be increasingly important to harness the full potential of emerging scientific leads as the potential technological approaches and disease targets has expanded and as the costs of developing, licensing, and delivering vaccines has increased. The focus of Goal 1 is to address research and development aspects of vaccines. The research needs of other aspects of vaccines and immunization (e.g., operations research, translational research, behavior and communications research) are included within their respective Goals.

Goal 1 Indicators

- Within one year, create an evidence-based list of new vaccine targets to prevent infectious diseases that are high priorities for development.

- Identify X candidate vaccines (*e.g.*, for HIV, malaria, TB, and a cross protective vaccine for influenza) and advance y priority vaccine candidates along the

research and development pipeline including Z candidates into advanced clinical trials.

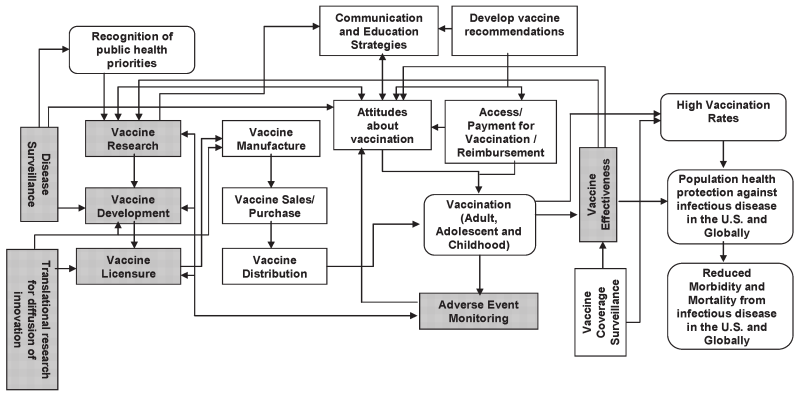
- Advance X new delivery strategies that will improve effectiveness, feasibility, acceptability, safety, or ease of administration of new or improved vaccines into clinical trials.

- In X years, have the capability to test potential vaccine candidates in clinical trials developed in response to an emerging infectious disease health threat within six months of the identification of the need for a vaccine.

Identifying Goal 1 Objectives and Strategies

Figure 3 is the same as Figures 1 and 2, but it shows the components of the vaccine and immunization enterprise (i.e., the shaded rectangular boxes) that play a role in achieving Goal 1 – developing new and improved vaccines. While these components, including disease surveillance, vaccine research, translational research, development and licensure, occur mainly in the early part of the overall process, they are influenced by others such as surveillance related to vaccine effectiveness and adverse event monitoring, which occur later in the process. Disease surveillance continues throughout the process and provides information and feedback for multiple activities. The information from these components feeds back into and informs new vaccine research and development priorities.

Figure 3. Components of the Vaccine and Immunization Enterprise Relevant to Goal 1



Proposed Objectives

Objective 1.1: **Prioritize the needs for developing new vaccines.**

Federal Departments and Agencies[7]: HHS (BARDA, CDC, FDA, IHS, NIH, NVPO), DoD, USAID, VA
Non-federal Stakeholders[8]: Academia, health care providers, philanthropic organizations, the public, state, local, and tribal governments and public health agencies, vaccine industry, WHO

Strategies:

1.1.1 With stakeholder input, develop, implement, and evaluate a process for prioritizing the needs for new vaccines that considers the leading causes of morbidity and mortality from infectious diseases in populations for which vaccines could be a component of an effective prevention strategy.

1.1.2 Conduct surveillance to continuously inform the priorities for potential new vaccines.

Objective 1.2: **Support research to develop new vaccine candidates and improve current vaccines to prevent infectious diseases, particularly those determined to be priorities.**

Federal Departments and Agencies: HHS (BARDA, CDC, FDA, NIH), DoD, USAID, VA
Non-federal Stakeholders: Academia, philanthropic organizations, vaccine investors, vaccine industry

Strategies:

1.2.1 Advance research and development toward new and/or improved vaccines that prevent diseases, including those that protect against emerging, re-emerging, and important biodefense related pathogens.

1.2.2 Conduct and support expanded vaccine research to meet medical and public health needs of specific populations including neonates, infants, the elderly, pregnant women, and immunocompromised individuals.

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[7] Federal Departments and Agencies having a significant role in each objective are listed after the objective, with HHS as the first Department, followed by its agencies in parentheses, then by other Federal Departments and agencies in alphabetical order. These Departments and agencies are listed in Appendix 3.
[8] Non-federal stakeholder sectors considered to have a significant role in an objective are listed after the objective in alphabetical order. The sectors are defined in Appendix 3.

1.2.3 Advance the science of neonatal and maternal immunization including the development of immunological models with which to study maternal immunization and effects on offspring.

1.2.4 Develop a process that identifies current vaccines that would benefit from improved performance characteristics (effectiveness, safety, number of doses, and/or delivery characteristics) and conduct and support studies to bring them to licensure.

Objective 1.3: **Support research on novel vaccine delivery methods.**

Federal Departments and Agencies: HHS (BARDA, CDC, NIH), DoD (DARPA), USAID, VA
Non-federal Stakeholders: Academia, philanthropic organizations, vaccine investors, vaccine industry,

Strategies:

1.3.1 Develop and evaluate alternate delivery methods to improve the protective immune response, safety, effectiveness, and/or efficiency (e.g. number of doses) of immunization.

1.3.2 Expand knowledge of the mechanisms by which induction of protective immunity can be stimulated by immunization through mucosal surfaces and other routes of administration. Include studies to identify and mitigate host factors that may have an impact on the effectiveness of immunizing by these routes.

Objective 1.4: **Support development of vaccine candidates and the scientific tools needed to evaluate these candidates for licensure.**

Federal Departments and Agencies: HHS (BARDA, CDC, FDA, NIH), DoD (DTRA), DHS, USAID
Non-federal Stakeholders: Academia, vaccine industry, philanthropic foundations, vaccine investors

Strategies:

1.4.1 Support applied research to develop rapid and cost efficient production, and optimize formulations and stability profiles of currently available vaccines.

1.4.2 Support research on and development of platform technologies that are applicable to vaccine design and production.

1.4.3 Improve access to appropriately designed pilot lot manufacturing facilities that produce clinical grade material for promising vaccine candidates.

1.4.4 Improve identification of useful biomarkers and immune correlates of protection.

1.4.5 Support translational research that accelerates the development of information that can be used in the product evaluation and licensure process.

1.4.6 Enhance methods and timeliness for conducting risk assessments of emerging variants or strains of vaccine-preventable disease agents, such as emerging strains of human and animal influenza virus.

1.4.7 Establish and strengthen partnerships to address urgent needs in vaccine research and development.

1.4.8. Establish alternative development and manufacturing approaches to support licensure for those vaccines which have a limited market.

Objective 1.5: **Increase understanding of how the host immune system influences vaccine response.**

Federal Departments and Agencies: HHS (CDC, FDA, NIH) DoD (DARPA), VA
Non-federal Stakeholders: Academia, philanthropic organizations, vaccine industry

Strategies:

1.5.1 Expand basic and applied research on innate and adaptive immune responses to infections at different stages of life (e.g., neonate, infant, pregnancy, elderly) in order to advance the understanding of immune protection.

1.5.2 Gain a better understanding of how induction and recall of immune memory may inform the development of vaccines that provide life-long protection.

1.5.3 Enhance research on vaccine effectiveness by continuing to support development of immunomodulators such as new adjuvants and use insights from such research to create novel vaccines and novel formulations of existing vaccines.

1.5.4 Expand knowledge of host related factors that impact severity of disease, and use this information to inform vaccine development.

Objective 1.6: **Strengthen the science base for the development and licensure of safe and effective vaccines.**

Federal Departments and Agencies: HHS (CDC, FDA, NIH), DoD
Non-federal Stakeholders: Academia, vaccine industry

Strategies:

1.6.1 Better characterize product safety and efficacy through research in areas including assay development and characterization of novel cell substrates.

1.6.2 Develop better animal models to study potential correlates of immune response to predict safety and efficacy in humans.

1.6.3 Conduct research to inform feasible ways to provide data to support evaluation and licensure of new vaccines for biodefense related pathogens and rare diseases.

1.6.4 Develop better methods for ensuring control and quality for laboratory, clinical and manufacturing practices related to developing a vaccine.

Goal 2: Enhance the safety of vaccines and vaccination practices

Introduction

The United States has a robust vaccine safety system that has the goal of minimizing the occurrence of serious adverse events from routinely administered vaccines and detecting them in a timely manner when they do occur. Enhancing the current vaccine safety system is important in order to keep pace with a number of factors influencing the system, including: an increasing number of vaccines and vaccine combinations, expanding target populations, and a better understanding of human biology, especially the human immune system. Learning from historic successes and failures (e.g. the Cutter incident) in vaccine safety also offers opportunities for enhancements to the vaccine safety system. In addition to advances in vaccine research and development, pre-licensure evaluation, and post-licensure monitoring advances in medical and information technologies are creating opportunities to further enhance immunization safety. For example, advances in genomics may lead to new ways to identify those at increased risk of adverse events following immunization (AEFI). Expansion of healthcare databases and new approaches to statistical analysis will also provide opportunities to more rapidly identify and evaluate AEFI.

Vaccine safety is a focus of virtually all stakeholders in the vaccine and immunization enterprise including government, research scientists, manufacturers, healthcare providers, professional medical societies, philanthropic foundations, and vaccine recipients. Goal 2 specifically addresses safety-related issues of vaccines and their biological effects as well as the system that monitors the safety of vaccines from production to vaccine administration and use in vaccination programs. Several important vaccine safety issues are also considered elsewhere in this plan. For example, research and development of safer vaccines, including pre-clinical and clinical safety evaluation of candidate vaccines and licensure, are addressed in Goal 1 (Develop new and improved vaccines). Issues related to behavioral science research, education, risk communications and public engagement on vaccine safety are included in Goal 3 (Support informed vaccine decision-making by the public, providers, and policy-makers). Vaccine safety is an important component of every immunization program. These other factors are included in Goal 4 (Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability, and death in the United States) and Goal 5 (Increased global prevention of death and disease through safe and effective vaccination).

Throughout Goal 2, two terms are used that deserve clarification: 'adverse event following immunization' (AEFI), and 'signal.' Respectively, these are defined:

- *Adverse event following immunization* (AEFI) is an adverse event temporally associated with an immunization that may or may not be causally related to the immunization. The term "vaccine adverse event" is also commonly used to convey the same meaning.
- *Signal:* While there are multiple definitions of signals, in this document a signal refers to a concern that an AEFI could be temporally occurring more often than anticipated based on chance alone (i.e., that the event could be related to the

receipt of the vaccine). Signals may arise from a variety of sources, including from pre-licensure clinical trials, case series, surveillance, clinical experience, the literature, expert committee reviews, the media, and/or the public. A signal may also arise from a single individual with a convincing clinical pattern such as a challenge/rechallenge case or instances where the vaccine strain organism (e.g., attenuated virus) is isolated and associated with a pathologic process.

Goal 2 Indicators

- Conduct and disseminate the results of active and passive surveillance-based safety assessments for newly recommended vaccines or for vaccines with expanded recommendations:
    - Within 1 year of publication in CDC's Morbidity and Mortality Weekly Report of new or revised ACIP recommendations.
    - Within 1 year after X million doses have been distributed

- Develop and disseminate plans for further investigation, if any, of newly detected AEFI signals and the rationale for those plans within X months of signal detection.

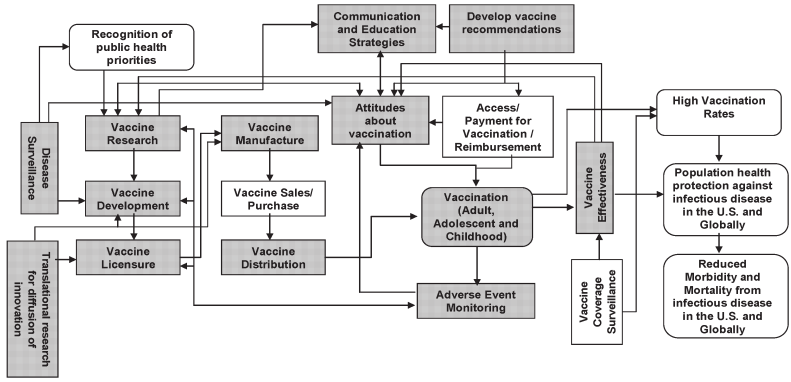
- By X year, X % of infants, children, adolescents, adults, and pregnant women will be under active surveillance for AEFIs.

- Conduct research to explore host factors and biological mechanisms associated with serious AEFIs and annually report results to the Assistant Secretary for Health, vaccine advisory committees, vaccine policy makers and other stakeholders.

Identifying Goal 2 Objectives and Strategies

Figure 4 is the same as Figures 1 and 2, but it shows the components of the vaccine and immunization enterprise (i.e., the shaded rectangular boxes) that play a role in achieving Goal 2 – enhancing the safety of vaccines and vaccination programs. The vaccine safety-related components shown here occur both pre- and post-licensure. However, as noted before, the focus of Goal 2 is on those components which contribute to enhancing the safety of vaccines and vaccination programs post licensure. These components include disease surveillance, vaccine research and development, translational research, manufacturing, developing vaccine recommendations, communications and education strategies, distribution, administration, vaccination of target populations, and monitoring vaccine effectiveness and AEFIs through both passive and active surveillance. The pre-licensure safety-related components, such as research and development of safer vaccines, and the associated objectives and strategies are captured in Goal 1.

Figure 4. Components of the Vaccine Process Relevant to Goal 2



Objective 2.1: Facilitate the continuous modernization of manufacturing sciences and regulatory approaches relevant to manufacturing, inspection and oversight to enhance product quality and patient safety.

Federal Departments and Agencies: HHS (FDA)
Primary Non-HHS Stakeholders: Academia, vaccine industry

Strategies:

Strategy 2.1.1: Facilitate the enhancement of vaccine manufacturing sciences and quality systems, including production technologies, in process controls and testing, and identification of best practices in preventive quality systems and oversight.

Strategy 2.1.2: Develop, implement and periodically reassess risk-based scientific approaches to identify inspectional priorities and best practices.

Strategy 2.1.3: Support new technologies and modernization of both industry and FDA testing of product quality to better prevent and more rapidly detect potential quality or safety issues.

Strategy 2.1.4: Evaluate current regulations, guidance documents, policies and procedures that are relevant to manufacturing to determine enhancements that could be made to promote and enhance product safety.

Objective 2.2: Enhance timely detection and evaluation of vaccine safety signals.

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HRSA, IHS), DoD, VA
Non-federal Stakeholders: Academia, health care system, the public, public and private payers and plans, state, local, and tribal governments and public health agencies, vaccine industry

Strategies:

2.2.1: Improve the effectiveness and timeliness of AEFI signal identification and assessment through coordinated use of national passive and active surveillance systems.

2.2.2: Enhance collection of medical histories and biological specimens from selected persons experiencing serious AEFI reported to the Vaccine Adverse Event Reporting System (VAERS), petitioning the National Vaccine Injury Compensation Program (VICP), and available through active surveillance to enhance study of biological mechanisms and individual risk factors.

2.2.3: Assess lay public and professional questions and concerns about vaccine safety.

2.2.4: Improve the process for assessing AEFI signals to determine which signals should be evaluated further in epidemiological and clinical studies.

Objective 2.3. Improve timeliness of the evaluation of vaccine safety signals when a high priority new vaccine safety concern emerges, a new vaccine is recommended or vaccination recommendations are expanded, and during public health emergencies such as in an influenza pandemic or other mass vaccination campaign.

Federal Departments and Agencies: HHS (BARDA, CDC, FDA, HRSA, IHS), DoD, VA
Non-federal Stakeholders: Academia, health care system, public and private payers and plans, state, local and tribal governments/public health agencies, vaccine industry

Strategies:

2.3.1: Increase the size of the population under active surveillance for serious AEFIs that can be included in high quality, rigorously conducted epidemiological studies to test vaccine safety hypotheses.

2.3.2: Expand collaboration with clinical, laboratory, genetic and statistical experts to conduct clinical research studies to investigate the role of host genetics in AEFI.

2.3.3: Enhance capacity to monitor immunization safety in the event of a mass vaccination campaign.

2.3.4: Provide safety data necessary to conduct informed risk-benefit assessments for utilization of vaccines in mass vaccinations for public health emergencies.

Objective 2.4: Improve causality assessments of vaccines and related AEFIs.

Federal Departments and Agencies: HHS (CDC, FDA, HRSA, IHS), DoD, VA
Non-federal Stakeholders: Academia, health care system, public and private payers and plans, state, local and tribal governments/public health agencies, vaccine industry

Strategies:

2.4.1 As appropriate, develop algorithms and assess the evidence on an individual-level for a causal relationship between certain vaccines and specific serious AEFI.

2.4.2 Assess the evidence on a population level for a causal relationship between certain vaccines and specific serious AEFI.

2.4.3 Regularly update the Vaccine Injury Table based upon individual and population level causality assessments.

Objective 2.5: Improve scientific knowledge about the risk of vaccine adverse events and their mechanisms.

Federal Departments and Agencies: HHS (CDC, FDA, HRSA, NIH), DoD, VA
Non-federal Stakeholders: Academia, Vaccine industry

Strategies:

2.5.1 Identify host risk factors, such as previous or concurrent illness or genetic characteristics that may be associated with increased risk for specific AEFI through basic, clinical, or epidemiological research.

2.5.2 Identify the biological mechanism(s) for specific AEFI that, based upon causality assessments (Strategy 2.4.2), are likely to be causally associated with vaccination.

2.5.3 Assess whether the risk of specific AEFI is increased in specific populations such as pregnant women, premature infants, elderly persons, those with immunocompromising or other medical conditions, or based on gender or race/ethnicity.

Objective 2.6: Improve clinical practice to prevent, identify and manage AEFIs.

Federal Departments and Agencies: HHS (CDC, HRSA, IHS), DoD, VA
Non-federal Stakeholders: Academia, health care system, MCOs, public and private payers and plans, state, local, tribal governments and public health agencies, vaccine industry

Strategies:

2.6.1 Improve training, availability of and access to vaccine safety clinical experts to provide consultation to healthcare providers and public health practitioners.

2.6.2 Develop additional evidence-based guidelines for vaccination or revaccination, as appropriate, for persons at increased risk of AEFI. Identify additional contraindications and precautions to vaccination, as needed.

2.6.3 Reduce errors in vaccine administration (e.g., wrong vaccine, dose, injection site, or timing) and associated adverse patient outcomes.

Objective 2.7: Improve cross-cutting scientific capabilities to enhance vaccine safety and the vaccination safety system.

Federal Departments and Agencies: HHS (CDC, FDA, IHS, NIH), DoD, VA
Non-federal Stakeholders: Academia, the Brighton Collaboration, vaccine industry

Strategies:

2.7.1 Enhance the immunization safety science workforce to recruit and retain additional highly trained scientists and clinicians.

2.7.2 Develop additional standard case definitions for AEFI for use in immunization safety surveillance and research, vaccine safety standards such as concept definitions, standardized abbreviations, and standardized study designs.

2.7.3 Improve laboratory, epidemiological and statistical methods used in vaccine safety research.

Objective 2.8: Enhance integration and collaboration of vaccine safety activities

Federal Departments and Agencies: HHS (AHRQ, CDC, CMS, FDA, HRSA, NVPO), DoD, VA, USAID
Non-federal Stakeholders: Academia, MCOs, public and private payers and plans, vaccine industry, World Health Organization

Strategies:

2.8.1 Improve collaboration, such as data sharing arrangements, across agencies and departments.

2.8.2 Improve information and data sharing with international partners (e.g., national vaccine safety programs) as consistent with ethical and human subjects protections.

Goal 3: Support informed vaccine decision-making by the public, providers, and policy-makers

Introduction

HHS is committed to providing accurate, timely, transparent, complete, and audience-appropriate information about immunizations and vaccines to parents making vaccination decisions for their children (birth through age 18), adults considering vaccines for themselves, public health partners, providers, and others. Communication tools and channels used to disseminate immunization and vaccine information span the spectrum: publication of evidence-based recommendations, use of mass media and new media in campaigns throughout the year, provider education and training in a variety of formats, and support to partner organizations and state immunization programs through provision of resources, trainings, updates, and announcements. HHS also provides immunization and vaccine information to decision-makers in a variety of settings (e.g., health system, executive and legislative government entities).

Current communication efforts are informed by adequate research as well as the principles of effective risk communication. Communication research should be enhanced to facilitate the development of the best messages and methods for transparently, clearly, and effectively communicating about the benefits and risks of vaccines, and addressing information needs and concerns unique to various audiences. The importance of timely audience and message testing research to inform effective communications must not be underestimated. Uninformed strategies could be detrimental to public confidence and ultimately to vaccine coverage and control of vaccine-preventable diseases. By working together, communication scientists, health services researchers and others can develop and implement comprehensive, long-term, sustainable plans for gathering real-time, reliable, and representative data about facilitators of, and barriers to, vaccine acceptance and translate those data into practical solutions.

While the focus of Goal 3 is on communication and education issues relevant to informed decision-making, they are also relevant to each of the other goals of the National Vaccine Plan. Topic-specific communications and education activities are described in Goals 2, 4, and 5.

Goal 3 Indicators:

- By Y (year), enhance communication with stakeholders and the public to more rapidly inform them (within _X_ days) about urgent and high-priority vaccine and vaccine-preventable disease issues (e.g., outbreaks, supply shortages, vaccine safety concerns).

- _X___ % of the public will report that they are satisfied with how their health care provider answers their questions about the benefits and risks of vaccines by Y (year).

- _X___% of the public will report they have access to information which allows them to make informed vaccination decisions for themselves or their children by Y (year).

- __X__% of health care providers will report that they have access to accurate and complete information about vaccine benefits and risks and are able to adequately answer questions of parents and patients by Y (year).

- __X__ % of key decision- and policy-makers will report they have access to vaccine benefits, risks, and costs to make informed decisions about vaccine policy by Y (year).

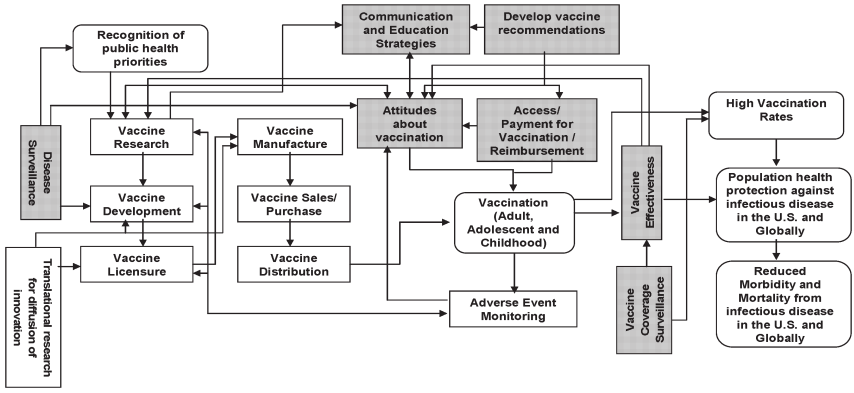
- By Y year, all health professional schools and training programs will include vaccine and vaccine-preventable disease content in their curricula, and assess students' and trainees' knowledge.

- By Y year, all relevant health professional certifying examinations will include vaccine and vaccine-preventable disease questions.

Identifying Goal 3 Objectives and Strategies

Figure 5 is the same as Figures 1 and 2, but it shows the components of the vaccine and immunization enterprise (i.e., the shaded rectangular boxes) that play a role in achieving Goal 3 - supporting informed vaccine decision-making by the public, providers, and policy-makers. The key components include communication and education strategies, development of vaccine recommendations, attitudes about vaccination, access to, and payment for, vaccination, vaccine effectiveness, disease surveillance, and assessment of vaccine coverage.

Figure 5. Components of the Vaccine and Immunization Enterprise Relevant to Goal 3



Proposed Objectives

Objective 3.1: Conduct research and utilize findings in an ongoing fashion to identify communication and education needs and inform communication and education efforts.

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HIS), DoD, VA
Non-federal Stakeholders: Healthcare payers and plans (public and private), healthcare Systems, the public, state, local and Tribal Governments and public health agencies, vaccine industry

Strategies:

3.1.1 Conduct ongoing research to regularly take a "pulse of the public" to identify knowledge, beliefs and concerns about vaccines and vaccine-preventable diseases.

3.1.2 Conduct research on factors (positive influences and barriers) that go into decision-making about vaccination for individuals and families, providers, and policymakers.

3.1.3 Develop and test educational strategies that better enable public audiences and policymakers to read, understand, and use information about vaccine benefits and risks when making immunization decisions.

3.1.4 Continue to assess the effectiveness of specific messages and materials in addressing information needs and concerns based on public and provider attitudes toward the benefits and risks of vaccines.

3.1.5 Evaluate the effectiveness of vaccine benefit and risk communication, overall and for populations known to be at risk of under immunization, and, as needed, update communications.

3.1.6 Gather data to inform communications about the accessibility of vaccines (i.e., where and when to get vaccinated).

3.1.7 Gather data to inform communications activities and vaccine program managers on the direct and indirect costs of vaccination. This includes, but is not limited to, information on federal and state programs that offer low cost vaccines.

Objective 3.2: **Utilize collaborations and partnerships to leverage communication efforts.**

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HRSA, IHS), USAID, VA

Non-federal Stakeholders: Healthcare payers and plans (public and private), healthcare systems, the public, state, local and tribal governments and public health agencies, vaccine industry

Strategies:

3.2.1 Emphasize cross-agency and intra-agency collaboration to inform development of communication research agendas, protocols, campaigns and messages.

3.2.2 Strengthen partnerships and coalitions supporting immunization of children, adolescents, and adults.

3.2.3 Collaborate with partners and stakeholders to communicate vaccine benefits and risks in appropriate languages, methods, and literacy levels.

Objective 3.3: Enhance delivery of timely, accurate, and transparent information to public audiences and key intermediaries (such as media) about what is known and unknown about the benefits and risks of vaccines and the vaccination program.

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HRSA, IHS), USAID
Non-federal Stakeholders: Healthcare payers and plans (public and private), healthcare Systems, the public, state, local and Tribal Governments and public health agencies, vaccine industry

Strategies:

3.3.1 Enhance communication of scientific findings about vaccine safety and effectiveness studies to the public, partners, and providers in a clear, transparent and timely manner.

3.3.2 Consistently and effectively respond in a rapid and coordinated manner to emerging vaccine issues and concerns (e.g. supply, safety or public health emergencies).

3.3.3 More rapidly and completely disseminate research findings through peer-reviewed journals, conferences, and partner communications to facilitate implementation of evidence-based strategies.

Objective 3.4: **Increase public awareness of vaccine preventable diseases, and benefits and risks of vaccines and immunization, especially among populations at risk of under immunization.**

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HRSA, IHS)
Non-federal Stakeholders: Healthcare payers and plans (public and private), healthcare Systems, the public, state, local and Tribal Governments and public health agencies, travel industry, vaccine industry

Strategies:

3.4.1 Develop, implement, and evaluate a long-term strategic communications plan and program aimed at educating parents of children and adolescents about vaccine preventable diseases and the benefits and risks of vaccines.

3.4.2 Maintain up-to-date, easily accessible, evidence based web-based information on vaccine preventable diseases and vaccines, including benefits and risks and the basis of immunization recommendations, for all audience groups.

3.4.3 Use and evaluate new media (such as mobile technologies and social networking), as appropriate, to reach target audiences with accurate and timely information about vaccines and to respond to emerging concerns and issues.

3.4.4 Develop, use, and evaluate evidence-based communication tools to educate parents, adolescents, and adults about vaccine-preventable diseases, recommended vaccines, and preventive health care visits.

3.4.5 Develop, implement, and evaluate interventions to increase knowledge among all travelers about benefits and risks of immunizations before travel.

Objective 3.5: Assure that key decision and policy-makers (e.g., third-party payers, employers, legislators, community leaders, hospital administrators, health departments) receive accurate and timely information on vaccine benefits, risks, and economics, and on public and stakeholder knowledge, attitudes, and beliefs.

Federal Departments and Agencies: HHS (CDC,CMS, FDA, HRSA, IHS), VA
Non-federal Stakeholders: Healthcare payers and plans (public and private), healthcare systems, the public, state, local and tribal governments and public health agencies, vaccine industry

Strategies:

3.5.1 Develop, disseminate, and evaluate business case evidence and guidance for purchasers of health care and for health plans that address the coverage of vaccines in routine health care.

3.5.2 Develop, disseminate, and evaluate broad-based education of key groups (e.g., legislators, community leaders, hospital administrators, health departments) on the benefits, risks, and economics of vaccines, the basis of immunization recommendations, vaccine policy development, and on the standards of immunization practice.

3.5.3 Improve capacity for public engagement initiatives at the national, state and local levels.

Objective 3.6: **Improve the knowledge of vaccines and vaccine-preventable diseases, understanding of basis for immunization recommendations, and immunization practices of all healthcare providers.**

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HRSA, IHS), DoD, USAID, VA
Non-federal Stakeholders: Academia, healthcare payers and plans (public and private), healthcare system, the public, state, local and tribal governments and public health agencies, vaccine industry

Strategies:

3.6.1 Expand and implement training and education of immunization providers at all levels of their education on the proper use of vaccines, the proper storage and handling of vaccines, the basis of immunization recommendations, vaccine safety, and on the standards of immunization practice.

3.6.2 Develop and implement educational strategies for providers on vaccine-preventable diseases, including diagnosis, modes of transmission, prevention and control, and reporting requirements.

3.6.3 Widely disseminate information about vaccines and vaccine use that will assist clinicians assess, report, and manage vaccine adverse events.

3.6.4 Determine the most effective and efficient mechanisms to communicate to health care providers about reporting to VAERS.

Objective 3.7: **Develop and disseminate communication materials that help facilitate active and involved immunization decision-making.**

Federal Departments and Agencies: HHS (AHRQ, CDC, CMS, FDA, HRSA, IHS), DoD, USAID, VA
Non-federal Stakeholders: Healthcare payers and plans (public and private), healthcare system, the public, state, local and tribal governments and public health agencies, vaccine industry

Strategies:

3.7.1 Conduct research on factors that go into decision-making about vaccination.

3.7.2 Conduct research to identify the kinds of information that would support decision-making about vaccination for individuals and families, providers, and policymakers.

3.7.3 Develop evidence-based tools to assist individuals, parents, and providers synthesize relevant vaccine-related information to make informed decisions regarding vaccination.

Goal 4: Ensure a stable supply of recommended vaccines, and achieve better use of existing vaccines to prevent disease, disability, and death in the United States

Introduction

Vaccine-preventable disease incidence is at or near record-low levels for most diseases against which children are routinely vaccinated and vaccination rates are at or near record high levels for infants and children. However, coverage levels are below *Healthy People 2010* targets for many vaccines targeted to adolescents and adults, and substantial disparities exist among racial and ethnic groups in vaccination levels for adults. Ongoing efforts through partnerships among national, state, local, private, and public entities are needed to sustain and improve the use of vaccines in the United States.

Challenges remain for further improving vaccination rates, and for incorporating new vaccines into child and adolescent vaccination schedules. Three new vaccines have been recommended for adolescents by the Advisory Committee for Immunization Practices (ACIP) since 2005: meningococcal conjugate vaccine (1 dose), tetanus, diphtheria, acellular pertussis vaccine (1 dose), and quadrivalent human papillomavirus vaccine (3 doses). ACIP also recommends that adolescents should receive recommended vaccinations that were missed during childhood.

Vaccination rates for adults remain below the HealthyPeople 2010 targets and indicate where substantial challenges lie. These challenges include overcoming health access and financial barriers as well as barriers related to knowledge and attitudes of the public, health care professionals, and health policy and decision-makers. Translational research to assess how best to implement strategies to overcome such barriers is also important.

An additional barrier is assuring a reliable and steady supply of all vaccines in the United States, where shortages of several commonly used vaccines have occurred since 2000 (including *Haemophilus influenzae* type b, hepatitis A, influenza, meningococcal conjugate, pneumococcal conjugate, and rabies). New 21st century vaccine supply concerns are vaccines for pandemic influenza, emerging diseases, and biothreats that present different models for sustainability and surge manufacturing capacity as compared to traditional vaccine models.

Strong public health surveillance that monitors and evaluates vaccine-preventable diseases and the effectiveness of licensed vaccines provides the link between vaccination policy and outcomes. Such public health surveillance is a key component of strategies to overcoming barriers and achieving better use of existing vaccines.

Goal 4 identifies eight objectives and related strategies to keep our nation's vaccination program strong and overcome barriers to continue to improve it. Enhancing communication and education activities to allow improved decision-making about vaccination, are also a key approach to overcome many of the current challenges. Those

concepts are discussed in Goal 3, and have significant relationships to the objectives and strategies presented in Goal 4.

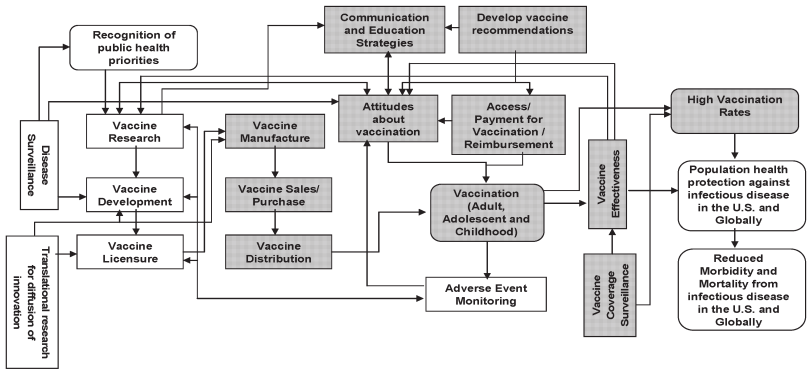
Goal 4 Indicators

- The United States will have 6 months' supply of all vaccines appropriate to stockpile.
- Reduce financial and non-financial barriers to access immunization services, such as cost, availability, and language, by Y (year) so that:
  - _X_% of parents of infants and children report no barriers to immunization;
  - _X_% of parents of adolescents report no barriers to immunization; and
  - _X_% of adults report no barriers to immunization.
- Reach or exceed HealthyPeople 2020 vaccine coverage levels, once established, for pediatric, adolescent and adult populations using coverage levels in 2010 as a baseline.
- X% of electronic health record systems and Y% of immunization information systems will include reminder and recall systems for vaccination by Y (year).
- Implement surveillance for at least one major disease outcome for each routinely recommended vaccine in X% of states within Y years after its ACIP recommendation.
- Through the evaluation of evolving science, ensure that the Vaccine Injury Table is updated on an as needed basis (at least every X years).

Identifying Goal 4 Objectives and Strategies

Figure 6 is the same as Figures 1 and 2, but it shows components of the vaccine and immunization process (i.e., the shaded rectangular boxes) that play a role in achieving Goal 4 - ensuring a stable supply of recommended vaccines and achieving better use of existing vaccines. These focus on what happens post licensure, and include processes related to vaccine manufacturing, purchasing/sales of vaccines, and distribution channels and process for getting vaccines to people, and processes related to vaccine administration. Importantly, they also include processes related to determining which vaccines are recommended for use, and their indications, communication and education about vaccines — to and from the public, providers, and policymakers, as well as assessing attitudes about vaccination. Finally, surveillance related to disease and to coverage levels informs efforts to achieve high vaccination rates through communication and education strategies, and addresses financial and non financial barriers to vaccines.

Figure 6. Components of the Vaccine and Immunization Enterprise Relevant to Goal 4



Proposed Objectives

Objective 4.1: Ensure consistent and adequate availability of vaccines for the United States.

Federal Departments and Agencies: HHS (BARDA, CDC, FDA, IHS, NVPO)
Non-Federal Stakeholders: Health care system, international organizations, national regulatory agencies, state, local, and tribal governments/public health, vaccine industry

Strategies:

4.1.1 Increase US licensed vaccine suppliers to have at least two suppliers of each vaccine antigen recommended for routine use by infants, children, adolescents and adults.

4.1.2 Promote development of high quality harmonized vaccine standards internationally.

4.1.3 Improve product quality and availability through advancing manufacturing sciences, through communication and training in best practices and through better manufacturing and production oversight.

4.1.4 Improve vaccine ordering, distribution and tracking systems for routine use, for public health emergencies, and for management of supply disruptions.

4.1.5 Optimize use, and content, and distribution of vaccine stockpiles.

4.1.6 Improve the development, communication, and tracking of adherence to recommended changes in vaccine use during national vaccine shortages.

4.1.7 Enhance support for international regulatory information sharing and collaboration.

Objective 4.2: Reduce financial and non-financial barriers to vaccination.

Federal Departments and Agencies: HHS (BARDA, CDC, CMS, HRSA, IHS), USAID, VA
Non-Federal Stakeholders: Health care payers and plans (public and private), health care system, state, local, and tribal governments and public health agencies, vaccine industry

Strategies:

4.2.1 Ensure that out of pocket costs for purchase and administration of all ACIP recommended vaccines for children, adolescents, and adults by publicly funded health insurance plans do not represent a significant financial barrier (i.e., Medicare, Medicaid, TRICARE, VA, FEHBP, DoD).

4.2.2 Reduce financial barriers to immunization by increasing the proportion of people with private healthcare insurance who have only minimal cost sharing for purchase, counseling, and administration of all ACIP recommended vaccines for children, adolescents, and adults (regardless of where the vaccines are administered).

4.2.3 Identify and regularly monitor financial and non-financial (e.g., vaccine availability and language) barriers to receipt of ACIP recommended vaccines for children, adolescents, and adults, and regularly publicize the findings.

4.2.4 Strengthen the ability of States to purchase and expand access to ACIP recommended vaccines for people who qualify for publicly supported vaccinations.

4.2.5 Develop, implement, and evaluate strategies to reduce the financial burden on vaccination providers for purchase of initial and ongoing vaccine inventories.

4.2.6 Enhance public sector infrastructure to support and sustain adult immunization activities.

4.2.7 Expand access to vaccination at medical care sites for children, adolescents, and adults.

4.2.8 Expand access to vaccination at sites outside of traditional medical settings.

Objective 4.3: Maintain and enhance the capacity to monitor immunization coverage for vaccines routinely administered to infants, children, adolescents, and adults.

Federal Departments and Agencies: HHS (CDC, IHS), DoD, USAID, VA
Non-federal Stakeholders: Health care payers and plans (public and private), health care system (e.g., electronic health record vendors), state, local, and tribal governments and public health agencies

Strategies:

4.3.1 Identify, implement, and evaluate cost-effective and rapid methods for assessing vaccination coverage:

a. among children, adolescents, adults overall and by State, immunization grantee, and within states and grantees;
b. among persons in key population subgroups (e.g., racial/ethnic groups, pregnant women, healthcare workers); and
c. by type of vaccination financing (e.g., VFC, other public sector program, private sector).

4.3.2 Improve the completeness and use of Immunization Information Systems (IIS) and electronic medical records (EMR) to monitor vaccination coverage.

Objective 4.4: Enhance tracking of vaccine preventable diseases and monitoring of the effectiveness of licensed vaccines.

Federal Departments and Agencies: HHS (CDC, IHS), DoD, USAID, VA
Non-federal Stakeholders: Academia, health care system, public and private payers, philanthropic organizations, state, local, and tribal governments/public health, vaccine industry

Strategies:

4.4.1 Strengthen epidemiologic and laboratory methods and tools to diagnose vaccine-preventable diseases and characterize the impact of vaccination coverage on relevant clinical outcomes.

4.4.2 Monitor circulating strains of relevant vaccine-preventable pathogens.

4.4.3 Monitor ongoing disease burden and determine epidemiologic and clinical characteristics of cases of relevant vaccine-preventable diseases.

4.4.4 Conduct studies to assess vaccine effectiveness and indirect (community or herd) protection.

4.4.5 Monitor long term protection from vaccines administered to infants, children, adolescents, and adults.

4.4.6 Assure rapid and comprehensive identification, investigation, and control of vaccine preventable disease outbreaks.

Objective 4.5: Educate about, and support, healthcare and other vaccination providers in vaccination counseling and delivery.

Federal Departments and Agencies: HHS (CDC, CMS, FDA, HRSA, IHS), DoD, USAID, VA
Non-federal Stakeholders: Health care payers and plans (public and private), health care system (including health care provider organizations), philanthropic organizations, state, local, and tribal governments/public health, vaccine industry

Strategies:

4.5.1 Expand knowledge regarding the value of vaccination, the vaccination program, and vaccine administration by traditional healthcare providers, medical and nursing trainees, and other vaccinators (e.g., pharmacists, community vaccinators).

4.5.2 Improve counseling and referral of patients for immunization by healthcare providers who do not offer immunization services.

4.5.3 Promote and support educational and technical assistance to improve business practices associated with providing immunizations.

4.5.4 Incentivize direct health care providers, health systems, and health insurers to provide vaccines by incorporating vaccination in quality assessment programs (e.g., HEDIS, Quality Measures and Pay for Performance programs).

4.5.5 Ensure appropriate reimbursement for vaccine counseling and administration by providers under public sector and private health plans.

4.5.6 Support research to evaluate the capacity (accommodating the increased number of patient visits required to receive recommended vaccines) of health care providers to implement childhood, adolescent, and adult vaccination recommendations.

4.5.7 Develop, implement, and evaluate communication tools as part of comprehensive programs to ensure health care professionals are appropriately immunized with recommended vaccines.

4.5.8 Promote the development, implementation, and evaluation of employer-based immunization programs (including free vaccines, convenient access, education, and compliance monitoring) to increase the coverage of health-care personnel with recommended vaccines.

4.5.9 Assess whether changes in health care facility and professional licensure and regulation can improve the safety of the health care environment by increasing vaccination rates of health care professionals.

4.5.10 Develop and monitor policies promoting vaccination for patients and health care personnel in long-term care facilities and hospitals.

Objective 4.6: Maintain a strong, science-based, transparent process for developing and evaluating immunization recommendations.

Federal Departments and Agencies: HHS, (BARDA, CDC, FDA, HRSA, NVPO, IHS), DoD, USAID, VA
Non-federal Stakeholders: Academia, health care system (including health care provider organizations), media, the public and citizen advocacy groups, state, local, and tribal governments and public health agencies, vaccine industry,

Strategies:

4.6.1 Obtain broad-based input from the public and stakeholders contributing to new immunization policies and to assessment of existing policies.

4.6.2 Support and strengthen immunization advisory committees at the state and national levels.

4.6.3 Assess the impact of new vaccines and vaccine recommendations on the overall immunization schedule, including programmatic implementation, safety, and efficacy.

4.6.4 Evaluate the cost-effectiveness of proposed and existing immunization recommendations.

Objective 4.7: Strengthen the Vaccine Injury Compensation Program (VICP) and Public Readiness and Emergency Preparedness (PREP) Act compensation fund

Federal Departments and Agencies: HHS (BARDA, CDC, HRSA, IHS, NVPO), DoJ

Non-federal Stakeholders: Academia, health care system, media, state, local, and tribal governments/public health, the public, media, vaccine industry, citizen advocacy groups

Strategies:

4.7.1 Increase knowledge about the VICP and PREP act among all stakeholders.

4.7.2 Assure the program is responsive to evolving science, including regularly updating the Vaccine Injury Table.

4.7.3 Continue to ensure fair and efficient compensation.

4.7.4 Examine alternative approaches for adjudication of claims for illnesses not included in the Vaccine Injury Table (and seek Federal legislation as necessary).

Objective 4.8: Enhance the effectiveness of state and federal immunization programs

Federal Departments and Agencies: HHS (ASPR, CDC, HRSA, IHS), DoD, DHS, VA
Non-federal Stakeholders: Health care system, health care payers and plans (public and private) state, local, and tribal governments and public health agencies, vaccine industry

Strategies:

4.8.1 Implement, monitor, and evaluate evidence-based interventions, and translational research, designed to raise and sustain high vaccination coverage in children, adolescents, and adults.

4.8.2 Monitor and evaluate the impact of state immunization laws including childcare, school, and college prematriculation requirements, the role of exemptions, insurance mandates, and immunization information systems requirements.

4.8.3 Prepare, practice, and evaluate mass vaccination activities for containment of an outbreak of a vaccine-preventable disease, for a biological attack, for the critical workforce in advance of an influenza pandemic, and for the entire population, prior to and during, an influenza pandemic.

Objective 4.9: Enhance Immunization Coverage of International Travelers Who Are at Risk of Acquiring Vaccine-Preventable Diseases.

Federal Departments and Agencies: HHS (CDC), USAID

Non-federal Stakeholders: Health care system, health care payers and plans (public and private) state, local, and tribal governments and public health agencies, travel industry, vaccine industry

Strategies:

4.9.1 Define the populations at risk for acquiring international travel-related vaccine-preventable diseases, and identify and address barriers to their receiving immunizations.

4.9.2 Implement and evaluate activities to enhance immunization coverage among travelers.

Goal 5: Increase global prevention of death and disease through safe and effective vaccination

Introduction

Infectious diseases are the leading cause of death among children globally and contribute substantially to disease and disability among persons of all ages. Immunization programs have been remarkably successful preventing millions of childhood deaths, eradicating smallpox, and eliminating circulation of polio and measles from many countries around the world. However, the continued morbidity and mortality burden from diseases for which vaccination already is routinely recommended, for which vaccines are available but not used in most countries (e.g., pneumococcus and rotavirus), and from diseases for which vaccines are being developed (e.g., HIV, tuberculosis, and malaria) highlights the substantial challenges that remain. Achieving the United Nations Millennium Development Goals of reducing the under-five mortality rate and the proportion of 1 year-old children immunized against measles by two-thirds will require addressing these challenges.

The goals of global vaccination are to eradicate, eliminate or control infectious diseases in a way that supports and strengthens health systems and can be sustained and expanded as new vaccines are developed and introduced. Success in global immunization requires action by the full range of stakeholders involved in the vaccine and immunization enterprise, from research and development, through regulation and manufacturing, to program implementation and monitoring. New partnerships such as the Global Alliance for Vaccines and Immunization (the GAVI Alliance) have led to increased focus and support for immunization worldwide and have catalyzed introduction of new vaccines in most countries and expanded vaccination coverage. U.S. governmental and non-governmental organizations have contributed to progress through vaccine research and development, participation in multilateral and bilateral partnerships, and technical assistance and program support.

Given the breadth of global immunization activities, some of the Objectives and Strategies relevant to this topic are included elsewhere in this Plan. All vaccine research and development are included under Goal 1 as the approach to achieving these objectives and the key stakeholders are not different for the U.S. and the rest of the world. By contrast, issues related to vaccine safety, communications, and program implementation are included under the Global Immunization goal as well as under other goals of the Plan. Whereas many of the objectives in these areas are similar for the U.S. and abroad, the strategies differ as internationally, U.S. stakeholders focus on partnerships and providing assistance rather than on direct implementation as described elsewhere in the Plan. Because the role of U.S. stakeholders in reaching global immunization targets, many of which were established by international organizations such as the World Health Organization, is largely indirect, achievement of these indicators will require actions by the involved countries and international stakeholders and, thus, may be largely outside the control of the United States.

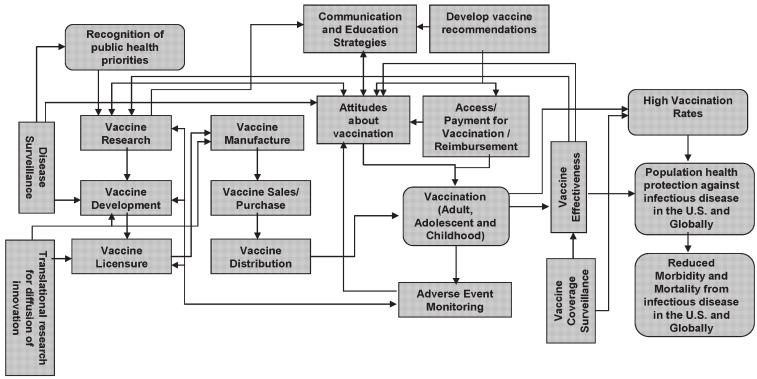
Goal 5 Indicators

- Transmission of wild polio virus will be eradicated by Y (year).
- Mortality from measles will be reduced by X% by Y (year) compared with a X (year) baseline.
- X% of countries will achieve DTP3 vaccination coverage of 90% or greater nationally (and 80% or greater in each country's district) by Y (year).
- Support introduction of new vaccines as part of national vaccination programs:
  - Meningococcal vaccine in all African countries in the "meningitis belt" by Y (year);
  - Rotavirus vaccine in X countries by Y (year); and
  - Pneumococcal conjugate vaccine in Z countries by Y (year).
- X countries establish immunization advisory committees by Y (year) that make evidence-based decisions on adding new vaccines to the routine program and monitor program quality, vaccination coverage, and vaccine safety.
- X countries enhance injection safety by Y (year) through the use of auto-disable syringes or other safe injection devices (e.g., needle free delivery) for all immunizations.

Identifying Goal 5 Objectives and Strategies

Figure 7 is the same as Figures 1 and 2, but it shows components of the vaccine and immunization enterprise (i.e., the shaded rectangular boxes) which contribute to achieving Goal 5 – increasing global prevention of death and disease through safe and effective vaccination. In essence, Goal 5 incorporates elements of each of the other domestically-oriented goals and considers them from a global perspective. The process begins with global disease surveillance informing the recognition of global public health priorities and guiding vaccine research and development activities. The steps from vaccine development to vaccination proceed through a set of activities related to vaccine licensure, developing vaccine recommendations, manufacturing, distribution, communication and education about vaccines, and monitoring adverse events and vaccine effectiveness. Vaccine coverage is influenced by financial and non-financial factors, including attitudes toward vaccination and payment policies. Attitudes and coverage are, in turn, influenced by issues related to vaccine safety and vaccine effectiveness. Issues related to safety and effectiveness inform the next generation of vaccine research and development. The desired outcomes of this process include high vaccination rates which lead to reduced morbidity and mortality from infectious disease, and improved population health around the world. All of these components take place across a wide range of countries with different cultures, environments, and levels of infrastructure. Developing objectives and strategies that recognize and account for these differences is critical for achieving Goal 5.

Figure 7. Components of the Vaccine Process Relevant to Goal 5



Proposed Objectives

Objective 5.1: Improve global surveillance for VPDs and strengthen health information systems to monitor vaccine coverage, effectiveness, and safety.

Federal Departments and Agencies: HHS (CDC, NIH), USAID, DoD
Non-federal stakeholders: Academia, international organizations, NGOs, public and private philanthropic organizations, UNICEF, World Health Organization

Strategies:

5.1.1 Achieve sustainable WHO certification quality surveillance for eradication targeted VPDs.

5.1.2 Expand and improve sustainable surveillance systems for all current VPDs and for diseases for which vaccine introduction is being considered.

5.1.3 Strengthen all levels of global laboratory networks (including national, regional, and global reference laboratories) to sustain and improve VPD diagnosis in order to establish baseline disease burden, detect outbreaks, detect newly emerging variants of vaccine-preventable diseases, and monitor the impact of new vaccines.

5.1.4 Enhance assessments of emerging variants or strains of vaccine-preventable disease agents.

5.1.5 Develop new diagnostic tests, tools and procedures to improve both field-based and laboratory confirmation of diagnoses.

5.1.6 Improve coverage monitoring of vaccines and other health services linked with the vaccination program and the use of information at district and local levels.

5.1.7 Introduce and improve programs that monitor the occurrence of AEFI.

Objective 5.2: Improve and sustain immunization programs that deliver vaccines safely and effectively as a component of healthcare delivery systems and promote opportunities to link immunization delivery with other priority health interventions, where appropriate.

Federal Departments and Agencies: HHS (CDC), USAID
Non-federal stakeholders: Academia, international organizations, NGOs, public and private philanthropic organizations, UNICEF, World Health Organization

Strategies:

5.2.1 Provide support to countries and partners to strengthen key components of immunization program management and implementation, including epidemiological analysis, comprehensive planning, vaccine distribution and administration, monitoring, and program evaluation.

5.2.2 Provide technical support to countries to introduce, sustain, and monitor recommended safe injection practices for all vaccinations, including the use of auto disable syringes or needle-free devices.

5.2.3 Support linking delivery of immunization and other health services in ways that do not jeopardize immunization coverage, and develop standardized methods for monitoring and evaluating the efficiency, effectiveness and impact of combined interventions to improve coverage and public health.

5.2.4 Encourage establishment of programs, as appropriate, for vaccination beyond the traditional infant target age groups (e.g., among older children, adolescents and adults).

Objective 5.3: Support introduction and availability of new and under-utilized vaccines to prevent diseases of public health importance.

Federal Departments and Agencies: HHS (CDC, FDA, NIH), USAID

Non-federal stakeholders: Academia, international organizations, NGOs, public and private philanthropic organizations, UNICEF, World Health Organization

Strategies:

5.3.1 Collaborate with global organizations and partners to accelerate the clinical testing and licensure, where appropriate, in developing countries of vaccines already licensed in developed countries.

5.3.2 Strengthen country capacity to make informed decisions on introduction of new vaccines based on evaluation of epidemiology, financial sustainability, safety, and programmatic considerations.

5.3.3 Support the integration of new and under-utilized vaccine into each GAVI-eligible country's multi-year national plan of action and provide training and logistical support necessary to successfully incorporate new vaccines into routine programs.

5.3.4 Conduct post-licensure evaluations of the impact of new vaccines on immunization programs, disease patterns, and the occurrence of AEFI.

Objective 5.4: Improve communication of research-based and culturally and linguistically appropriate information about the benefits and risks of vaccines to the public, providers, and policy-makers.

Federal Departments and Agencies: HHS (CDC), USAID
Non-federal stakeholders: Academia, international organizations, NGOs, public and private philanthropic organizations, UNICEF, World Health Organization

Strategies:

5.4.1 Support appropriate economic studies to inform the understanding of the costs and benefits of immunization among key decision and policy-makers.

5.4.2 Develop and support capabilities to communicate vaccine risks and to respond to emerging vaccine safety issues and concerns to the public, providers, and other stakeholders in a clear, transparent and timely manner.

5.4.3 Provide assistance in determining the most effective and efficient mechanisms to communicate with health care providers about reporting on AEFI; evaluate providers' knowledge and adherence to recommendations to prevent AEFI; and improve and assess adherence to these recommendations.

5.4.4 Assist countries to develop, implement and assess comprehensive evidence-based communication plans to increase provider and public awareness of vaccine preventable

diseases and promote immunization recommendations, especially among populations at risk of under-immunization.

5.4.5 Assist countries to develop and implement sustainable communication research to gather timely and reliable data from the public and providers on knowledge, attitudes and beliefs about the benefits and risks of vaccines.

5.4.6 Provide technical assistance and training to behavioral and communications scientists and promote their participation on Technical Advisory Groups.

Objective 5.5: Support the development of regulatory environments and manufacturing capabilities that facilitate access to safe and effective vaccines in all countries.

Federal Departments and Agencies: HHS (BARDA, CDC, FDA), USAID
Non-federal stakeholders: Academia, international organizations, NGOs, public and private philanthropic organizations, vaccine industry, World Health Organization

Strategies:

5.5.1 Promote and support the efforts of the World Health Organization to develop and harmonize international standards and norms to assure the quality, safety and efficacy of vaccines and to provide a predictable environment for vaccine development.

5.5.2 Promote and support the efforts of the World Health Organization to improve regulatory capacity in countries with limited infrastructures to assure vaccine quality, evaluate new vaccines when appropriate and assure that clinical trials are conducted in accordance with Good Clinical Practices.

5.5.3 Support efforts to harmonize international vaccine licensing regulations.

5.5.4 Provide technical assistance to developing country vaccine manufacturers to support development and production of safe and effective vaccines and related technologies.

Objective 5.6: Build and strengthen multilateral and bilateral partnerships and other collaborative efforts to support global immunization and eradication programs.

Federal Departments and Agencies: HHS (CDC, FDA, NIH), USAID
Non-federal stakeholders: Academia, international organizations, public and private philanthropic organizations, UNICEF, World Health Organization

Strategies:

5.6.1 Participate in establishing global immunization priorities, goals and objectives and provide technical assistance at global, regional, and national forums.

5.6.2 Strengthen international collaborations for basic and applied research, especially onsite research in disease endemic areas or those with the greatest burden of disease.

5.6.3 Work with global partners to establish an international system that facilitates rapid response to emerging infections through the development of vaccine reference strains and candidate vaccines.

5.6.4 Contribute to development and implementation of a research agenda establishing the scientific basis for VPD eradication/elimination; identifying optimal vaccination approaches; and developing strategies to minimize risks in the post-eradication period.

5.6.5 Build and strengthen bilateral and multilateral partnerships and other collaborative efforts to support availability, access, sustainable financing, and use of current, under-utilized, and new vaccines.

5.6.6 Work with global partners to secure and maintain adequate stockpiles/strategic reserves of vaccines to maintain uninterrupted supply, for emergency response to outbreaks, and for special purposes.

5.6.7 Work with global partners to develop a global advocacy agenda and create a positive environment for vaccine use.

Appendix 1. Anticipated outcomes from the 1994 National Vaccine Plan and the extent to which each has been achieved at the time the release of draft strategic National Vaccine Plan (November 2008)

Anticipated outcome	Status
Age-appropriate immunization with all recommended vaccines will be extended to at least 90% of infants and children, and access to affordable vaccination services will be made available for every person in the United States.	• ≥90% coverage for all routinely recommended childhood vaccines that have been licensed for >5 years except for DTaP (4 doses – 85.1%) and pneumococcal conjugate (88.9%). • VFC has enhanced coverage levels in children. 43% of US children are receiving vaccines through the VFC program that was implemented first in 1994. Coverage levels for 19-35 month old children in the VFC program and outside of it are similar. Financial barriers to access still exist among children who are underinsured and not eligible for the Vaccine for Children's (VFC) program. • Financial barriers to access exist among adults <65 years who are uninsured, underinsured, or whose health insurance coverage does not include vaccinations or includes a high co-pay. Medicare part D to date has complex payment mechanisms for vaccination.
Diphtheria, tetanus, poliomyelitis, measles, rubella mumps, some forms of hepatitis, pertussis (whooping cough), and bacterial meningitis (from *Haemophilus influenzae* type b) will be essentially eliminated as significant causes of death, disease and disability in the United States.	• Diphtheria, tetanus, poliomyelitis, rubella, and invasive Hib disease, including meningitis have been virtually eliminated in the U.S. • Hepatitis A and B have declined 90% and 81%, respectively, since vaccines were licensed to prevent these diseases. • Despite greater than an estimated 95% reduction in cases compared with the pre-vaccine era, pertussis continues to occur endemically and in outbreaks. • Despite an estimated 99% reduction in cases compared with the pre-vaccine era, for both measles and mumps, sporadic outbreaks continue to occur. • Vaccine-type invasive pneumococcal disease has been reduced by 92% in all ages. • Estimated varicella illnesses have been reduced by 99% compared with the pre-vaccine burden of disease.
Educational communication networks will be in place that will inform all healthcare providers, communities, and families of the benefits and risks of	• Vaccine Information Statements, by law, are to be provided to all vaccine recipients receiving vaccines covered under National Childhood Vaccine Injury Act, informing them about benefits and risks of vaccination. • Information on vaccine benefits and risks is available on a variety of relevant federal websites. • While no single educational communication network exists that actively reaches out to and informs all healthcare

vaccination.	providers, families, and communities about vaccine benefits and risks, internet-based information is significantly more available than it was in 1994. For example, for providers, the AAP and AAFP newsletters and email blasts constitute a network, as does IDSA's similar capacity with members. CDC/NCIRD's Immunization Works is a regular effort to update programs and partners, and DoD's Milvax internet site has abundant information about their vaccination programs.
In a global context, polio will be drastically reduced, if not eliminated, and neonatal tetanus and measles will be better controlled.	• Polio cases have been reduced to 1,385 in 2007 from just under 10,000 in 1994 and 35,252 in 1988. • Measles cases have been reduced 68% worldwide. • Of 57 countries with high risk of maternal and neonatal tetanus in 1999, 12 have eliminated the disease, and 38 have reduced it by at least 50%.
Pneumococcal pneumonia and influenza in American adults over the age of 65 will be significantly reduced.	• Since 1999, pneumonia and influenza rates among older adults have dropped slightly in those 65-84 years, and significantly in those 85 years and older (see table 9 at http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_10.pdf). Influenza is unique among the vaccine-preventable diseases in that annual vaccination is required in order to provide protection and impact of the vaccination program must be measured within individual influenza seasons as opposed to being considered over a several year period as with other vaccine-preventable diseases in which the vaccine provides long-term protection and/or prevents carriage of the pathogen. Further, the disease burden and vaccine effectiveness for influenza can vary substantially from one year to the next. • Annual influenza vaccination coverage among adults ≥65 years old has increased to more than 70%. CMS has likely assisted in raising coverage in older adults by quadrupling its vaccine administration payment since 1994. • Studies of pneumococcal vaccination in adults have shown some effectiveness in preventing invasive pneumococcal disease, but no impact on the occurrence of pneumococcal pneumonia in older adults; however, childhood pneumococcal vaccination is assumed largely responsible for the drop in adult invasive pneumococcal disease, from 61.5/100,000 in 1999 to 39.6/100,00 in 2007
A nationwide system will monitor the vaccines that children receive, and will remind parents when	• Although there is no nationwide system, immunization information systems have been established by every State except one. • The ability of State-based systems to monitor vaccination coverage and provide reminders for infant and child

individual infants and children should be vaccinated.	vaccination varies (see http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5711a4.htm)
A nationwide surveillance system will report and investigate cases of vaccine-preventable-diseases.	• Most vaccine preventable diseases are notifiable diseases; however, the completeness of reporting in this "passive" surveillance system varies • Case-investigations occur for some, less common vaccine preventable diseases • Complete reporting ("active" surveillance) and investigation occur for some vaccine preventable diseases in certain geographical areas
Vaccine safety and efficacy will be continuously monitored, and adverse events following immunization will be reported and carefully analyzed.	• The Vaccine Adverse Events Reporting System (VAERS) is a national system that continuously monitors adverse events reported by healthcare providers, manufacturers or the public • Other systems exist to do active surveillance, clinical assessment of persons with suspected adverse events following vaccination, and study design and implementation.
Improved vaccines will replace some of the vaccines in current use.	• DTaP has replaced DTP vaccines to reduce adverse events • Tdap has replaced Td to address pertussis in older ages • IPV has replaced OPV to eliminate the risk of vaccine-associated paralytic poliomyelitis (VAPP) • Hib and pneumococcal conjugate vaccines have replaced polysaccharide vaccines in infants and children to increase effectiveness • Meningococcal conjugate vaccine has replaced the polysaccharide vaccine in children to increase effectiveness
Some vaccines requiring multiple doses and multiple contacts with the health care system will be replaced by more cost-effective ones that will improve people's access to immunization.	• Combination vaccines have been licensed that reduce the number of injections needed to completely vaccinate infants and children • Use of combination vaccines has not clearly increased cost-effectiveness because of higher pricing for some these products, compared to the separate vaccines, and has not affected access to immunization
Many new vaccines will be developed or be much closer to licensure, for diseases for which effective	• Since 1994, new vaccines have been licensed and recommended for routine use against varicella, hepatitis A, pneumococcal conjugate, rotavirus, influenza, herpes zoster, and human papillomavirus

vaccines do not now exist.	
New mechanisms for the more rapid assessment of vaccines proposed for licensure will be in place.	• Mechanism to use immune endpoint surrogates reasonably likely to predict clinical benefit created by regulation, and has been utilized to increase influenza vaccine supply • Mandated under the Modernization Act in 1997, guidance for fast track designation and priority review policies were written, and have been used for vaccines. (More than a dozen guidances have been issued to industry since 1994). The former allows for more frequent interactions with FDA during development; the latter allows 6 month review of an application versus 10 month review for a product for serious or life-threatening disease. Initial fast track draft guidance was published in 1998; final guidance was issued July, 2004.
A reliable supply of all recommended vaccines and a capability to respond to emergencies and emergent threats to public health will be achieved and sustained.	• Supply shortages for a number of routinely recommended vaccines have occurred since 2000 (e.g., pneumococcal conjugate, influenza, meningococcal conjugate, Hib, varicella, tetanus-diphtheria toxoid) • As a result of FDA initiatives (including provision of accelerated approval based on a likely surrogate) and intense interaction with manufacturers, supplies of influenza vaccine, and the diversity of the supply in terms of numbers of US manufacturers, have been doubled from 2004 to 2008. The number of US licensed influenza vaccine manufacturers has increased during this time from two to six. • Stockpiles of routinely recommended vaccines for children have been established to mitigate the risk of shortages • Emergency response capacity for vaccination is being established by State and local health departments • Stockpiles of, and/or production plans for, pre-pandemic influenza vaccines, and smallpox and anthrax vaccines are in place
Information on the costs and benefits of the National Vaccine Plan will be made available on an ongoing basis to the American people.	• Cost -effectiveness analyses of the childhood schedule through vaccines routinely recommended in 1999 have been disseminated. Routine childhood immunization with the 7 vaccines then recommended was cost saving from the direct cost and societal perspectives, with net savings of 9.9 billion dollars and 43.3 billion dollars, respectively (Zhou et al., Arch Pediatr Adolesc Med. 2005 Dec;159(12):1136-44). Several studies have demonstrated the cost-effectiveness of several vaccines in adults, such as influenza, pneumococcal polysaccharide, and pertussis.

Appendix 2: IOM committee recommendations from the June 11, 2008 letter report "Initial Guidance for an Update of the National Vaccine Plan: A Letter Report to the National Vaccine Program Office" and National Vaccine Program Office responses[9]

The National Vaccine Program Office (NVPO) and other offices and agencies in the Department of Health and Human Services (HHS) have reviewed the recommendations in the June 11, 2008 letter report of the Institute of Medicine's Committee on the Review of Priorities in the National Vaccine Plan. We appreciate the Committee's work and thoughtful recommendations. Our response to each recommendation follows its citation below.

Recommendation 1: The committee recommends that NVPO and its partners include for each strategic initiative listed under the four plan goals the following details:

- **The primary responsible party (government agency or other stakeholder)**
- **Secondary participant(s) (government agency or other stakeholder)**
- **Measurable short, mid, and longer term outcomes to assess success of the initiative**
- **Identification of costs and potential funding sources (e.g., professional judgment budgets) to support pursuit of the initiative**
- **The plan also should include a timetable and process for regular updates that reflect the dynamic nature of the field.**

The draft strategic National Vaccine Plan has listed HHS agencies and other federal Departments responsible for each objective in it, as well as possible non-federal stakeholder sectors. . Input and comments from non-federal stakeholders (including the public), and recommendations from the IOM committee all will contribute to final Plan to be released in the fall, 2009. This Plan, in turn, will serve as the basis for implementation planning by Federal agencies and non-Federal stakeholders which will define specific actions that will be undertaken to accomplish each of the strategies in the Plan and timelines and measurable outcomes to assess progress.

Identification of resource needs will follow identification of specific actions in the implementation plan, in consultation with stakeholders.

NVPO will be responsible for assuring coordination and for monitoring federal actions and accomplishments on an ongoing basis. NVAC will establish a working group to promote coordination and monitor progress by the broader group of stakeholders. Each year, NVPO and NVAC will report their findings to the Assistant Secretary for Health.

[9] Recommendations from the Institute of Medicine Committee on the Review of Priorities in the National Vaccine Plan letter report "Initial Guidance for an Update of the National Vaccine Plan: A Letter Report to the National Vaccine Program Office," June 11, 2008 available at http://www.iom.edu/CMS/3793/55143.aspx.

This report will include a summary of progress, identify areas where progress is lagging, and propose corrective action where needed. The report also will be summarized annually at an NVAC meeting, which is open to the public and is attended by many stakeholders not represented directly on the Committee.

Recommendation 2: The committee recommends that NVPO and its partners identify specific and creative strategies (not limited to funding) that federal agencies and programs could use to motivate stakeholders to implement objectives in the national vaccine plan.

NVPO believes the three following steps will be essential strategies motivating stakeholders to implement the National Vaccine Plan: 1) reviewing and commenting on the Goals, Objectives and Strategies in the draft Plan; 2) participating in developing, and assuming responsibility for implementing, measurable milestones for the implementation plan; and 3) working with NVPO and NVAC to monitor progress in implementing these milestones.

Recommendation 3: The committee recommends that NVPO and its partners explain in the draft update to the National Vaccine Plan what was important to include and why, and the process by which items were selected for inclusion or discarded.

The draft strategic National Vaccine Plan represents the aggregate input from HHS federal agencies and Departments most involved in vaccine issues about how to improve the current United States vaccine system. The component maps of the vaccine and immunization enterprise address these issues and offer a framework for the Goals, Objectives, and Strategies. Some elements have not been included, post-exposure prophylaxis, and therapeutic vaccines. The National Vaccine Program was established by congressional legislation (Title XXI of the Public Health Service Act [Public Law 99-660]) in 1986 to ***achieve optimal prevention of infectious diseases through immunization and optimal prevention of adverse reactions to vaccines.*** *NVPO recognizes the need for strategic planning for therapeutic vaccines and will seek to identify mechanisms to address this need separately from this Plan.*

Recommendation 4: The committee recommends that NVPO and its partners include in the update to the National Vaccine Plan mechanisms to assess the "horizon" of innovation and new developments in vaccines, and explore strategic objectives or initiatives that enable timely consideration of and decision making to address emerging opportunities and challenges.

NVPO agrees that a flexible approach is important to assure timely response to emerging opportunities and challenges. In developing this draft Plan, NVPO analyzed the strengths, weaknesses, opportunities, and threats to the U.S. vaccine system. The draft Plan has incorporated the results of that analysis, and believes the regular monitoring of the progress in the Plan, as well as its objectives and strategies, will permit rapid assessment and response to those emerging opportunities and challenges.

Recommendation 5: The committee recommends that the update to the National Vaccine Plan include a comprehensive framework for communicating with the public and other key stakeholders such as healthcare providers about the benefits (both individual and community) and risks of vaccination. Communication strategies that are implemented should be evaluated for their effect on knowledge and behavior.

The draft Plan has maintained the focus of Goal 3 from the 1994 Plan on communications and education issues, including benefits and risks of vaccines, and including vaccine issues in health professional schools' curricula and training programs. Evaluation and monitoring of proposed communication and education strategies is outlined in the draft, and are essential to improving this area, as they are for all aspects of the Plan.

Recommendation 6: The committee recommends that NVPO and its partners consider ways the update to the National Vaccine Plan could spur research for creative solutions to vaccine supply problems.

Goal 4 is now entitled ***Ensure a stable supply of recommended vaccines, and increase uptake of existing vaccines to prevent disease, disability, and death in the United States,*** *demonstrating the importance of vaccine supply issues in the draft Plan. The Plan discusses improving vaccine stockpiles, centralized vaccine distribution, and Good Manufacturing Practices. The Committee also emphasized the importance of addressing health disparities in vaccination levels, including access and financial issues. Concepts from the NVAC Vaccine Financing Working Group's recommendations have been incorporated into the draft Plan.*

Appendix 3: Stakeholders In the United States National Vaccine System*

Academic research

- Researchers
    - Universities
    - Vaccine manufacturers
    - Research Organizations
- Research funders
    - National Institutes of Health
    - Philanthropic organizations
- Institute of Medicine
- The Brighton Collaboration

Adocacy groups

Federal government Departments and Agencies

- Department of Health and Human Services
    - Office of the Assistant Secretary for Health
        - National Vaccine Program Office
        - Office of the Surgeon General
    - Office of the Assistant Secretary for Legislation
    - Office of the Assistant Secretary for Planning and Evaluation
    - Office of the Assistant Secretary for Public Affairs
    - Office of the Assistant Secretary for Preparedness and Response
        - Biomedical Advanced Research and Development Authority
    - Office of the Assistant Secretary for Public Affairs
    - Office of the General Counsel
    - Office of Global Health Affairs
    - Office of Intergovernmental Affairs
    - Office of the National Coordinator for Health Information Technology
    - Administration on Aging
    - Agency for Healthcare Research and Quality
    - Centers for Disease Control and Prevention
    - Centers for Medicare and Medicaid Services
    - Food and Drug Administration
    - Health Resources and Services Administration
    - Indian Health Service
    - National Institutes of Health
    - Substance Abuse and Mental Health Services Administration
- Department of Agriculture
- Department of Defense
    - Assistant Secretary for Health Affairs
    - US Army Medical Research Institute of Infectious Diseases (USAMRIID)
    - The Military Vaccine (MILVAX) Agency
    - Defense Advanced Research Projects Agency

    - Defense Threat Reduction Agency
- Department of Homeland Security
- Department of Justice
- Department of Labor
    - Occupational Safety and Health Administration
- Department of State
    - U.S. Agency for International Development
- Department of Veterans Affairs

The general public
- Individuals
- Families
- Schools
- Employers
- Churches and other faith-based institutions

HHS Federal advisory committees
- Advisory Commission on Childhood Vaccines (ACCV)
- Advisory Committee on Immunization Practices (ACIP)
- National Advisory Allergy and Infectious Disease Council (NAAIDC)
- National Biodefense Science Board (NBSB)
- National Vaccine Advisory Committee (NVAC)
- Vaccines and Related Biologicals Products Advisory Committee (VRBPAC)

Health care system
- Health care providers, hospitals, clinics, and federally qualified health centers, long-term care facilities, managed care organizations (MCOs)
- Medical professional societies
- Health care professional schools
- Health care training programs
- Pharmacies
- Community vaccinators
- Electronic health record vendors

Health care payers and plans (public and private)
- Benefit managers
- Coverage policy, reimbursement
- Quality monitoring systems

International organizations
- WHO, UNICEF
- Other countries
- National regulatory agencies

Media

Non-governmental organizations

Philanthropic organizations

State, local, and tribal governments and public health agencies

Travel industry

Vaccine industry (manufacturers [large companies, biotechnology companies, both foreign and U.S.-based]

Vaccine distributors

Vaccine investors

*Adapted from the Initial Guidance for an Update of the National Vaccine Plan, A Letter Report to the National Vaccine Program Office, June 11, 2008, available at http://www.iom.edu/CMS/3793/55143.aspx,
The sectors, and groups listed under each sector, are examples and may not be all-inclusive.

Appendix 4: Roles and Responsibilities of Department of Health and Human Services Agencies and Offices, and other federal Departments in the draft strategic National Vaccine Plan

Secretary of Health and Human Services	• Directs all HHS activities
Office of the Assistant Secretary for Health	• Directs the National Vaccine Program • Advises Secretary on Public Health and Science as he directs HHS vaccination activities • Coordinates operations planning efforts of HHS agencies, operational divisions and offices • Assists with public communications and coordination with state and local public health partners
Office of the Assistant Secretary, Administration on Aging	• Help the elderly maintain dignity and independence through comprehensive, coordinated and cost-effective systems of long-term care and livable communities. • Advances the concerns and interests of older people and their caregivers. • Works with the Aging Services Network to promote the development of a comprehensive and coordinated system of home and community-based long term care, including vaccination services.
Office of the Assistant Secretary, Administration for Children and Families	• Communicates with and supports vaccine-preventable disease response activities of state, local, tribal, and nonprofit (including faith-based and community) human services organizations • Communicates information on child and family well-being, including the importance and availability of vaccinations • Encourages the participation of human services providers (e.g., Head Start centers, child care centers, family resource centers, community action agencies, runaway and homeless youth shelters, and shelters for unaccompanied alien children) in making vaccines available to vulnerable populations

Office of the Assistant Secretary for Legislation	• Coordinates Congressional outreach and communications, including on vaccination issues.
Office of the Assistant Secretary for Planning and Evaluation	• Conducts research and evaluation studies on vaccine topics, develops policy analyses, and estimates the cost and benefits of policy alternatives under consideration by the Department or Congress. • Advises the Secretary on policy development in health, disability, human services, data, and science, and provides advice and analysis on economic policy. • Leads special initiatives, coordinates the Department's evaluation, research and demonstration activities, and manages cross-Department planning activities such as strategic planning, legislative planning, and review of regulations. • Monitors effectiveness of response activities and modifies strategies, as needed.

Office of Assistant Secretary for Preparedness and Response (ASPR)	• Coordinates and communicates with other federal departments and agencies
	• Coordinates HHS pandemic and biodefense vaccine response activities
	  • Provides an integrated, systematic approach to the development and purchase of the necessary vaccines, drugs, therapies, and diagnostic tools for public health medical emergencies.
	  • Manages Project BioShield, which includes the procurement and advanced development of medical countermeasures for chemical, biological, radiological, and nuclear agents, as well as the advanced development and procurement of medical countermeasures for pandemic influenza and other emerging infectious diseases that fall outside the auspices of Project BioShield.

Office of the Assistant Secretary for Public Affairs	• Coordinates public information and communications, including all aspects of vaccination, vaccine supply, vaccine preventable diseases and vaccine safety issues
Office of Intergovernmental Affairs	• Advises and coordinates outreach and communications to state, local and tribal officials and national intergovernmental organizations
Office of the Surgeon General	• Oversees the operations of the 6,200 active duty officers of the Commissioned Corps of the U.S. Public Health Service • Deploys commissioned officers to meet urgent public health needs and provide public health and medical services in response to natural and man-made disasters. • Provides trusted and credible health and medical information to the public, improving health and reducing the risk of illness and injury • Assigns officers to HHS and non-HHS Federal agencies to provide clinical, technical, regulatory, disease surveillance, program management and research services. • Coordinates nearly 800 local units of the Civilian Volunteer Medical Reserve Corps, representing over 170,000 health volunteers. • Coordinates the USPHS Inactive Reserve Corps comprising over 1,000 health professionals in 11 professional categories who are Federalized to respond to disasters or urgent public health need.
Office of the General Counsel	• Advises on legal issues and authorities related to key vaccination activities
Office of Global Health Affairs	• Coordinates interactions with health authorities in other governments and international organizations in

	coordination with the Department of State
Office of the National Coordinator for Health Information Technology	• Coordinates the Department of Health and Human Services' (HHS) health information technology policies and programs internally and with other relevant executive branch agencies • Develops, maintains, and directs the implementation of HHS' strategic plan to guide the nationwide implementation of interoperable health information technology in both the public and private health care sectors, to the extent permitted by law, including immunization information systems • Provides comments and advice at the request of OMB regarding specific Federal health information technology programs.
National Vaccine Program Office (NVPO)	• Coordinates communication between vaccine manufacturers and HHS agencies • Coordinates National Vaccine Plan development and periodic review • Coordinates vaccine safety planning and public engagement • Coordinates and provides direction on vaccine research and development • Coordinates vaccine supply activities • Coordinates governmental and non-governmental vaccine activities
Agency for Healthcare Research and Quality	• Communicates with and supports federal, state, and local public health partners on vaccination and healthcare delivery plans
Centers for Disease Control and Prevention (CDC)	• Conducts and supports clinical and laboratory vaccine-preventable disease and microorganism surveillance, as well for diseases and microorganisms that may become vaccine preventable • Coordinates vaccine-preventable disease response

activities with state, local and tribal public health agencies
- Investigates epidemiology, environmental contributions to, and clinical characteristics, of vaccine-preventable disease
- Leads in federal vaccination program implementation and supports state and health care provider immunization through vaccine purchase, distribution, guidance, evaluation, and quality control
- Distributes public sector vaccines
- Co-leads with FDA in monitoring and investigating vaccine adverse events
- Assesses vaccine effectiveness in population-based studies
- Makes recommendations on diagnosis, management, and prevention of vaccine-preventable disease illness
- Conducts and supports basic and applied research on vaccine-preventable diseases
- Leads federal activities for surveillance, detection, and response to pandemic influenza
- Provides training and reagents for diagnosis of vaccine-preventable diseases
- Conducts and supports research and development of diagnostic test and immunologic assays for vaccine-preventable diseases
- Conducts human health risk assessment of new and emerging vaccine-preventable diseases in the US and globally
- Conducts laboratory and animal studies of emerging vaccine-preventable diseases to identify markers for virulence and transmission among humans
- Communicates with state and local health departments and other public health partners
- Communicates information on vaccine-preventable disease health impacts and vaccination in collaboration with ASPA and other partners
- Maintains close communication with vaccine manufacturers
- Provides reference strains for influenza vaccine manufacturing
- Works with WHO and other international organizations to promote global health through vaccination
- Provides scientific leadership and support to global laboratory networks for vaccine preventable diseases, technical support to eradication and elimination

	efforts and accelerating use of new and underutilized vaccines
Centers for Medicare and Medicaid (CMS)	• Provides streamlined payment mechanisms and works with prescription drug plans, Medicare managed care plans, and Medicare providers, as necessary, to ensure ready access to vaccines for Medicare's population • Communicates specific vaccine-preventable disease guidance to the nation's hospitals, home health agencies, skilled nursing facilities and other health care providers, suppliers and practitioners that participate in Medicare and Medicaid • Communicates vaccine-preventable disease related information through existing outreach networks to Medicare and Medicaid beneficiary populations • Supports tracking and surveillance of Medicare and Medicaid patients, including high-risk and vulnerable patients, who have received vaccines, including review of Medicare and Medicaid claims and quality data
Food and Drug Administration (FDA)	• Performs research to 1) facilitate vaccine development and evaluation, including through innovation in regulatory pathways, and 2) enhance manufacturing and product quality (including assays, biomarkers and models for product safety, quality and efficacy, and methods for statistical and epidemiological analysis) • Regulates vaccines' manufacturing processes and promotes enhancement of manufacturing quality and problem prevention • Prepares reference strains, assays, standards, and reagents appropriate for vaccine manufacturing • Evaluates and licenses vaccines • Monitors vaccine quality, releases vaccine lots for distribution, performs testing of vaccine quality and potency • Facilitates the development, evaluation and clearance or approval of diagnostic tests and devices • Reviews vaccine supply issues • Evaluates and issues Emergency Use Authorizations when appropriate • With CDC, monitors vaccine adverse events • Maintains close communication with vaccine manufacturers

	• Makes necessary changes in prescribing and patient information, including dosing, target populations, and other direction for use, for vaccines based on research and adverse events • Monitors to protect against the distribution of counterfeit vaccines • Designated as a WHO Collaborating Center for Biological Standardization, which encompasses responsibilities of setting and providing standards needed to assure products are high quality, safe, and available, and supporting efforts to harmonize product development and regulation.
National Institutes of Health (NIH)	• Studies the evolution and emergence of microorganisms, including the identification of factors that affect their host-range and virulence • Determines the molecular basis of virulence in humans and animals • Supports laboratory-based surveillance studies of the distribution of microorganisms that are, or may be, vaccine-preventable • Develops sensitive, specific, and rapid diagnostic tests for vaccine-preventable diseases • Develops and clinically evaluates novel vaccines and vaccination strategies (e.g., adjuvants, delivery systems) • Evaluates the immune response to infection and vaccination • Supports basic research, with the goal of identifying new therapeutic targets • Evaluates the molecular and/or environmental factors that influence the transmission of viruses, bacteria and other organisms, including drug-resistant strains • Maintains close communication with vaccine manufacturers • Prepares reference strains appropriate for vaccine manufacturing
Health Resources and Services Administration (HRSA)	• Provides national leadership, program resources and services needed to improve access to culturally, competent (including linguistic and health literate), quality health care. • As the Nation's access agency, focuses on uninsured, underserved, and special needs populations in its

	goals and program activities (including vaccine preventable diseases and vaccine administration). • Communicates with and provides technical assistance and training to support vaccine-preventable disease control activities of state primary care associations, health centers, and other community-based providers • Operates the National Vaccine Injury Compensation Program to ensure an adequate supply of vaccines, stabilize vaccine costs, establish and maintain an accessible and efficient forum for individuals found to be injured by certain vaccines to receive compensation.
Indian Health Service	• Communicates with and supports state, local, and tribal vaccination and vaccine-preventable disease response activities at HHS, tribal, and urban Indian sites serving American Indian and Alaska Native populations
Substance Abuse & Mental Health Services Administration	• Brings effective alcohol and drug treatment to every community. • Provides national leadership to expand the availability of effective treatment and recovery services for alcohol and drug problems; to improve access, reduce barriers and promote high-quality effective treatment and medical care services (including vaccination services) for people with alcohol and drug problems, abuse, or addiction as well as for their families and communities.
Department of Agriculture	• Manages Women, Infant, and Children's program for supplemental nutrition that also provides vaccination services. • Performs research on animal vaccines to prevent disease
Department of Defense	
Assistant Secretary of	• Serves as the principal civilian advisor to the Deputy

Defense for Health Affairs	Secretary of Defense for health service support for pandemic influenza preparedness and response • Responsible for overall leadership of the Military Health System • Serves as the principal advisor to the Secretary of Defense for all Department of Defense (DoD) health policies and programs • Oversees all DoD health resources
Defense Advanced Research Projects Agency	• Maintains the technological superiority of the U.S. military and prevent technological surprise from harming our national security. • Funds researchers in industry, universities, government laboratories and elsewhere to conduct high-risk, high-reward research and development projects that will benefit U.S. national security. • Develops technologies to accelerate the development and production of vaccines and other medical therapeutics from 12 years to only 12 weeks
Defense Threat Reduction Agency	• Provides capabilities to reduce, eliminate, and counter the threat of weapons of mass destruction (chemical, biological, radiological, nuclear and high explosives), and mitigate its effects. • Analyzes weapons of mass destruction threats, develops requirements forecasts and integrates the results into DTRA's future resource planning • Develops, provides, and maintains security, counterintelligence, and force protection products and services in support of the agency's global missions.
The Military Vaccine (Milvax) Agency	• Synchronize information among the Military Services and DoD staff elements • Deliver education for healthcare workers and the public (e.g., Immunization University, www.vaccines.mil, (877) GET-VACC, Vaccines@amedd.army.mil • Promote quality in immunization understanding and delivery • Coordinate and assess U.S. military immunization programs worldwide

	• Assist senior DoD leaders with policy development, especially related to biodefense and pandemic issues • Safeguard shipping and handling of temperature-sensitive medical products • Enhance scientific understanding of the benefits and risks of vaccines • Foster mutually beneficial relationships between DoD, other government agencies, and professional associations related to immunizations • Integrate electronic immunization tracking efforts of DoD and the Services
United States Army Medical Institute for Infectious Diseases	• Conducts basic and applied research on biological threats resulting in medical solutions to protect the warfighter. • Plays a key role as the only laboratory in the Department of Defense (DoD) equipped to safely study highly hazardous infectious agents requiring maximum containment at biosafety level (BSL)-4. • Ensures that research is conducted in a safe and secure environment. • Delivers competitive products to the advanced developer on schedule with the best value and quality.
United States Agency for International Development	• Participates in the Global Alliance for Vaccines and Immunization and introduces new and under-utilized vaccines into developing countries. • Provides technical and commodity assistance to more than 100 countries in support of routine child immunization programs, working closely with host-country Ministry's of Health, Non-governmental Organizations, International Organizations such as WHO and UNICEF, foundations and other international partners • Maintains a vaccine development program targeting malaria and HIV/AIDS in developing countries in coordination with DoD, HHS, and non-federal partners. • Provides technical assistance and funding for the Global Polio Eradication Initiative • Supports global goals to eliminate and control other

	vaccine preventable diseases such as measles and neonatal tetanus. • Raises awareness and helps generate greater resources, from both the public and private sectors, to help countries improve and sustain their capacity to deliver lifesaving vaccines and address diseases of international and domestic public health importance
Department of Veterans Affairs (VA)	• Mounts a system-wide annual seasonal influenza campaign for VHA patients and health care providers • Actively monitors, on a national basis, receipt of influenza and pneumococcal vaccine among at risk VHA patients • Monitors adverse events to vaccinations as part of a national pharmacovigilance program • Supports health services research in the area of improving vaccine delivery within VHA healthcare settings • Educates, communicates with, and provides technical assistance to VHA providers to support vaccine-preventable disease control activities in all VA health care facilities • Participates in clinical trials to determine efficacy of new/improved vaccines • Monitors national influenza vaccination rates of employees working in VHA health care facilities • Developing an occupational health record system for employees to track vaccination status • Contributes support and provides expertise to national bodies focused on vaccine and immunization programs.

Appendix 5: HHS Agency and Other Federal Department Strategic Plans relevant to the draft strategic National Vaccine Plan

HHS: U.S. Department of Health and Human Services Strategic Plan - FY 2007-2012

http://aspe.hhs.gov/hhsplan/2007/

ASPR: HHS PHEMCE Strategy and HHS PHEMCE Implementation Plan

http://www.hhs.gov/aspr/barda/phemce/enterprise/strategy/index.html

Draft BARDA Strategic Plan for Medical Countermeasure Research, Development, and Procurement

http://www.hhs.gov/aspr/barda/phemce/enterprise/strategy/bardaplan.html

CDC: National Immunization Program Strategic Plan 2000-2005
http://www.cdc.gov/ncird/downloads/strategic-plan.rtf

Immunization Information Systems Strategic Plan 2002-2007
http://www.cdc.gov/vaccines/programs/iis/activities/strategic-plan.htm

CDC Global Immunization Strategic Framework 2006-2010
http://www.cdc.gov/vaccines/programs/global/downloads/gisf-2006-2010.pdf

FDA: FDA Strategic Action Plan, Fall, 2007
http://www.fda.gov/ope/stratplan07/stratplan07.htm

ODPHP: HealthyPeople 2010
http://www.healthypeople.gov/Publications/

HealthyPeople 2020
http://www.healthypeople.gov/hp2020/

HRSA: HRSA Strategic Plan FY 2005-2010
http://www.hrsa.gov/about/strategicplan.htm

NIH: NIAID Strategic Plan for Biodefense Research, 2007
http://www3.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/about/strategicplan.htm

NIAID: Planning for the 21st Century
http://www3.niaid.nih.gov/about/overview/planningPriorities/strategicplan/

Department of Agriculture

USDA Strategic Plan 2005-2010
http://www.ocfo.usda.gov/usdasp/sp2005/sp2005.pdf

DoD: U.S. Department of Defense Military Health System Strategic Plan
http://www.health.mil/StrategicPlan/Default.aspx

DARPA Defense Advanced Research Projects Agency Strategic Plan 2007
http://www.darpa.mil/body/pdf/DARPA2007StrategicPlanfinalMarch14.pdf

DoJ U.S. Department of Justice Strategic Plan 2007-2012
http://www.usdoj.gov/jmd/mps/strategic2007-2012/

VA: VA Strategic Plan (2006-2011)
http://www1.va.gov/op3/docs/VA_2006_2011_Strategic_Plan.pdf

USAID: Strategic Plan: Fiscal Years 2007-2012
http://www.usaid.gov/policy/coordination/stratplan_fy07-12.html

Appendix B

Letter to the Committee from the National Vaccine Advisory Committee

DEPARTMENT OF HEALTH AND HUMAN SERVICES Office of the Secretary

Assistant Secretary for Health
Office of Public Health and Science
Washington D.C. 20201

Claire Broome, M.D., M.P.H.
IOM Committee Chair
Institute of Medicine
500 5th Street NW
Washington DC 20001

MAR 13 2009

Re: Incorporation of recommendations to National Vaccine Plan to ensure coordination of vaccination activities within the Federal government and with non-governmental partners

Dear Dr. Broome:

The National Vaccine Advisory Committee (NVAC), an advisory group to the U.S. Department of Health and Human Services (HHS) authorized by Section 2105 of Title XXI of the Public Health Service Act, would like to offer comment on the update to the National Vaccine Plan.

As stated in Section 2105(4) of Title XXI of the Public Health Service Act (P.L. 99-660), the NVAC shall "advise the Director of the [National Vaccine] Program in the implementation of sections 2102 and 2103 of the Act, which include coordinating governmental and non-governmental activities. As part of this charge, NVAC recently adopted its 2008 State of the Program Report which includes a series of recommendations. A copy of the Report is attached. A central concern of NVAC in the current conduct of the National Vaccine Program (NVP) is the need for better coordination by NVPO, particularly of federal agency vaccine efforts, and sufficient resources to carry this out. The NVAC's four recommendations in the Report are:

1. The NVP should be given the resources and effective organizational authority within HHS necessary to carry out its mission to coordinate and direct the vaccine-related efforts of the federal PHS agencies. Having the NVP report directly to the Secretary of HHS would achieve the needed organizational authority.

2. The National Vaccine Plan should specifically address how the NVP will improve its effectiveness.

3. The NVP should be evaluated regularly and its effectiveness reviewed as part of each revision of the National Vaccine Plan.

4. The NVPO should improve the effectiveness of the NVAC based on the recommendations of the pending NVAC evaluation report.

U.S. Public Health Service

The NVAC feels that the draft National Vaccine Plan does not go far enough to address coordination of vaccine-related activities both at the Federal level and with non-governmental partners. This role was highlighted in the 1994 National Vaccine Plan, and again in the June 2008 Initial Guidance for an Update of the National Vaccine Plan: A Letter Report to the National Vaccine Program Office, which stated:

> [T]he principal coordinating organization for the [National Vaccine Program] NVP is the National Vaccine Program Office (NVPO), within the Public Health Service (PHS). The NVPO's responsibilities include providing overall leadership for the collaborative effort and monitoring the progress being made in achieving the plan's goals. Within the PHS, the NVPO has the task of reviewing all budget requests associated with vaccine development and immunization programs to ensure that all major priorities are adequately covered and that there is no duplication of effort.

The NVAC urges the Institute of Medicine recommend as part of its critique of the draft National Vaccine Plan that the final Plan adequately and appropriately addresses the ability of the National Vaccine Program to coordinate between the many varied partners and stakeholders involved in immunization in the United States, and that it be given an adequate administrative structure and resources to do so.

Please don't hesitate to contact me if I can provide more information on behalf of the Committee. I can be reached through the National Vaccine Program Office, HHS at 202-690-5566.

Sincerely,

Guthrie Birkhead MD

Guthrie S. Birkhead, M.D., M.P.H., Chair
National Vaccine Advisory Committee

cc: Dr. Gellin

Enclosures

Appendix C

1986 National Childhood Vaccine Injury Act (Public Law 99-660)

tive service, and may pay such executive director and other personnel without regard to the provisions of chapter 51 and subchapter 111 of chapter 53 of such title relating to classification and General Schedule pay rates, except that the rate of pay for such executive director and other personnel may not exceed the rate payable for GS-18 of the General Schedule under section 5332 of such title. 5 USC 5101 *et seq.* 5 USC 5331.

(c) APPLICABILITY OF OTHER FEDERAL LAWS.—Service of an individual as a member of the Commission or employment of an individual by the Commission on a part-time or full-time basis and with or without compensation shall not be considered as service or employment bringing such individual within the provisions of any Federal law relating to conflicts of interest or otherwise imposing restrictions, requirements, or penalties in relation to the employment of persons, the performance of services, or the payment or receipt of compensation in connection with claims, proceedings, or matters involving the United States. Service as a member of the Commission or as an employee of the Commission, shall not be considered service in an appointive or elective position in the Government for purposes of section 8344 of title 5, United States Code, or comparable provisions of Federal law.

(d) EXPERTS AND CONSULTANTS.—Subject to such rules as may be prescribed by the Commission, the Chairman of the Commission may procure temporary and intermittent services under section 3109 of title 5, United States Code, at rates for individuals not to exceed the daily rate payable for GS-18 of the General Schedule under section 5332 of such title.

SEC. 207. SUNSHINE PROVISION. 42 USC 285g note.

The Commission shall establish procedures to ensure its proceedings are open to the public to the maximum extent practicable.

SEC. 208. TERMINATION OF THE COMMISSION. 42 USC 285g note.

Ninety days after the Commission submits its recommendations as required by section 204(b)(4) the Commission shall terminate.

SEC. 209. AUTHORIZATION OF APPROPRIATIONS. 42 USC 285g note.

There are authorized to be appropriated to the Commission such sums as may be necessary. Amounts appropriated under this section shall remain available until the day on which the Commission terminates under section 208.

TITLE III—VACCINE COMPENSATION

National Childhood Vaccine Injury Act of 1986. 42 USC 201.

SEC. 301. SHORT TITLE.

This title may be cited as the "National Childhood Vaccine Injury Act of 1986".

PART A—VACCINES

SEC. 311. AMENDMENT TO PUBLIC HEALTH SERVICE ACT. 42 USC 300aa *et seq.*, 300cc *et seq.*

(a) NEW TITLE.—The Public Health Service Act is amended by redesignating title XXI as title XXIII, by redesignating sections 2101 through 2116 as sections 2301 through 2316, respectively, and by inserting after title XX the following new title:

"TITLE XXI—VACCINES

"Subtitle 1—National Vaccine Program

"ESTABLISHMENT

42 USC 300aa-1. "SEC. 2101. The Secretary shall establish in the Department of Health and Human Services a National Vaccine Program to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines. The Program shall be administered by a Director selected by the Secretary.

"PROGRAM RESPONSIBILITIES

42 USC 300aa-2. "SEC. 2102. (a) The Director of the Program shall have the following responsibilities:

"(1) VACCINE RESEARCH.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for research carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development on means to induce human immunity against naturally occurring infectious diseases and to prevent adverse reactions to vaccines.

"(2) VACCINE DEVELOPMENT.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for activities carried out in or through the National Institutes of Health, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development to develop the techniques needed to produce safe and effective vaccines.

"(3) SAFETY AND EFFICACY TESTING OF VACCINES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for safety and efficacy testing of vaccines carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development.

"(4) LICENSING OF VACCINE MANUFACTURERS AND VACCINES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for the allocation of resources in the implementation of the licensing program under section 353.

42 USC 263a.

"(5) PRODUCTION AND PROCUREMENT OF VACCINES.—The Director of the Program shall, through the plan issued under section 2103, ensure that the governmental and non-governmental production and procurement of safe and effective vaccines by the Public Health Service, the Department of Defense, and the Agency for International Development meet the needs of the United States population and fulfill commitments of the United States to prevent human infectious diseases in other countries.

"(6) DISTRIBUTION AND USE OF VACCINES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction to the Centers for Disease

Control and assistance to States, localities, and health practitioners in the distribution and use of vaccines, including efforts to encourage public acceptance of immunizations and to make health practitioners and the public aware of potential adverse reactions and contraindications to vaccines.

"(7) EVALUATING THE NEED FOR AND THE EFFECTIVENESS AND ADVERSE EFFECTS OF VACCINES AND IMMUNIZATION ACTIVITIES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction to the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the National Center for Health Statistics, the National Center for Health Services Research and Health Care Technology Assessment, and the Health Care Financing Administration in monitoring the need for and the effectiveness and adverse effects of vaccines and immunization activities.

"(8) COORDINATING GOVERNMENTAL AND NON-GOVERNMENTAL ACTIVITIES.—The Director of the Program shall, through the plan issued under section 2103, provide for the exchange of information between Federal agencies involved in the implementation of the Program and non-governmental entities engaged in the development and production of vaccines and in vaccine research and encourage the investment of non-governmental resources complementary to the governmental activities under the Program.

"(9) FUNDING OF FEDERAL AGENCIES.—The Director of the Program shall make available to Federal agencies involved in the implementation of the plan issued under section 2103 funds appropriated under section 2106 to supplement the funds otherwise available to such agencies for activities under the plan.

"(b) In carrying out subsection (a) and in preparing the plan under section 2103, the Director shall consult with all Federal agencies involved in research on and development, testing, licensing, production, procurement, distribution, and use of vaccines.

"PLAN

"SEC. 2103. The Director of the Program shall prepare and issue a plan for the implementation of the responsibilities of the Director under section 2102. The plan shall establish priorities in research and the development, testing, licensing, production, procurement, distribution, and effective use of vaccines, describe an optimal use of resources to carry out such priorities, and describe how each of the various departments and agencies will carry out their vaccine functions in consultation and coordination with the Program and in conformity with such priorities. The first plan under this section shall be prepared not later than January 1, 1987, and shall be revised not later than January 1 of each succeeding year. 42 USC 300aa-3.

"REPORT

"SEC. 2104. The Director shall report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate not later than January 1, 1988, and annually thereafter on the implementation of the Program and the plan prepared under section 2103. 42 USC 300aa-4.

"NATIONAL VACCINE ADVISORY COMMITTEE

42 USC 300aa-5. "SEC. 2105. (a) There is established the National Vaccine Advisory Committee. The members of the Committee shall be appointed by the Director of the Program, in consultation with the National Academy of Sciences, from among individuals who are engaged in vaccine research or the manufacture of vaccines or who are physicians, members of parent organizations concerned with immunizations, or representatives of State or local health agencies or public health organizations.

"(b) The Committee shall—

"(1) study and recommend ways to encourage the availability of an adequate supply of safe and effective vaccination products in the States,

"(2) recommend research priorities and other measures the Director of the Program should take to enhance the safety and efficacy of vaccines,

"(3) advise the Director of the Program in the implementation of sections 2102, 2103, and 2104, and

"(4) identify annually for the Director of the Program the most important areas of government and non-government cooperation that should be considered in implementing sections 2102, 2103, and 2104.

"AUTHORIZATIONS

42 USC 300aa-6. "SEC. 2106. (a) To carry out this subtitle other than section 2102(9) there are authorized to be appropriated $2,000,000 for fiscal year 1987, $2,500,000 for fiscal year 1988, $3,000,000 for fiscal year 1989, $3,500,000 for fiscal year 1990, $4,000,000 for fiscal year 1991.

"(b) To carry out section 2102(9) there are authorized to be appropriated $20,000,000 for fiscal year 1987, $22,500,000 for fiscal year 1988, $25,000,000 for fiscal year 1989, $27,500,000 for fiscal year 1990, $30,000,000 for fiscal year 1991.

"Subtitle 2—National Vaccine Injury Compensation Program

"PART A—PROGRAM REQUIREMENTS

"ESTABLISHMENT OF PROGRAM

42 USC 300aa-10. "SEC. 2110. (a) PROGRAM ESTABLISHED.—There is established the National Vaccine Injury Compensation Program to be administered by the Secretary under which compensation may be paid for a vaccine-related injury or death.

"(b) ATTORNEY'S OBLIGATION.—It shall be the ethical obligation of any attorney who is consulted by an individual with respect to a vaccine-related injury or death to advise such individual that compensation may be available under the program for such injury or death.

"PETITIONS FOR COMPENSATION

42 USC 300aa-11. "SEC. 2111. (a) GENERAL RULE.—

"(1) A proceeding for compensation under the Program for a vaccine-related injury or death shall be initiated by service upon the Secretary and the filing of a petition with the United States district court for the district in which the petitioner resides or in which the injury or death occurred.

"(2)(A) No person may bring a civil action for damages in an amount greater than $1,000 or in an unspecified amount against a vaccine manufacturer in a State or Federal court for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle, and no such court may award damages in an amount greater than $1,000 in a civil action for damages for such a vaccine-related injury or death, unless—

"(i) a petition has been filed, in accordance with section 2116, under subsection (b) for compensation under the Program for such injury or death,

"(ii) a district court of the United States has issued a judgment under section 2112 on such petition, and Courts, U.S.

"(iii) such person elects under section 2121(a) to file such an action.

"(B) If a civil action which is barred under subparagraph (A) is filed in a State or Federal court, the court shall dismiss the action. If a petition is filed under this section with respect to the injury or death for which such civil action was brought, the date such dismissed action was filed shall, for purposes of the limitations of actions prescribed by section 2116, be considered the date the petition was filed if the petition was filed within one year of the date of the dismissal of the civil action. Courts, U.S.

"(3) No vaccine manufacturer may be made a party to a civil action (other than a civil action which may be brought under paragraph (2)) for damages for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle.

"(4) If in a civil action brought against a vaccine manufacturer before the effective date of this subtitle damages were denied for a vaccine-related injury or death or if such civil action was dismissed with prejudice, the person who brought such action may file a petition under subsection (b) for such injury or death.

"(5)(A) A plaintiff who on the effective date of this subtitle has pending a civil action for damages for a vaccine-related injury or death may, at any time within 2 years after the effective date of this title or before judgment, whichever occurs first, elect to withdraw such action without prejudice and file a petition under subsection (b) for such injury or death.

"(B) If a plaintiff who on the effective date of this subtitle had pending a civil action for damages for a vaccine-related injury or death does not withdraw the action under subparagraph (A), such person may not file a petition under subsection (b) for such injury or death.

"(6) If a person brings a civil action after the effective date of this subtitle for damages for a vaccine-related injury or death associated with the administration of a vaccine before the effective date of this subtitle, such person may not file a petition under subsection (b) for such injury or death.

"(7) If in a civil action brought against a vaccine manufacturer for a vaccine-related injury or death damages are awarded under a judgment of a court or a settlement of such action, the person who brought such action may not file a petition under subsection (b) for such injury or death.

(b) PETITIONERS.—

"(1)(A) Except as provided in subparagraph (B), any person who has sustained a vaccine-related injury, the legal representative of such person if such person is a minor or is disabled, or the legal representative of any person who died as the result of the administration of a vaccine set forth in the Vaccine Injury Table may file a petition for compensation under the Program.

"(B) No person may file a petition for a vaccine-related injury or death associated with a vaccine administered before the effective date of this subtitle if compensation has been paid under this subtitle for 3500 petitions for such injuries or deaths.

"(2) Only one petition may be filed with respect to each administration of a vaccine.

"(c) PETITION CONTENT.—A petition for compensation under the Program for a vaccine-related injury or death shall contain—

"(1) an affidavit, and supporting documentation, demonstrating that the person who suffered such injury or who died—

"(A) received a vaccine set forth in the Vaccine Injury Table or, if such person did not receive such a vaccine, contracted polio, directly or indirectly, from another person who received an oral polio vaccine,

"(B)(i) if such person received a vaccine set forth in the Vaccine Injury Table—

"(I) received the vaccine in the United States or in its trust territories,

"(II) received the vaccine outside the United States or a trust territory and at the time of the vaccination such person was a citizen of the United States serving abroad as a member of the Armed Forces or otherwise as an employee of the United States or a dependent of such a citizen, or

"(III) received the vaccine outside the United States or a trust territory and the vaccine was manufactured by a vaccine manufacturer located in the United States and such person returned to the United States not later than 6 months after the date of the vaccination,

"(ii) if such person did not receive such a vaccine but contracted polio from another person who received an oral polio vaccine, was a citizen of the United States or a dependent of such a citizen,

"(C)(i) sustained, or had significantly aggravated, any illness, disability, injury, or condition set forth in the Vaccine Injury Table in association with the vaccine referred to in subparagraph (A) or died from the administration of such vaccine, and the first symptom or manifestation of the onset or of the significant aggravation of any such illness, disability, injury, or condition or the death occurred within the time period after vaccine administration set forth in the Vaccine Injury Table, or

"(ii)(I) sustained, or had significantly aggravated, any illness, disability, injury, or condition not set forth in the Vaccine Injury Table but which was caused by a vaccine referred to in subparagraph (A), or

"(II) sustained, or had significantly aggravated, any illness, disability, injury, or condition set forth in the Vaccine Injury Table the first symptom or manifestation of the onset or significant aggravation of which did not occur

within the time period set forth in the Table but which was caused by a vaccine referred to in subparagraph (A),

"(D)(i) suffered the residual effects or complications of such illness, disability, injury, or condition for more than 1 year after the administration of the vaccine, (ii) incurred unreimbursable expenses due in whole or in part to such illness, disability, injury, or condition in an amount greater than $1,000, or (iii) died from the administration of the vaccine, and

"(E) has not previously collected an award or settlement of a civil action for damages for such vaccine-related injury or death,

"(2) all available relevant medical records (including autopsy reports, if any) relating to the person who suffered such injury or who died from the administration of the vaccine and an identification of any unavailable records known to the petitioner and the reasons for their unavailability, and

"(3) appropriate assessments, evaluations, and prognoses and such other records and documents as are reasonably necessary for the determination of the amount of compensation to be paid to, or on behalf of, the person who suffered such injury or who died from the administration of the vaccine.

"COURT JURISDICTION

"SEC. 2112. (a) GENERAL RULE.—The district courts of the United States shall have jurisdiction (1) over proceedings to determine if a petitioner under section 2111 is entitled to compensation under the Program and the amount of such compensation, and (2) to issue and enforce such orders as the courts deem necessary to assure the prompt payment of any compensation awarded. 42 USC 300aa-12.

"(b) PARTIES.—

"(1) The Secretary shall be named as the respondent in all proceedings brought by the filing of a petition under section 2111(b). Except as provided in paragraph (2), no other person may intervene in any such proceeding.

"(2) Within 30 days after the Secretary receives service of any petition filed under section 2111 the Secretary shall publish notice of such petition in the Federal Register. The special master designated with respect to such petition under subsection (c) shall afford all interested persons an opportunity to submit relevant, written information— Federal Register, publication.

"(A) relating to the existence of the evidence described in section 2113(a)(1)(B), or

"(B) relating to any allegation in a petition with respect to the matters described in section 2111(c)(1)(C)(ii).

"(c) SPECIAL MASTERS.—

"(1) Following receipt of a petition under subsection (a), the district court of the United States in which the petition is filed shall designate a special master to carry out the functions authorized by paragraph (2).

"(2) A special master shall serve as an adjunct to the court and may—

"(A) require such evidence as may be appropriate for the preparation of proposed findings of fact and conclusions of law with respect to whether compensation is to be provided

under the Program and the amount of any such compensation,

"(B) require the submission of such information as may be reasonable and necessary to determine if the petitioner is entitled to compensation,

"(C) require the testimony of any person and the production of any document as may be reasonable and necessary to determine if the petitioner is entitled to compensation,

"(D) conduct such hearings as may be appropriate, and

"(E) prepare and submit to the court proposed findings of fact and conclusions of law.

Information submitted to a special master in a proceeding on a petition may not be disclosed to a person who is not a party to the proceeding without the express, written consent of the person who submitted the information. There may be no discovery in a proceeding on a petition other than the discovery required under this paragraph.

"(d) ACTION BY THE COURT.—

Records.

"(1) Upon objection by the petitioner or respondent to the proposed findings of fact or conclusions of law prepared by the special master or upon the court's own motion, the court shall undertake a review of the record of the proceedings and may thereafter make a de novo determination of any matter and issue its judgment accordingly, including findings of fact and conclusions of law, or remand for further proceedings.

"(2) If no objection is filed under paragraph (1) or if the court does not choose to review the proceeding, the court shall adopt the proposed findings of fact and conclusions of law of the special master as its own and render judgment thereon.

"(3) The court shall render its judgment on any petition filed under the Program as expeditiously as practicable but not later than 365 days after the date on which the petition was filed.

"(e) ADMINISTRATION OF AWARD.—The Program shall administer the payments of such compensation. The Program shall audit the payments of compensation under a judgment. A petitioner awarded compensation shall notify the Program of any changes which significantly affect the compensation to be paid.

"(f) REVISION OF AWARD.—

"(1) If the court issues a judgment awarding to a petitioner compensation described in section 2115(a)(1)(A) for unreimbursable expenses and the compensation is insufficient to meet such expenses, such petitioner may petition the court to (A) review such award, and (B) increase the award to make it sufficient to meet such expenses or amend the periodic payment schedule established under section 2115, or both.

"(2) If an audit conducted under subsection (e) discloses the improper use of compensation awarded under a judgment or the termination of a need for an item of compensation, the Program shall petition the court which awarded the compensation to make an appropriate revision in the compensation.

"(g) APPEALS.—The findings of fact and conclusions of law of a district court of the United States on a petition shall be final determinations of the matters involved, except that the Secretary or any petitioner aggrieved by the findings or conclusions of the court may obtain review of the judgment of the court in the United States court of appeals for the circuit in which the court is located upon petition filed with such court of appeals.

"DETERMINATION OF ELIGIBILITY AND COMPENSATION

"SEC. 2113. (a) GENERAL RULE.— Courts, U.S. Records. 42 USC 300aa-13.

"(1) Compensation shall be awarded under the Program to a petitioner if the court finds on the record as a whole—

"(A) that the petitioner has demonstrated by a preponderance of the evidence the matters required in the petition by section 2111(c)(1), and

"(B) that there is not a preponderance of the evidence that the illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition.

The court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion.

"(2) For purposes of paragraph (1), the term 'factors unrelated to the administration of the vaccine'—

"(A) does not include any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness, or condition, and

"(B) may, as documented by the petitioner's evidence or other material in the record, include infection, toxins, trauma (including birth trauma and related anoxia), or metabolic disturbances which have no known relation to the vaccine involved, but which in the particular case are shown to have been the agent or agents principally responsible for causing the petitioner's illness, disability, injury, condition, or death.

"(b) MATTERS TO BE CONSIDERED.—

"(1) In determining whether to award compensation to a petitioner under the Program, the court shall consider, in addition to all other relevant medical and scientific evidence contained in the record— Courts, U.S. Records.

"(A) any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death, and

"(B) the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions.

Any such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the court. In evaluating the weight to be afforded to any such diagnosis, conclusion, judgment, test result, report, or summary, the court shall consider the entire record and the course of the injury, disability, illness, or condition until the date of the judgment of the court.

"(2) The court may find the first symptom or manifestation of onset or significant aggravation of an injury, disability, illness, condition, or death described in a petition occurred within the time period described in the Vaccine Injury Table even though the occurrence of such symptom or manifestation was not recorded or was incorrectly recorded as having occurred outside such period. Such a finding may be made only upon demonstration by a preponderance of the evidence that the onset or significant aggravation of the injury, disability, illness, condi-

tion, or death described in the petition did in fact occur within the time period described in the Vaccine Injury Table.

"(c) RECORD DEFINED.—For purposes of this section, the term 'record' means the record established by a distict court of the United States in a proceeding on a petition filed under section 2111.

"VACCINE INJURY TABLE

42 USC 300aa-14.

"SEC. 2114. (a) INITIAL TABLE.—The following is a table of vaccines, the injuries, disabilities, illnesses, conditions, and deaths resulting from the administration of such vaccines, and the time period in which the first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths is to occur after vaccine administration for purposes of receiving compensation under the Program:

"VACCINE INJURY TABLE

I.	DTP; P; DTP/Polio Combination; or Any Other Vaccine Containing Whole Cell Pertussis Bacteria, Extracted or Partial Cell Bacteria, or Specific Pertussis Antigen(s).	
	Illness, disability, injury, or condition covered:	Time period for first symptom or manifestation of onset or of significant aggravation after vaccine administration:
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)	3 days
	C. Shock-collapse or hypotonic-hyporesponsive collapse	3 days
	D. Residual seizure disorder in accordance with subsection (c)(2)	3 days
	E. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
II.	Measles, mumps, rubella, or any vaccine containing any of the foregoing as a component; DT; Td; or Tetanus Toxoid.	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)	15 days (for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component). 3 days (for DT, Td, or tetanus toxoid).
	C. Residual seizure disorder in accordance with subsection (c)(2)	15 days (for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component). 3 days (for DT, Td, or tetanus toxoid).
	D. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
III.	Polio Vaccines (other than Inactivated Polio Vaccine).	
	A. Paralytic polio	

	—in a non-immunodeficient recipient	30 days
	—in an immunodeficient recipient	6 months
	—in a vaccine-associated community case	Not applicable
	B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
IV.	Inactivated Polio Vaccine.	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable

"(b) QUALIFICATIONS AND AIDS TO INTERPRETATION.—The following qualifications and aids to interpretation shall apply to the Vaccine Injury Table in subsection (a):

"(1) A shock-collapse or a hypotonic-hyporesponsive collapse may be evidenced by indicia or symptoms such as decrease or loss of muscle tone, paralysis (partial or complete), hemiplegia or hemiparesis, loss of color or turning pale white or blue, unresponsiveness to environmental stimuli, depression of consciousness, loss of consciousness, prolonged sleeping with difficulty arousing, or cardiovascular or respiratory arrest.

"(2) A petitioner may be considered to have suffered a residual seizure disorder if the petitioner did not suffer a seizure or convulsion unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit before the first seizure or convulsion after the administration of the vaccine involved and if—

"(A) in the case of a measles, mumps, or rubella vaccine or any combination of such vaccines, the first seizure or convulsion occurred within 15 days after administration of the vaccine and 2 or more seizures or convulsions occurred within 1 year after the administration of the vaccine which were unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit, and

"(B) in the case of any other vaccine, the first seizure or convulsion occurred within 3 days after administration of the vaccine and 2 or more seizures or convulsions occurred within 1 year after the administration of the vaccine which were unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit.

"(3)(A) The term 'encephalopathy' means any significant acquired abnormality of, or injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurologic signs, increased intracranial pressure, or changes lasting at least 6 hours in level of consciousness, with or without convulsions. The neurological signs and symptoms of encephalopathy may be temporary with complete recovery, or may result in various degrees of permanent impairment. Signs and symptoms such as high

pitched and unusual screaming, persistent unconsolable crying, and bulging fontanel are compatible with an encephalopathy, but in and of themselves are not conclusive evidence of encephalopathy. Encephalopathy usually can be documented by slow wave activity on an electroencephalogram.

"(B) If in a proceeding on a petition it is shown by a preponderance of the evidence that an encephalopathy was caused by infection, toxins, trauma, or metabolic disturbances the encephalopathy shall not be considered to be a condition set forth in the table. If at the time a judgment is entered on a petition filed under section 2111(b) for a vaccine-related injury or death it is not possible to determine the cause, by a preponderance of the evidence, of an encephalopathy, the encephalopathy shall be considered to be a condition set forth in the table. In determining whether or not an encephalopathy is a condition set forth in the table, the court shall consider the entire medical record.

"(4) For purposes of paragraphs (2) and (3), the terms 'seizure' and 'convulsion' include grand mal, petit mal, absence, myoclonic, tonic-clonic, and focal motor seizures and signs. If a provision of the table to which paragraph (1), (2), (3), or (4) applies is revised under subsection (c) or (d), such paragraph shall not apply to such provision after the effective date of the revision unless the revision specifies that such paragraph is to continue to apply.

"(c) ADMINISTRATIVE REVISION OF THE TABLE.—

Regulations.

"(1) The Secretary may promulgate regulations to modify in accordance with paragraph (3) the Vaccine Injury Table. In promulgating such regulations, the Secretary shall provide for notice and opportunity for a public hearing and at least 180 days of public comment.

"(2) Any person (including the Advisory Commission on Childhood Vaccines) may petition the Secretary to propose regulations to amend the Vaccine Injury Table. Unless clearly frivolous, or initiated by the Commission, any such petition shall be referred to the Commission for its recommendations. Following—

"(A) receipt of any recommendation of the Commission, or

Federal Register, publication.

"(B) 180 days after the date of the referral to the Commission,

whichever occurs first, the Secretary shall conduct a rulemaking proceeding on the matters proposed in the petition or publish in the Federal Register a statement of reasons for not conducting such proceeding.

"(3) A modification of the Vaccine Injury Table under paragraph (1) may add to, or delete from, the list of injuries, disabilities, illnesses, conditions, and deaths for which compensation may be provided or may change the time periods for the first symptom or manifestation of the onset or the significant aggravation of any such injury, disability, illness, condition, or death.

"(4) Any modification under paragraph (1) of the Vaccine Injury Table shall apply only with respect to petitions for compensation under the Program which are filed after the effective date of such regulation.

"(d) ROLE OF COMMISSION.—Except with respect to a regulation recommended by the Advisory Commission on Childhood Vaccines, the Secretary may not propose a regulation under subsection (c) or any revision thereof, unless the Secretary has first provided to the Commission a copy of the proposed regulation or revision, requested recommendations and comments by the Commission, and afforded the Commission at least 90 days to make such recommendations. Regulations.

"(e) RECOMMENDATION.—The Secretary may recommend to Congress revisions of the table to change the vaccines covered by the table.

"COMPENSATION

"SEC. 2115. (a) GENERAL RULE.—Compensation awarded under the Program to a petitioner under section 2111 for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle shall include the following: 42 USC 300aa-15.

"(1)(A) Actual unreimbursable expenses incurred from the date of the judgment awarding such expenses and reasonable projected unreimbursable expenses which—

"(i) result from the vaccine-related injury for which the petitioner seeks compensation,

"(ii) have been or will be incurred by or on behalf of the person who suffered such injury, and

"(iii)(I) have been or will be for diagnosis and medical or other remedial care determined to be reasonably necessary, or

"(II) have been or will be for rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary.

The amount of unreimbursable expenses which may be recovered under this subparagraph shall be limited to the amount in excess of the amount set forth in section 2111(c)(1)(D)(ii).

"(B) Subject to section 2116(a)(2), actual unreimbursable expenses incurred before the date of the judgment awarding such expenses which—

"(i) resulted from the vaccine-related injury for which the petitioner seeks compensation,

"(ii) were incurred by or on behalf of the person who suffered such injury, and

"(iii) were for diagnosis, medical or other remedial care, rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary.

The amount of unreimbursable expenses which may be recovered under this subparagraph shall be limited to the amount in excess of the amount set forth in section 2111(c)(1)(D)(ii).

"(2) In the event of a vaccine-related death, an award of $250,000 for the estate of the deceased.

"(3)(A) In the case of any person who has sustained a vaccine-related injury after attaining the age of 18 and whose earning

capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded, compensation for actual and anticipated loss of earnings determined in accordance with generally recognized actuarial principles and projections.

"(B) In the case of any person who has sustained a vaccine-related injury before attaining the age of 18 and whose earning capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded and whose vaccine-related injury is of sufficient severity to permit reasonable anticipation that such person is likely to suffer impaired earning capacity at age 18 and beyond, compensation after attaining the age of 18 for loss of earnings determined on the basis of the average gross weekly earnings of workers in the private, non-farm sector, less appropriate taxes and the average cost of a health insurance policy, as determined by the Secretary.

"(4) For actual and projected pain and suffering and emotional distress from the vaccine-related injury, an award not to exceed $250,000.

Payments for projected expenses shall be paid on a periodic basis (but no payment may be made for a period in excess of 1 year). Payments for pain and suffering and emotional distress and incurred expenses may be paid in a lump sum.

"(b) VACCINES ADMINISTERED BEFORE THE EFFECTIVE DATE.—Compensation awarded under the Program to a petitioner under section 2111 for a vaccine-related injury or death associated with the administration of a vaccine before the effective date of this subtitle shall only include the compensation described in paragraphs (1)(A) and (2) of subsection (a).

"(c) RESIDENTIAL AND CUSTODIAL CARE AND SERVICE.—The amount of any compensation for residential and custodial care and service expenses under subsection (a)(1) shall be sufficient to enable the compensated person to remain living at home.

"(d) TYPES OF COMPENSATION PROHIBITED.—Compensation awarded under the Program may not include the following:

"(1) Punitive or exemplary damages.

"(2) Except with respect to compensation payments under paragraphs (2) and (3) of subsection (a), compensation for other than the health, education, or welfare of the person who suffered the vaccine-related injury with respect to which the compensation is paid.

"(e) ATTORNEYS' FEES.—

Courts, U.S.

"(1) The judgment of a court on a petition filed under section 2111 awarding compensation shall include an amount to cover—

"(A) reasonable attorneys' fees, and

"(B) other costs,

incurred in any proceeding on such petition. If the judgment of a court on such a petition does not award compensation, the court may include in the judgment an amount to cover petitioner's reasonable attorneys' fees and other costs incurred in any proceeding on such petition if the court determines that the civil action was brought in good faith and there was a reasonable basis for the claim for which the civil action was brought.

"(2) If the petitioner, before the effective date of this title, filed a civil action for damages for any vaccine-related injury or death for which compensation may be awarded under the Pro-

gram, and elected under section 2111(a)(4) to withdraw such action and to file a petition for compensation under the Program, the judgment of the court on such petition may include an amount limited to the costs and expenses incurred by the petitioner and the attorney of the petitioner before the effective date of this subtitle in preparing, filing, and prosecuting such civil action (including the reasonable value of the attorney's time if the civil action was filed under contingent fee arrangements).

"(3) No attorney may charge any fee for services in connection with a petition filed under section 2111 which is in addition to any amount included under paragraph (1) in a judgment on such petition.

"(f) PAYMENT OF COMPENSATION.—

"(1) Except as provided in paragraph (2), no compensation may be paid until an election has been made, or has been deemed to have been made, under section 2121(a) to receive compensation.

"(2) Compensation described in subsection (a)(1)(A)(iii) shall be paid from the date of the judgment of the district court of the United States under section 2112 awarding the compensation. Such compensation may not be paid after an election under section 2121(b) to file a civil action for damages for the vaccine-related injury or death for which such compensation was awarded.

"(3) Payments of compensation shall be exempt from reduction under any order issued under part C of the Balanced Budget and Emergency Deficit Control Act of 1985. 2 USC 901 *et seq.*

"(f) PROGRAM NOT PRIMARILY LIABLE.—Payment of compensation under the Program shall not be made for any item or service to the extent that payment has been made, or can reasonably be expected to be made, with respect to such item or service (1) under any State compensation program, under an insurance policy, or under any Federal or State health benefits program, or (2) by an entity which provides health services on a prepaid basis.

"(g) LIABILITY OF HEALTH INSURANCE CARRIERS, PREPAID HEALTH PLANS, AND BENEFIT PROVIDERS.—No policy of health insurance may make payment of benefits under the policy secondary to the payment of compensation under the Program and—

"(1) no State, and

"(2) no entity which provides health services on a prepaid basis or provides health benefits,

may make the provision of health services or health benefits secondary to the payment of compensation under the Program.

"LIMITATIONS OF ACTIONS

"SEC. 2116. (a) GENERAL RULE.—In the case of— 42 USC 300aa-16.

"(1) a vaccine set forth in the Vaccine Injury Table which is administered before the effective date of this title, if a vaccine-related injury or death occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such injury or death after the expiration of 24 months after the effective date of this title,

"(2) a vaccine set forth in the Vaccine Injury Table which is administered after the effective date of this title, if a vaccine-related injury occurred as a result of the administration of such

vaccine, no petition may be filed for compensation under the Program for such injury after the expiration of 36 months after the date of the occurrence of the first symptom or manifestation of onset or of the significant aggravation of such injury, and

"(3) a vaccine set forth in the Vaccine Injury Table which is administered after the effective date of this title, if a death occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such death after the expiration of 24 months from the date of the death and no such petition may be filed more than 48 months after the date of the occurrence of the first symptom or manifestation of onset or of the significant aggravation of the injury from which the death resulted.

"(b) EFFECT OF REVISED TABLE.—If at any time the Vaccine Injury Table is revised and the effect of such revision is to permit an individual who was not, before such revision, eligible to seek compensation under the Program, such person may file a petition for such compensation not later than 2 years after the effective date of the revision, except that no compensation may be provided under the Program with respect to a vaccine-related injury or death covered under the revision of the table if—

"(1) the vaccine-related death occurred more than 8 years before the date of the revision of the table, or

"(2) the vaccine-related injury occurred more than 8 years before the date of the revision of the table.

"(c) STATE LIMITATIONS OF ACTIONS.—If a petition is filed under section 2111(b) for a vaccine-related injury or death, limitations of actions under State law shall be stayed with respect to a civil action brought for such injury or death for the period beginning on the date the petition is filed and ending on the date a final judgment is entered on the petition.

"SUBROGRATION

42 USC 300aa-17.

"SEC. 2117. (a) GENERAL RULE.—

"(1) Upon payment of compensation to any petitioner under the Program, the trust fund which has been established to provide such compensation shall be subrogated to all rights of the petitioner with respect to the vaccine-related injury or death for which compensation was paid, except that the trust fund may not recover under such rights an amount greater than the amount of compensation paid to the petitioner.

Courts, U.S. Records. Claims.

"(2) In any case in which it deems such action appropriate, a district court of the United States may, after entry of a final judgment providing for compensation to be paid under section 2115 for a vaccine-related injury or death, refer the record of such proceeding to the Secretary and the Attorney General with such recommendation as the court deems appropriate with respect to the investigation or commencement of a civil action by the Secretary under paragraph (1).

"(b) DISPOSITION OF AMOUNTS RECOVERED.—Amounts recovered under subsection (a) shall be collected on behalf of, and deposited in, the trust fund which has been established to provide compensation under the Program.

"INCREASE FOR INFLATION

"SEC. 2118. The compensation under subsections (a)(2) and (a)(4) of section 2115 and the civil penalty under section 2127(b) shall, effective December 1 of each year beginning 1 year after the effective date of this title, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest 1/10 of 1 percent. For purposes of this section, the term 'base quarter', as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

Effective date.
42 USC 300aa-18.

"ADVISORY COMMISSION ON CHILDHOOD VACCINES

"SEC. 2119. (a) ESTABLISHMENT.—There is established the Advisory Commission on Childhood Vaccines. The Commission shall be composed of:

42 USC 300aa-19.

"(1) Nine members appointed by the Secretary as follows:

"(A) Three members who are health professionals, who are not employees of the United States, and who have expertise in the health care of children, the epidemiology, etiology, and prevention of childhood diseases, and the adverse reactions associated with vaccines, of whom at least two shall be pediatricians.

"(B) Three members from the general public, of whom at least two shall be legal representatives of children who have suffered a vaccine-related injury or death.

"(C) Three members who are attorneys, of whom at least one shall be an attorney whose specialty includes representation of persons who have suffered a vaccine-related injury or death and of whom one shall be an attorney whose specialty includes representation of vaccine manufacturers.

"(2) The Director of the National Institutes of Health, the Assistant Secretary for Health, the Director of the Centers for Disease Control, and the Commissioner of Food and Drugs (or the designees of such officials), each of whom shall be a nonvoting ex officio member.

The Secretary shall select members of the Commission within 90 days of the effective date of this subtitle. The members of the Commission shall select a Chair from among the members.

"(b) TERM OF OFFICE.—Appointed members of the Commission shall be appointed for a term of office of 3 years, except that of the members first appointed, 3 shall be appointed for a term of 1 year, 3 shall be appointed for a term of 2 years, and 3 shall be appointed for a term of 3 years, as determined by the Secretary.

"(c) MEETINGS.—The Commission shall first meet within 60 days after all members of the Commission are appointed, and thereafter shall meet not less often than four times per year and at the call of the chair. A quorum for purposes of a meeting is 5. A decision at a meeting is to be made by a ballot of a majority of the voting members of the Commission.

"(d) COMPENSATION.—Members of the Commission who are officers or employees of the Federal Government shall serve as members of the Commission without compensation in addition to that received in their regular public employment. Members of the

Commission who are not officers or employees of the Federal Government shall be compensated at a rate not to exceed the daily equivalent of the rate in effect for grade GS-18 of the General Schedule for each day (including traveltime) they are engaged in the performance of their duties as members of the Commission. All members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703, title 5, United States Code, for employees serving intermittently.

5 USC 5332.

"(e) STAFF.—The Secretary shall provide the Commission with such professional and clerical staff, such information, and the services of such consultants as may be necessary to assist the Commission in carrying out effectively its functions under this section.

"(f) FUNCTIONS.—The Commission shall—

"(1) advise the Secretary on the implementation of the Program,

"(2) on its own initiative or as the result of the filing of a petition, recommend changes in the Vaccine Injury Table,

"(3) advise the Secretary in implementing the Secretary's responsibilities under section 2127 regarding the need for childhood vaccination products that result in fewer or no significant adverse reactions,

"(4) survey Federal, State, and local programs and activities relating to the gathering of information on injuries associated with the administration of childhood vaccines, including the adverse reaction reporting requirements of section 2125(b), and advise the Secretary on means to obtain, compile, publish, and use credible data related to the frequency and severity of adverse reactions associated with childhood vaccines, and

"(5) recommend to the Director of the National Vaccine Program research related to vaccine injuries which should be conducted to carry out this subtitle.

"PART B—ADDITIONAL REMEDIES

"AUTHORITY TO BRING ACTIONS

42 USC 300aa-21.

"SEC. 2121. (a) ELECTION.—After the judgment of a district court of the United States under section 2111 on a petition filed for compensation under the Program for a vaccine-related injury or death has become final, the person who filed the petition shall file with the court—

"(1) if the judgment awarded compensation, an election in writing to receive the compensation or to file a civil action for damages for such injury or death, or

"(2) if the judgment did not award compensation, an election in writing to accept the judgment or to file a civil action for damages for such injury or death.

An election shall be filed under this subsection not later than 90 days after the date of the entry of the court's judgment with respect to which the election is to be made. If a person required to file an election with a court under this subsection does not file the election within the time prescribed for filing the election, such person shall be deemed to have filed an election to accept the judgment of the court. If a person elects to receive compensation under a judgment of a court or is deemed to have accepted the judgment of a court,

such person may not bring or maintain a civil action for damages against a vaccine manufacturer for the vaccine-related injury or death for which the judgment was entered.

"(b) LIMITATIONS OF ACTIONS.—A civil action for damages arising from a vaccine-related injury or death for which a petition was filed under section 2111 shall, except as provided in section 2116(c), be brought within the period prescribed by limitations of actions under State law applicable to such civil action. State and local governments.

"STANDARDS OF RESPONSIBILITY

"SEC. 2122. (a) GENERAL RULE.—Except as provided in subsections (b), (c), and (e) State law shall apply to a civil action brought for damages for a vaccine-related injury or death. State and local governments. Claims. 42 USC 300aa–22.

"(b) UNAVOIDABLE ADVERSE SIDE EFFECTS; WARNINGS.—

"(1) No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.

"(2) For purposes of paragraph (1), a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with all requirements under the Federal Food, Drug, and Cosmetic Act and section 351 of the Public Health Service Act (including regulations issued under such provisions) applicable to the vaccine and related to vaccine-related injury or death for which the civil action was brought unless the plaintiff shows— 21 USC 301 note. 42 USC 262.

"(A) that the manufacturer engaged in the conduct set forth in subparagraph (A) or (B) of section 2123(d)(2), or

"(B) by clear and convincing evidence that the manufacturer failed to exercise due care notwithstanding its compliance with such Act and section (and regulations issued under such provisions).

"(c) DIRECT WARNINGS.—No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle solely due to the manufacturer's failure to provide direct warnings to the injured party (or the injured party's legal representative) of the potential dangers resulting from the administration of the vaccine manufactured by the manufacturer.

"(d) CONSTRUCTION.—The standards of responsibility prescribed by this section are not to be construed as authorizing a person who brought a civil action for damages against a vaccine manufacturer for a vaccine-related injury or death in which damages were denied or which was dismissed with prejudice to bring a new civil action against such manufacturer for such injury or death.

"(e) PREEMPTION.—No State may establish or enforce a law which prohibits an individual from bringing a civil action against a vaccine manufacturer for damages for a vaccine-related injury or death if such civil action is not barred by this subtitle. State and local governments.

"TRIAL

42 USC 300aa-23.

"SEC. 2123. (a) GENERAL RULE.—A civil action against a vaccine manufacturer for damages for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle which is not barred by section 2111(a)(2) shall be tried in three stages.

"(b) LIABILITY.—The first stage of such a civil action shall be held to determine if a vaccine manufacturer is liable under section 2122.

"(c) GENERAL DAMAGES.—The second stage of such a civil action shall be held to determine the amount of damages (other than punitive damages) a vaccine manufacturer found to be liable under section 2122 shall be required to pay.

"(d) PUNITIVE DAMAGES.—

"(1) If sought by the plaintiff, the third stage of such an action shall be held to determine the amount of punitive damages a vaccine manufacturer found to be liable under section 2122 shall be required to pay.

Fraud.

"(2) If in such an action the manufacturer shows that it complied, in all material respects, with all requirements under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act applicable to the vaccine and related to the vaccine injury or death with respect to which the action was brought, the manufacturer shall not be held liable for punitive damages unless the manufacturer engaged in—

21 USC 301 note.
42 USC 201 note.

"(A) fraud or intentional and wrongful withholding of information from the Secretary during any phase of a proceeding for approval of the vaccine under section 351,

42 USC 262.

Safety.

"(B) intentional and wrongful withholding of information relating to the safety or efficacy of the vaccine after its approval, or

Safety.

"(C) other criminal or illegal activity relating to the safety and effectiveness of vaccines,

which activity related to the vaccine-related injury or death for which the civil action was brought.

"(e) EVIDENCE.—In any stage of a civil action, the Vaccine Injury Table, any finding of a district court of the United States or a master appointed by such court in a proceeding on a petition filed under section 2111 and the final judgment of a district court of the United States on such a petition shall not be admissible.

"PART C—ASSURING A SAFER CHILDHOOD VACCINATION PROGRAM IN THE UNITED STATES

"RECORDING AND REPORTING OF INFORMATION

42 USC 300aa-25.

"SEC. 2125. (a) GENERAL RULE.—Each health care provider who administers a vaccine set forth in the Vaccine Injury Table to any person shall record, or ensure that there is recorded, in such person's permanent medical record (or in a permanent office log or file to which a legal representative shall have access upon request) with respect to each such vaccine—

"(1) the date of administration of the vaccine,

"(2) the vaccine manufacturer and lot number of the vaccine,

"(3) the name and address and, if appropriate, the title of the health care provider administering the vaccine, and

"(4) any other identifying information on the vaccine required pursuant to regulations promulgated by the Secretary.

"(b) REPORTING.—

"(1) Each health care provider and vaccine manufacturer shall report to the Secretary—

"(A) the occurrence of any event set forth in the Vaccine Injury Table, including the events set forth in section 2114(b) which occur within 7 days of the administration of any vaccine set forth in the Table or within such longer period as is specified in the Table or section,

"(B) the occurrence of any contraindicating reaction to a vaccine which is specified in the manufacturer's package insert, and

"(C) such other matters as the Secretary may by regulation require.

Reports of the matters referred to in subparagraphs (A) and (B) shall be made beginning 90 days after the effective date of this subtitle. The Secretary shall publish in the Federal Register as soon as practicable after such date a notice of the reporting requirement. Federal Register, publication.

"(2) A report under paragraph (1) respecting a vaccine shall include the time periods after the administration of such vaccine within which vaccine-related illnesses, disabilities, injuries, or conditions, the symptoms and manifestations of such illnesses, disabilities, injuries, or conditions, or deaths occur, and the manufacturer and lot number of the vaccine.

"(3) The Secretary shall issue the regulations referred to in paragraph (1)(C) within 180 days of the effective date of this subtitle. Regulations.

"(c) RELEASE OF INFORMATION.—

"(1) Information which is in the possession of the Federal Government and State and local governments under this section and which may identify an individual shall not be made available under section 552 of title 5, United States Code, or otherwise, to any person except— State and local governments.

"(A) the person who received the vaccine, or

"(B) the legal representative of such person.

"(2) For purposes of paragraph (1), the term 'information which may identify an individual' shall be limited to the name, street address, and telephone number of the person who received the vaccine and of that person's legal representative and the medical records of such person relating to the administration of the vaccine, and shall not include the locality and State of vaccine administration, the name of the health care provider who administered the vaccine, the date of the vaccination, or information concerning any reported illness, disability, injury, or condition resulting from the administration of the vaccine, any symptom or manifestation of such illness, disability, injury, or condition, or death resulting from the administration of the vaccine.

"(3) Except as provided in paragraph (1), all information reported under this section shall be available to the public. Public information.

"VACCINE INFORMATION

"SEC. 2126. (a) GENERAL RULE.—Not later than 1 year after the effective date of this subtitle, the Secretary shall develop and 42 USC 300aa-26.

disseminate vaccine information materials for distribution by health care providers to the legal representatives of any child receiving a vaccine set forth in the Vaccine Injury Table. Such materials shall be published in the Federal Register and may be revised.

Federal Register, publication.

"(b) DEVELOPMENT AND REVISION OF MATERIALS.—Such materials shall be developed or revised by rule—

"(1) after notice to the public, opportunity for a public hearing, and 90 days of comment thereon, and

"(2) in consultation with the Advisory Commission on Childhood Vaccines, appropriate health care providers and parent organizations, the Centers for Disease Control, and the Food and Drug Administration.

"(c) INFORMATION REQUIREMENTS.—The information in such materials shall be presented in understandable terms and shall include—

"(1) the frequency, severity, and potential long-term effects of the disease to be prevented by the vaccine,

"(2) the symptoms or reactions to the vaccine which, if they occur, should be brought to the immediate attention of the health care provider,

"(3) precautionary measures legal representatives should take to reduce the risk of any major adverse reactions to the vaccine that may occur,

"(4) early warning signs or symptoms to which legal representatives should be alert as possible precursors to such major adverse reactions,

"(5) a description of the manner in which legal representatives should monitor such major adverse reactions, including a form on which reactions can be recorded to assist legal representatives in reporting information to appropriate authorities,

"(6) a specification of when, how, and to whom legal representatives should report any major adverse reaction,

"(7) the contraindications to (and bases for delay of) the administration of the vaccine,

"(8) an identification of the groups, categories, or characteristics of potential recipients of the vaccine who may be at significantly higher risk of major adverse reaction to the vaccine than the general population,

"(9) a summary of relevant State and Federal laws concerning the vaccine, including information on—

"(A) the number of vaccinations required for school attendance and the schedule recommended for such vaccinations, and

"(B) the availability of the Program, and

"(10) such other relevant information as may be determined by the Secretary.

"(d) HEALTH CARE PROVIDER DUTIES.—On and after a date determined by the Secretary which is—

"(1) after the Secretary develops the information materials required by subsection (a), and

"(2) not later than 6 months after the date such materials are published in the Federal Register,

each health care provider who administers a vaccine set forth in the Vaccine Injury Table shall provide to the legal representatives of any child to whom such provider intends to administer such vaccine a copy of the information materials developed pursuant to subsection (a), or other written information which meets the requirements

of this section. Such materials or other information shall be provided prior to the administration of such vaccine.

"MANDATE FOR SAFER CHILDHOOD VACCINES

"SEC. 2127. (a) GENERAL RULE.—In the administration of this subtitle and other pertinent laws under the jurisdiction of the Secretary, the Secretary shall— 42 USC 300aa-27.

"(1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on the effective date of this subtitle and promote the refinement of such vaccines, and

"(2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.

"(b) REPORT.—Within 2 years after the effective date of this subtitle, and periodically thereafter, the Secretary shall prepare and transmit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report describing the actions taken pursuant to subsection (a) during the preceding 2-year period.

"MANUFACTURER RECORDKEEPING AND REPORTING

"SEC. 2128. (a) GENERAL RULE.—Each vaccine manufacturer of a vaccine set forth in the Vaccine Injury Table or any other vaccine the administration of which is mandated by the law or regulations of any State, shall, with respect to each batch, lot, or other quantity manufactured or licensed after the effective date of this subtitle— State and local governments. 42 USC 300aa-28.

"(1) prepare and maintain records documenting the history of the manufacturing, processing, testing, repooling, and reworking of each batch, lot, or other quantity of such vaccine, including the identification of any significant problems encountered in the production, testing, or handling of such batch, lot, or other quantity,

"(2) if a safety test on such batch, lot, or other quantity indicates a potential imminent or substantial public health hazard is presented, report to the Secretary within 24 hours of such safety test which the manufacturer (or manufacturer's representative) conducted, including the date of the test, the type of vaccine tested, the identity of the batch, lot, or other quantity tested, whether the batch, lot, or other quantity tested is the product of repooling or reworking of previous batches, lots, or other quantities (and, if so, the identity of the previous batches, lots, or other quantities which were repooled or reworked), the complete test results, and the name and address of the person responsible for conducting the test, Safety.

"(3) include with each such report a certification signed by a responsible corporate official that such report is true and complete, and

"(4) prepare, maintain, and upon request submit to the Secretary product distribution records for each such vaccine by batch, lot, or other quantity number.

Fraud.

"(b) SANCTION.—Any vaccine manufacturer who intentionally destroys, alters, falsifies, or conceals any record or report required under paragraph (1) or (2) of subsection (a) shall—

"(1) be subject to a civil penalty of up to $100,000 per occurrence, or

"(2) be fined $50,000 or imprisoned for not more than 1 year, or both.

Such penalty shall apply to the person who intentionally destroyed, altered, falsified, or concealed such record or report, to the person who directed that such record or report be destroyed, altered, falsified, or concealed, and to the vaccine manufacturer for which such person is an agent, employee, or representative. Each act of destruction, alteration, falsification, or concealment shall be treated as a separate occurrence.

"PART D—GENERAL PROVISIONS

"CITIZEN'S ACTIONS

42 USC 300aa-31.

"SEC. 2131. (a) GENERAL RULE.—Except as provided in subsection (b), any person may commence in a district court of the United States a civil action on such person's own behalf against the Secretary where there is alleged a failure of the Secretary to perform any act or duty under this subtitle.

"(b) NOTICE.—No action may be commenced under subsection (a) before the date which is 60 days after the person bringing the action has given written notice of intent to commence such action to the Secretary.

Courts, U.S.

"(c) COSTS OF LITIGATION.—The court, in issuing any final order in any action under this section, may award costs of litigation (including reasonable attorney and expert witness fees) to any party, whenever the court determines such award is appropriate.

"JUDICIAL REVIEW

Regulations. 42 USC 300aa-32.

"SEC. 2132. A petition for review of a regulation under this subtitle may be filed in a court of appeals of the United States within 60 days from the date of the promulgation of the regulation or after such date if such petition is based solely on grounds arising after such 60th day.

"DEFINITIONS

42 USC 300aa-33.

"SEC. 2133. For purposes of this subtitle:

"(1) The term 'health care provider' means any licensed health care professional, organization, or institution, whether public or private (including Federal, State, and local departments, agencies, and instrumentalities) under whose authority a vaccine set forth in the Vaccine Injury Table is administered.

"(2) The term 'legal representative' means a parent or an individual who qualifies as a legal guardian under State law.

"(3) The term 'manufacturer' means any corporation, organization, or institution, whether public or private (including Federal, State, and local departments, agencies, and instrumentalities), which manufactures, imports, processes, or distributes under its label any vaccine set forth in the Vaccine Injury Table, except that, for purposes of section 2128, such term shall include the manufacturer of any other vaccine cov-

ered by that section. The term 'manufacture' means to manufacture, import, process, or distribute a vaccine.

"(4) The term 'significant aggravation' means any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health.

"(5) The term 'vaccine-related injury or death' means an illness, injury, condition, or death associated with one or more of the vaccines set forth in the Vaccine Injury Table, except that the term does not include an illness, injury, condition, or death associated with an adulterant or contaminant intentionally added to such a vaccine.

"(6)(A) The term 'Advisory Commission on Childhood Vaccines' means the Commission established under section 2119.

"(B) The term 'Vaccine Injury Table' means the table set out in section 2114.". *Ante*, p. 3764.

(b) CONFORMING AMENDMENTS.—

(1) Sections 217(c), 465(f), and 497 of the Public Health Service Act (42 U.S.C. 218(c), 286(f), 289(f)) are each amended by striking out "2101" and inserting in lieu thereof "2301". 42 USC 218, 286, 289f.

(2) Section 305(h) of such Act (42 U.S.C. 242c(h)) is amended by striking out "2113" each place it occurs and inserting in lieu thereof "2313".

SEC. 312. RELATED STUDIES.

(a) REVIEW OF PERTUSSIS VACCINES AND RELATED ILLNESSES AND CONDITIONS.—Not later than 3 years after the effective date of this title, the Secretary of Health and Human Services shall complete a review of all relevant medical and scientific information (including information obtained from the studies required under subsection (e)) on the nature, circumstances, and extent of the relationship, if any, between vaccines containing pertussis (including whole cell, extracts, and specific antigens) and the following illnesses and conditions: 42 USC 300aa-1 note.

(1) Hemolytic anemia.
(2) Hypsarrhythmia.
(3) Infantile spasms.
(4) Reye's syndrome.
(5) Peripheral mononeuropathy.
(6) Deaths classified as sudden infant death syndrome.
(7) Aseptic meningitis.
(8) Juvenile diabetes.
(9) Autism.
(10) Learning disabilities.
(11) Hyperactivity.
(12) Such other illnesses and conditions as the Secretary may choose to review or as the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act recommends for inclusion in such review. *Ante*, p. 3771.

The review under this subsection shall include notice and opportunity for a public hearing, consideration of written information submitted by the public, and consultation with such Advisory Commission.

(b) FINDINGS WITH RESPECT TO PERTUSSIS.—Not later than 3 years after the effective date of this title, the Secretary shall make, and publish in the Federal Register, the following specific findings: Federal Register, publication.

(1) Whether each of the illnesses or conditions set forth in subsection (a) can reasonably be determined in some circumstances to be caused or significantly aggravated, by pertussis-containing vaccines.

(2) For each illness or condition for which a finding of causation or aggravation related to vaccines containing pertussis is made under paragraph (1), the circumstances under which such causation or aggravation can reasonably be determined to occur.

(3) For each illness or condition for which a finding of causation or aggravation related to vaccines containing pertussis is made under paragraph (1), and for each illness or condition set forth in the Vaccine Injury Table under section 2114 of the Public Health Service Act, the time periods within which the first symptom or manifestation of onset or aggravation of each such illness or condition can reasonably be determined to occur after pertussis vaccination.

Ante, p. 3764.

Regulations.

(c) REVISION OF TABLE WITH RESPECT TO PERTUSSIS VACCINES.—At the same time the Secretary publishes in the Federal Register findings under subsection (b), the Secretary shall propose regulations to amend the Vaccine Injury Table under section 2114 of the Public Health Service Act as a result of such findings. Not later than 42 months after the effective date of this title, the Secretary shall promulgate such proposed regulations with such modifications as may be necessary after opportunity for public hearing.

(d) REVIEW OF MMR VACCINES AND RELATED ILLNESSES AND CONDITIONS.—Not later than 3 years after the effective date of this title, the Secretary of Health and Human Services shall complete a review similar to the review conducted under subsection (a) with respect to the potential relationship between vaccines containing rubella (including MMR) and radiculoneuritis. The review under this subsection shall include notice and opportunity for a public hearing, consultation with the Advisory Commission on Childhood Vaccines and consideration of written information submitted by the public. Not later than 3 years after the effective date of this title, the Secretary shall make and publish in the Federal Register findings similar to those required by subsection (b) and shall, if appropriate, propose similar regulations (and thereafter promulgate such regulations) to those required by subsection (c), with respect to compensation under the National Vaccine Injury Compensation Program established under section 2110 of the Public Health Service Act for radiculoneuritis caused, contributed to, or significantly aggravated by vaccines containing rubella.

Federal Register, publication.

Ante, p. 3758.

(e) PERTUSSIS AND MMR STUDIES.—

(1) In order to assist the Secretary in making the findings required under subsections (b) and (d), the Secretary shall, in accordance with subparagraph (B), arrange for the conduct of studies of—

(A) the relationship between vaccines containing pertussis (including whole cell, extracts, and specific antigens) and the illnesses or conditions set forth in paragraphs (1) through (11) of subsection (a),

(B) the relationship between vaccines containing pertussis and any other illnesses and conditions, as selected by the Secretary or the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act, and

Ante, p. 3771.

(C) the relationship between vaccines containing rubella (including MMR) and radiculoneuritis.

(2)(A) The Secretary shall request the Institute of Medicine of the National Academy of Sciences to conduct the studies required by paragraph (1) under an arrangement by which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary.

(B) If the Institute of Medicine is unwilling to conduct such study under such an arrangement, the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study and prepare and submit the reports thereon as provided in paragraph (3). Reports.

(C) The Institute of Medicine or other group or association conducting the studies required by paragraph (1) shall conduct such studies in consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act. *Ante*, p. 3771.

(3) Reports on the results of the studies required by paragraph (1) shall be completed and submitted to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate and to the Secretary not later than 32 months after the effective date of this title. Upon submission to the Secretary, the reports shall be made available to the public. Reports. Public information.

(4) There are authorized to be appropriated such sums as are necessary for the purpose of making payments for the conduct of the studies required under this subsection. Appropriation authorization.

(f) DEFINITIONS.—For purposes of this section:

(1) The term "medical and scientific information" includes epidemiologic, clinical, biostatistical, pathological, toxicologic, and other laboratory data and case study information, observations, studies, and reports in peer-reviewed literature or official Government publications, as well as relevant unpublished information, data, studies, and observations.

(2) The term "MMR" means a vaccine containing material intended to prevent or confer immunity against measles, mumps, and rubella disease.

SEC. 313. STUDY OF OTHER VACCINE RISKS.

(a) STUDY.— 42 USC 300aa-1 note.

(1) Not later than 3 years after the effective date of this title, the Secretary shall, after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act—

(A) arrange for a broad study of the risks (other than the risks considered under section 102) to children associated with each vaccine set forth in the Vaccine Injury Table under section 2114 of such Act, and *Ante*, p. 3764.

(B) establish guidelines, after notice and opportunity for public hearing and consideration of all relevant medical and scientific information, respecting the administration of such vaccines which shall include—

(i) the circumstances under which any such vaccine should not be administered,

(ii) the circumstances under which administration of any such vaccine should be delayed beyond its usual time of administration, and

(iii) the groups, categories, or characteristics of potential recipients of such vaccine who may be at significantly higher risk of major adverse reactions to such vaccine than the general population of potential recipients.

(2)(A) The Secretary shall request the Institute of Medicine of the National Academy of Sciences to conduct the study required by paragraph (1) under an arrangement by which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary.

(B) If the Institute of Medicine is unwilling to conduct such study under such an arrangement, the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study.

(C) The Institute of Medicine or other group or association conducting the study required by paragraph (1) shall conduct such studies in consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act.

Ante, p. 3771.

Federal Register, publication.

(b) REVISION OF GUIDELINES.—The Secretary shall periodically, but at least every 3 years after establishing guidelines under subsection (a), review and revise such guidelines after notice and opportunity for public hearing and consideration of all relevant medical and scientific information, unless the Secretary finds that on the basis of all relevant information no revision of such guidelines is warranted and publishes such finding in the Federal Register.

(c) FACTORS AFFECTING GUIDELINES.—Guidelines under subsection (a) shall take into account—

(1) the risk to potential recipients of the vaccines with respect to which the guidelines are established,

(2) the medical and other characteristics of such potential recipients, and

(3) the risks to the public of not having such vaccines administered.

Physicians. Hospitals. Nurses. State and local governments.

(d) DISSEMINATION.—The Secretary shall widely disseminate the guidelines established under subsection (a) to—

(1) physicians and other health care providers,

(2) professional health associations,

(3) State and local governments and agencies, and

(4) other relevant entities.

42 USC 300aa-1 note.

SEC. 314. REVIEW OF WARNINGS, USE INSTRUCTIONS, AND PRECAUTIONARY INFORMATION.

Not later than 1 year after the effective date of this title and after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act and with other appropriate entities, the Secretary of Health and Human Services shall review the warnings, use instructions, and precautionary information presently issued by manufacturers of vaccines set forth in the Vaccine Injury Table set out in section 2114 of the Public Health Service Act and shall by rule determine whether such warnings, instructions, and information adequately warn health care providers of the nature and extent of dangers posed by such

Ante, p. 3764.

vaccines. If the Secretary determines that any such warning, instruction, or information is inadequate for such purpose in any respect, the Secretary shall at the same time require the manufacturers to revise and reissue such warning, instruction, or information as expeditiously as practical, but not later than 18 months after the effective date of this title.

SEC. 315. RECALL AUTHORITY.

Subsection (d) of section 351 of the Public Health Service Act (42 U.S.C. 262) is amended— *Ante*, p. 3751.

(1) by inserting "(1)" after "(d)", and

(2) by adding at the end thereof the following new paragraph:

"(2)(A) Upon a determination that a batch, lot, or other quantity of a product licensed under this section presents an imminent or substantial hazard to the public health, the Secretary shall issue an order immediately ordering the recall of such batch, lot, or other quantity of such product. An order under this paragraph shall be issued in accordance with section 554 of title 5, United States Code.

"(B) Any violation of subparagraph (A) shall subject the violator to a civil penalty of up to $100,000 per day of violation. The amount of a civil penalty under this subparagraph shall, effective December 1 of each year beginning 1 year after the effective date of this subparagraph, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest 1/10 of 1 percent. For purposes of this subparagraph, the term 'base quarter', as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.". Law enforcement and crime.

SEC. 316. STUDY OF IMPACT ON SUPPLY OF VACCINES. 42 USC 300aa-4 note.

On June 30, 1987, and on June 30 of each second year thereafter, the Secretary of Health and Human Services shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate—

(1) an assessment of the impact of the amendments made by this title on the supply of vaccines listed in the Vaccine Injury Table under section 2114 of the Public Health Service Act, and *Ante*, p. 3764.

(2) an assessment of the ability of the administrators of vaccines (including public clinics and private administrators) to provide such vaccines to children.

PART B—MISCELLANEOUS

SEC. 321. WAIVER OF PAPERWORK REDUCTION. 44 USC 3501 *et seq.*

Chapter 35 of title 44, United States Code, shall not apply to information required for purposes of carrying out this title and implementing the amendments made by this title. 42 USC 300aa-1 note.

SEC. 322. NONSEVERABILITY. 42 USC 300aa-1 note.

If any provision of this title or the application of any provision of this title to any person or circumstance is held invalid by reason of a violation of the Constitution, the entire title shall be considered invalid.

Appendix D

Initial Guidance for an Update of the National Vaccine Plan: A Letter Report to the National Vaccine Program Office

Initial Guidance for an Update of the National Vaccine Plan

A Letter Report to the National Vaccine Program Office

Committee on the Review of Priorities in the National Vaccine Plan
Board on Population Health and Public Health Practice

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

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NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

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"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

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COMMITTEE ON THE REVIEW OF PRIORITIES IN THE NATIONAL VACCINE PLAN

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REVIEWERS

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

Jo Ivey Boufford, New York Academy of Medicine
Julie S. Downs, Department of Social and Decision Science, Carnegie Mellon University
Barton F. Haynes, Duke Human Vaccine Institute
Lisa Jackson, Group Health Center for Health Studies
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Joshua P. Metlay, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania
Thomas W. Valente, Department of Preventive Medicine, Keck School of Medicine, University of Southern California

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Floyd E. Bloom,** The Scripps Research Institute. Appointed by the National Research Council, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

CONTENTS

June 10, 2008

Dr. Bruce Gellin, MD, MPH
Director
National Vaccine Program Office
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Hubert H. Humphrey Building
200 Independence Avenue, SW
Room 715H
Washington, DC 20201–0004

Dear Dr. Gellin:

The Committee on Review of Priorities in the National Vaccine Plan is pleased to offer you its letter report, *Initial Guidance for an Update to the National Vaccine Plan*. The committee has been given a statement of task in two parts (see Appendix B). The second part tasks the committee with reviewing priorities in the update to the National Vaccine Plan, which is currently under development by an interagency group led by the National Vaccine Program Office (NVPO). The first part of the statement of task asks the committee to review the 1994 National Vaccine Plan[1] and then provide guidance on the development of the update to the plan.[2] This letter report responds to the first part of the statement of task.

As part of its information-gathering activities, the committee held a meeting that included presentations from representatives of NVPO and several Department of Health and Human Services (DHHS) agencies on the development of the 1994 plan, on accomplishments since 1994, and on early thinking about the update to the plan (see Appendix C for the meeting agenda). The committee also reviewed relevant literature, and study staff along with one or two committee members held informal conversations with several individuals familiar with the 1994 plan and its development.

BACKGROUND

NVPO was established by the enactment of Title XXI of the Public Health Service Act (Public Law 99-660), which also called for the preparation of the National Vaccine Plan. The language of the 1994 plan provides the following description of NVPO's role:

[1] The 1994 National Vaccine Plan is available at http://www.hhs.gov/nvpo/vacc_plan/.
[2] The committee's other tasks include holding five workshops with national expert stakeholders in medicine, public health, industry, and vaccinology to review publicly available, draft planning documents from the Department of Health and Human Services, and then preparing a report with conclusions and recommendations about priority actions within the major components of the draft update to the new National Vaccine Plan.

> [T]he principal coordinating organization for the NVP is the National Vaccine Program Office (NVPO), within the Public Health Service (PHS). The NVPO's responsibilities include providing overall leadership for the collaborative effort and monitoring the progress being made in achieving the plan's goals. Within the PHS, the NVPO has the task of reviewing all budget requests associated with vaccine development and immunization programs to ensure that all major priorities are adequately covered and that there is no duplication of effort. (NVPO, 1994)

The legislation represented a response to several different developments. These developments included problems of vaccine safety; the reemergence of vaccine-preventable diseases, especially pertussis and measles, in the United States and other developed countries; the persistence of these and other vaccine-preventable diseases in developing countries; and vaccine industry concern regarding financial and liability-related impediments to the development of new vaccines. The legislation also contained provisions aimed at improved monitoring of the safety of recommended vaccines and at reducing industry concern about liability risks. The Vaccine Adverse Events Reporting System (VAERS) and the National Vaccine Injury Compensation Program both became operational in 1988.

The release of the 1994 National Vaccine Plan coincided with other federal action to expand immunization coverage among children and adults. Such actions included increased federal appropriations for state immunization efforts and passage of the Vaccines for Children (VFC) amendments to Medicaid (Public Law 103-66). VFC, building on the existing entitlement to immunizations for children enrolled in Medicaid, strengthened federal immunization coverage standards while extending the immunization entitlement to uninsured children, children served by American Indian and Alaska Native health programs, and underinsured children served through Federally Qualified Health Centers (FQHCs). In 1990, DHHS released *Healthy People 2000*, which set forth 19 objectives related to reducing infectious disease and improving immunization coverage among children and adults.

Various nonprofit organizations interested in children's health and welfare also were part of efforts in the early 1990s to improve immunization services. Every Child By Two, for example, sought to draw family and community attention to the need to ensure that young children received vaccines according to the recommended schedule, not simply in response to school entry requirements. The Children's Vaccine Initiative, begun in 1990 under the auspices of United Nations agencies, focused on delivery of vaccines to children in developing countries.

Features of the 1994 National Vaccine Plan

The plan was to "establish priorities in research and the development, testing, licensing, production, procurement, distribution, and effective use of vaccines, describe an optimal use of resources to carry out such priorities, and describe how each of the various departments and agencies will carry out their functions in consultation and coordination with the [National Vaccine] Program and in conformity with such priorities." The 1994 plan's aims included reducing "the incidence of infectious diseases through vaccine development and immunization" and integrating all U.S. efforts on vaccine development and immunization, whether their focus was domestic or global (NVPO, 1994: p. 13). The plan had four goals[3]: (1) to develop new and improved vaccines; (2) to ensure the optimal safety and effectiveness of vaccines and immunization; (3) to better educate the public and members of the health professions on the benefits and risks of immunizations; and (4) to achieve better use of existing vaccines to prevent disease, disability, and death. The plan also offered 26 objectives along with more than 70 strategies for achieving those objectives. In addition, 14 anticipated outcomes were offered as a basis for judging the success of the plan (see Appendix D).

The Committee's Approach to Reviewing the Plan

The committee reviewed the goals, objectives, strategies, and anticipated outcomes presented in the plan. In the interest of time and in recognition of the statement of task and the plan's acknowledged limitations (notably, the lack of measurable objectives), the committee did not undertake a point-by-point evaluation of what the plan has or has not achieved. Instead, in the first section of this letter report, the committee examines what has changed in the broader social, policy, and economic context of vaccine development and immunization, and highlights several areas where noteworthy progress has been made, particularly by federal agencies. The committee acknowledges that progress in developing and delivering vaccines has benefited from essential contributions by other stakeholders, including researchers, manufacturers, state and local public health agencies, and health care providers. In the second section of this letter report, the committee uses what it learned from reviewing the 1994 plan and the process of preparing it to distill key elements. Based on these elements, the committee offers guidance to NVPO and its partners on developing the update to the national vaccine plan.

CHANGES SINCE 1994

Important changes in the world, in American society, and in the delivery and financing of health care have occurred or have grown in prominence since 1994. For example, several key changes have been made in how the U.S. health care delivery system is organized. More elderly and underserved populations receive health care, including immunizations, through private health care delivery systems under the auspices of Medicaid and Medicare managed care programs.[4] With significant government-

[3] NVPO intends to retain these goals to structure the update to the plan.

[4] According to CMS, two-thirds of the Medicaid population is enrolled in managed care organizations (more than 90 percent in many states). There are now over 500 separate managed care plans nationally providing health services to more than 40 million enrollees (CMS, 2006).

financed immunization activity now occurring through private entities that have a role in and the ability to influence coverage and financing decisions, there is growing dependence on the private sector to ensure that immunization goals for senior and underserved populations are met.

Like other medical products, vaccines have benefits and risks, and in recent decades vaccine safety has emerged as an important topic both for the public health and medical communities and for the public. Research on vaccine safety has increased and regulatory attention to safety has intensified. Milestones include the withdrawal in 1999 of the first licensed rotavirus vaccine after cases of intussusception were reported to VAERS and subsequent research by CDC showed that this type of bowel obstruction occurred with significantly increased frequency after rotavirus vaccine administration, and the replacement of older pertussis and polio vaccines with safer products (see below). Multiple factors converged to facilitate the emergence of an increasingly organized and vocal movement that questions the need for vaccines and their safety in general and alleges that specific vaccines, features of vaccines, or the expansion of the pediatric immunization schedule in the past 15 years have caused health problems in some children. These factors include the decline in the incidence of vaccine-preventable diseases in the United States, the greater interest in complementary and alternative medicine, an increase in consumerism, broader public concern about the varied risks inherent in modern life, a growing public mistrust of government agencies, and the proliferation of electronic communication (Clements and Ratzan, 2003; Clements et al., 1999; Colgrove and Bayer, 2005).

Major transformation also has occurred in the area of funding for vaccine research, both globally and domestically. In the United States, the federal government has a greater role in funding and guiding the development and evaluation of vaccines, particularly those directed against pandemic influenza and potential agents of bioterrorism. Globally, the Bill & Melinda Gates Foundation and international partnerships such as the GAVI Alliance[5] fund new vaccine purchase, support strengthening immunization infrastructure in developing countries, and foster vaccine research and development.

PROGRESS SINCE 1994

As noted above, at its March 2008 meeting the committee heard a series of presentations from DHHS agencies, including the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), the National Institutes of Health (NIH), and the Centers for Medicare and Medicaid Services (CMS) (see Appendix C for the complete agenda).

Characteristics of the 1994 plan make it difficult to attribute specific activities to plan objectives, and accordingly, the presentations given to the committee in general did not attempt to link accomplishments to the plan, other than noting their relevance to the pertinent goal in the plan. These presentations described many remarkable achievements, both in process (e.g., enhanced regulatory tools) and substance (e.g., approval of safe and effective new vaccines), of federal agencies working in collaboration with other

[5] Global Alliance for Vaccines and Immunization

stakeholders in the U.S. vaccine system. Below, the committee highlights several examples of these achievements, as well as other areas of progress, and also notes the 1994 plan's anticipated outcomes in areas that coincide with areas of progress (see Appendix D for a complete list of the outcomes). However, the committee does not attempt to assess the extent to which each of the 14 anticipated outcomes was realized,[6] or to illustrate achievements related to all of the outcomes under each goal. Also, the committee did not undertake a systematic evaluation of achievements or failures to achieve plan objectives. The focus on progress in the field is intended to provide some context for the current environment for vaccine development and delivery, with the understanding that gaps and challenges remain in this complex domain of science, public health, and health care.

Goal 1: Develop new and improved vaccines.

Four of the 14 anticipated outcomes in the 1994 plan are associated with this goal and include: improved vaccines, vaccines for diseases without vaccines, and regulatory improvements to facilitate vaccine licensure. Much progress has been made in the area of vaccine development.

Since 1994, more than 20 new vaccine products resulting from the collaborative efforts of NIH, academic, and industry researchers were approved by FDA (IOM, 2008). Novel vaccines introduced include vaccines against pediatric pneumococcal disease, meningococcal disease, and human papilloma virus. Also, vaccines with improved safety profiles received regulatory approval. For example, the introduction of a new acellular pertussis vaccine led to a reduction in reports of adverse events compared with the older, whole-cell vaccine (Braun et al., 2000). Similarly, the 1996 recommendation by the Advisory Committee on Immunization Practices (ACIP) to begin replacing oral polio vaccine with inactivated polio vaccine,[7] and 2000 ACIP recommendation to replace all OPV with IPV led to the disappearance in the United States of vaccine-associated paralytic poliomyelitis (CDC, 2000; Wattigney et al., 2001).

NIH plays a crucial role in conducting and supporting both basic and applied vaccine research. In recent years, the agency has been involved in supporting a number of Investigational New Drug applications for vaccines, playing a role in the licensure of 17 different vaccines between 1994 and 2006, and has collaborated with the World Health Organization and nongovernmental organizations on vaccines of importance to developing countries. Most recently, NIH has been engaged in research related to vaccines for potential agents of bioterrorism and pandemic influenza (e.g., H5N1 inactivated vaccine).

[6] This was done to some extent by NVPO's evaluation of the 1994 (NVPO, 1997).

[7] This was done by changing the OPV vaccination schedule to a sequential OPV-IPV schedule, with two doses of IPV administered at ages 2 and 4 months, followed by two doses of OPV at ages 12–18 months and 4–6 years (CDC, 2000).

Goal 2: Ensure the optimal safety and effectiveness of vaccines and immunization.

One of the 14 anticipated outcomes in the 1994 plan is associated with this goal; it refers to continuous monitoring of vaccine efficacy and safety. There have been several notable activities in this area.

Since 1994, the FDA Center for Biologics Evaluation and Research (CBER), which regulates vaccines, has had an expanding array of regulatory tools and legislative requirements that facilitate the review and approval of safe and efficacious vaccines. For example, CBER has become better equipped to monitor manufacturer commitments to study the safety of vaccines after they are licensed.

In the past fourteen years, FDA and CDC have collaborated on surveillance for and evaluation of adverse events through their joint operation of VAERS. VAERS reporting procedures have been improved and simplified and better methods for monitoring and analyzing the data collected have been developed. Efforts have also been made to increase collaboration with CMS, the Department of Defense, and the Department of Veterans Affairs to improve surveillance and reporting of adverse events following immunization in the adult populations these agencies serve.

In addition, the Vaccine Safety Datalink (VSD) is a collaborative effort between CDC's Immunization Safety Office and several large managed care organizations to monitor immunization safety and address the "gaps in scientific knowledge about rare and serious side effects following immunization." Unlike VAERS, VSD permits systematic case finding and analysis of control data to assess potential adverse events, testing hypotheses concerning relationships between receipt of specific vaccines and the occurrence of specific adverse events. The VSD project, which has expanded from 4 to 8 participating managed care organization sites, not only conducts traditional epidemiologic studies on vaccine safety, but also has developed the capacity to conduct near real-time surveillance for adverse events after vaccination using Rapid Cycle Analysis methods.

In 2001, the Clinical Immunization Safety Assessment (CISA) Network was established. CISA is a network of six medical research centers with expertise in immunization safety. CISA sites focus on pathophysiologic mechanisms and identify biologic risks of adverse events following immunization (Iskander, 2007). Examples of CISA studies include research on possible genetic risk factors for post-vaccination Guillain-Barré syndrome and research on vaccine-associated encephalitis.

One of the objectives under Goal 2 in the 1994 plan was to "continue to ensure fair and efficient compensation to individuals injured by vaccines," in reference to the National Vaccine Injury Compensation Program (VICP), which is based at HRSA and has operated since 1988 (see Appendix D for a list of goals and objectives). The VICP is a no-fault mechanism through which compensation can be awarded for claims of vaccine-related injury or death. Since 1994, nine vaccines have been added to the program and the list of compensable injuries has been updated periodically to incorporate new findings on vaccine safety, including those from Institute of Medicine (IOM) reviews and CDC studies.[8]

[8] The IOM reviews were federally funded studies that brought together panels of experts to examine the available scientific evidence on specific vaccine safety concerns. Eight reports of the IOM Immunization

Goal 3: Better educate the public and members of the health professions about the benefits and risks of immunizations.

Two of the 14 anticipated outcomes in the 1994 plan are associated with this goal, and they include the establishment of educational communication networks to inform all potential audiences about vaccine risks and benefits, and providing information to the public on the costs and benefits of the plan. There have been several developments in this area.

Since 1999, the American Academy of Pediatrics (AAP) has received funding through a cooperative agreement with CDC for its Childhood Immunization Support Program (CISP). CISP has been providing educational resources on immunization and immunization-related issues to health care providers and parents.

In 2000, DHHS, CDC, and the American Medical Association co-sponsored the first National Influenza Vaccine Summit, a group that meets annually and has members representing 100 public and private organizations interested in preventing influenza. Major aims of this activity include finding new ways to communicate with and to the public and health care providers.

Between 2002 and 2003, NVPO, CDC, IOM, and the Keystone Center[9] collaborated on a proposal to stimulate public engagement in vaccine policy development. A National Vaccine Advisory Committee working group discussed the proposal and other models of public engagement during a 2004 workshop (NVAC, 2004). The collaboration among these organizations continued in 2005 in the form of a demonstration, or proof of principle, that vaccine policymaking could be well-informed by a substantive engagement of stakeholders and the public (The Keystone Center, 2005). The demonstration topic was pandemic influenza vaccine prioritization.

In 2007, FDA formed a risk communication advisory committee that will advise the agency on communication of risk and benefit information about the products the agency regulates.

Goal 4: Achieve better use of existing vaccines to prevent disease, disability, and death.

Seven of the 14 anticipated outcomes in the 1994 plan are associated with this goal and include extending age-appropriate immunization with recommended vaccines to at least 90 percent of infants and children (the only measurable outcome or objective provided in the plan), and eliminating childhood diseases (e.g., diphtheria, *Haemophilus influenzae* Type b) as significant causes of death. Below, the committee highlights examples of progress the use of vaccines.

For each birth cohort (the approximately 4 million children born each year), routine childhood immunization has been estimated to prevent approximately 33,500 premature deaths and 14.3 million cases of vaccine-preventable illnesses (Zhou et al., 2005). The introduction of *Haemophilus influenzae* Type b (Hib) and pertussis vaccines

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Safety Review Committee were published between 2001 through 2004 and may be viewed at www.nap.edu.

[9] The Keystone Center is a nonprofit that facilitates consensus-building for science-based public policy decisions (www.keystone.org).

illustrates the impact of immunization. Hib once affected 1 out of 200 children under age 5 and killed 600 U.S. children each year. One-quarter of children surviving Hib meningitis had neurologic damage. Conjugate Hib vaccine was recommended by ACIP for all infants in 1991. Between 1994 and 1998, fewer than 10 fatal cases of invasive Hib disease were reported (CDC, 2007a), and rates of the disease fell by 99 percent overall (Adams et al., 1993). Before pertussis vaccine became available in the 1940s, the disease caused between 150,000 and 260,000 cases and from 5,000 to a peak of 9,000 deaths annually (CDC, 2006, 2007a). Between 1990 and 1996, there were 57 pertussis deaths, most in infants under 6 months of age (CDC, 2007a).

Since 1994, the number of vaccines recommended for children and adolescents has increased from 9 to 16, including vaccines against varicella, pneumococcal disease, influenza, meningococcal disease, hepatitis A, rotavirus, and human papilloma virus (HPV). In 2006, immunization coverage for children aged 19–35 months exceeded 90 percent for several individual vaccines.[10] However, 77 percent of children in this age group had received all doses of a series of recommended vaccines[11] (CDC, 2007b).

GUIDANCE FOR DEVELOPING A NEW NATIONAL VACCINE PLAN

The committee learned from presentations at its March 2008 meeting and from conversations with individuals knowledgeable about the development of the 1994 National Vaccine Plan that its development served as (1) a tool to foster interagency dialogue, and (2) a mechanism for cataloguing activities and listing policy and research aspirations and prominent concerns that existed at that time (IOM, 2008; IOM Staff, 2008). However, there is little evidence that the plan served to guide or motivate activity that occurred after its preparation. As a result, it is difficult to attribute to the plan any changes that have occurred since 1994.

On the basis of its review of the 1994 plan and information gathered about its development, the committee has indentified several process and content areas that deserve particular attention as the update to the plan is developed.

Process Issues

The committee identified several limitations of the process of developing the 1994 plan that provide useful lessons in drafting the update to the National Vaccine Plan. These limitations include: the federal, rather than national, scope of the 1994 plan; the absence of a framework for evaluating and updating the plan; and the lack of explicit roles in the plan for stakeholders beyond the federal government (Figure 1 offers an illustration of the immunization system, which, despite being an incomplete representation, depicts the system's complexity). Also, NVPO and agencies involved in

[10] This is one area where a plan objective may be said to have been met and exceeded. As noted elsewhere, given the structure and contents of the 1994 plan, it is generally not possible to attribute specific changes to specific objectives in the plan.

[11] This refers to the series of ≥4 doses of diphtheria, tetanus toxoid, and any acellular pertussis vaccine; >3 doses of poliovirus vaccine; ≥1 dose of measles, mumps, and rubella vaccine; ≥3 doses of *Haemophilus influenzae* type b vaccine; ≥3 doses of hepatitis B vaccine; and ≥1 dose of varicella vaccine.

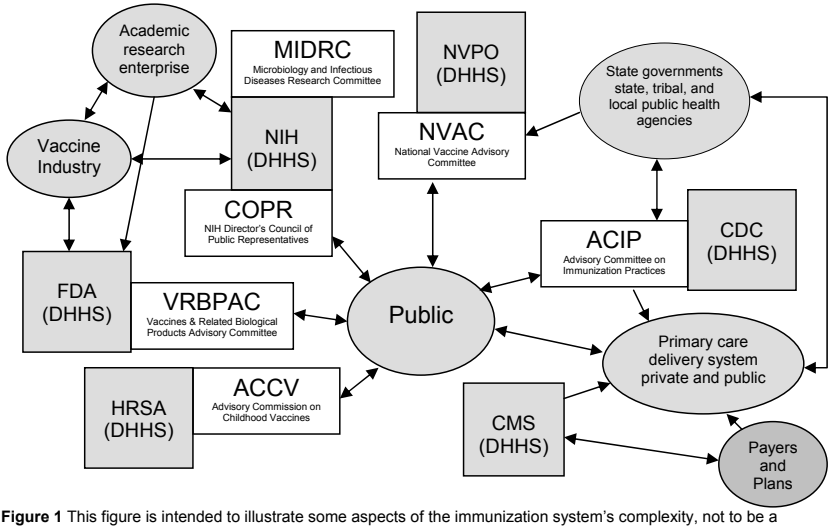

Figure 1 This figure is intended to illustrate some aspects of the immunization system's complexity, not to be a complete description of the system. A number of federal advisory committees exist to provide advice and guidance to agencies in the Department of Health and Human Services (DHHS). Several of these committees are associated with vaccine- or immunization-specific programs. Four such committees, as well as two additional relevant committees are depicted in the figure.
Legend: Gray boxes represent federal agencies in the Department of Health and Human Services (DHHS) (other departments, such as the Departments of Defense, Veterans Affairs, and Homeland Security, also play important roles in the immunization system); white boxes represent federal advisory committees associated with DHHS agencies, and gray ovals represent other stakeholders. **Acronyms:** CDC = Centers for Disease Control and Prevention; CMS = Centers for Medicare & Medicaid Services; FDA = Food and Drug Administration; HRSA = Health Resources and Services Administration; NIH = National Institutes of Health; NVPO = National Vaccine Program Office. **Notes about the federal advisory committees above:** ACCV includes attorneys for injured children and for industry; NVAC Includes public, industry, state public health, and health care (AHIP) representation; ACIP includes public and state and local public health representation and liaisons to the vaccine industry and professional associations; COPR includes patients, family members of patients, health care and education professionals and members of the general public who advise the Director of the NIH on "matters of public interest, outreach and participation in NIH's research-related activities"; VRBPAC includes public and nonvoting industry representation.

the development of the 1994 plan acknowledged that it did not serve as a central document for strategic planning among federal agencies.

To help avoid important limitations of the 1994 plan, the committee urges NVPO to give special attention to the following points as it coordinates the development of update to the plan.

1. A Plan of National Scope

A National Vaccine Plan provides a mechanism for defining national, state, and local vaccine and immunization priorities and potentially for coordinating the activities of multiple federal agencies with the private sector to achieve them. NVPO has stated its intention and the commitment of the interagency group involved in drafting the new National Vaccine Plan to prepare a *national* plan and not merely a federal plan.

Box 1: On the Coordinating Role of NVPO (excerpt from the 1994 plan)

Two formal mechanisms exist for coordinating Federal activity. The NVP Interagency Group includes those agencies with major vaccine-related responsibilities specifically mentioned in Public Law. 99-660, and the Interagency Committee on Immunization (ICI) includes all those Federal departments and agencies involved in immunization. . . . Each of these groups meets regularly to supplement day-to-day information exchange, and coordination, cooperation, and planning that is facilitated by the NVPO staff. In addition, the NVPO coordinates special cross-agency initiatives that are undertaken from time to time on specific topics of importance or other identified needs.
(Source: NVPO, 1994: p. 49.)

The committee is aware that the 1986 legislation for the National Vaccine Plan called for a plan to "describe how each of the various departments and agencies will carry out their functions in consultation and coordination" with NVPO and "in conformity" with priorities in the plan (NVPO, 1994: p. 60); see Box 1 for a description of NVPO's coordinating role as provided in the 1994 plan.

The relationship between NVPO and NVAC in the development of the National Vaccine Plan in 1994 and the current update is important to understand. The 1994 plan stated that "[v]arious entities participate in the process of guiding and coordinating NVP activities. For example, the National Vaccine Advisory Committee (NVAC) (composed of nongovernmental experts in vaccine development and immunization) provides overall advice on vaccine development and immunization, as specified under P.L. 99-660" (NVPO, 1994: p. 49). It is the committee's understanding that NVAC will play an important role in the development of the update to the plan, by reviewing early drafts and contributing white papers developed by NVAC subcommittees or working groups (e.g., on vaccine finance, on vaccine safety).

The statute does not mention the involvement of non-federal stakeholders, including the broad array described above. At the committee's March 2008 meeting, however, NVPO described the vision of a national plan involving broad stakeholder input. The committee believes this vision is consistent with NVPO's charge to "achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines" (Public Law 99-660, §2103 [300aa-3]), a charge that can only be met through the efforts of multiple stakeholders, in addition to those of the federal government.

To develop a national plan, it will be important to give essential partners beyond federal agencies an early and meaningful role in framing the plan's scope, goals, and objectives. Essential stakeholders in the U.S. immunization system include not only federal agencies but also the pharmaceutical industry, insurers, purchasers of health care services, health care providers, researchers in areas ranging from the basic sciences through health economics and health services research, state and local public health agencies responsible for vaccine delivery, schools and day care centers, foundations and other not-for-profit organizations, the mass media, and very importantly, a spectrum of the public, reflecting varying perspectives on the value of immunization (some, but not all relevant stakeholders are included in Figure 1).

This IOM committee has been asked to engage a broad range of expert stakeholders around each of the four goals in the national vaccine plan at a series of workshops. However, the committee underscores the importance of including the full

array of interested and relevant stakeholders as early as possible in the process of developing the plan. The committee recognizes the role of NVAC, which includes stakeholder representatives, in contributing to and reviewing the draft update to the plan. Other options for involving stakeholders early in the process include obtaining advance input from all relevant federal advisory committees (most of which include consumer, state public health agency, and industry representation), and notifying participants at the IOM committee's stakeholder meetings that the draft plan is fully open to stakeholder input.[12]

At the federal level, NVPO has already engaged many agencies within the DHHS, as well as the Department of Defense, the Department of Veterans Affairs, and the State Department (the U.S. Agency for International Development). Additional consideration, could be (if it has not already been) given to involving the Department of Homeland Security, the Department of Agriculture, and perhaps others.

Despite its support for efforts to generate a more truly national plan, the committee recognizes that there are formidable barriers to achieving meaningful collaboration in this complex field where public health, medical, ethical, economic, societal, and individual objectives collide. Participation of all potential stakeholders would involve a wide array of potentially conflicting agendas, accountabilities, as well as regulatory, legal, and other limitations. Effective collaboration will be challenging to achieve even among federal agencies such as CDC, NIH, FDA, and HRSA, each of which has its own priorities, resource constraints, and culture.

2. A Plan that Is Used, Evaluated, and Updated

Ideally, a national vaccine plan would serve as a critical reference and coordinating mechanism for federal agency strategic planning. It would also enable and sustain greater coordination among all stakeholders with a role in vaccine development, delivery, and policy. Empirical research in management shows that systematic evaluation leads to a higher likelihood of success in implementing strategic plans (Armstrong, 1982; Kaplan and Norton, 1992). The 1994 plan lacked activity milestones and specific role designations for initiatives, and it did not differentiate longer- and shorter-term outcomes to help measure plan success. The update to the National Vaccine Plan should contain appropriate evaluative mechanisms, objective measures, and milestones, if the plan is to fulfill its potential as a blueprint for action on national priorities in vaccine development and immunization.

Recommendation 1: The committee recommends that NVPO and its partners include for each strategic initiative listed under the four plan goals the following details:

- **The primary responsible party (government agency or other stakeholder)**
- **Secondary participant(s) (government agency or other stakeholder)**
- **Measurable short, mid, and longer term outcomes to assess success of the initiative**

[12] The IOM committee will manage a process to capture and organize stakeholder input throughout the course of the study.

- **Identification of costs and potential funding sources (e.g., professional judgment budgets) to support pursuit of the initiative**

The plan also should include a timetable and process for regular updates that reflect the dynamic nature of the field.

3. Facilitating and Sustaining Stakeholder Participation in Plan Implementation

The 1994 plan does not appear to have been coordinated with related efforts that were already under way when it was being developed, such as Healthy People 2000, or to have been a reference point for subsequent efforts, including Healthy People 2010. An exception appears to be the federally-sponsored Task Force on Safer Childhood Vaccines, which issued a report in 1998 and noted that its recommendations were consistent with the goals of the National Vaccine Plan (NIAID, 1998).

Obtaining input from a broad range of stakeholders, including the public, as described in (1) above, should be followed by finding ways to encourage and motivate continued involvement of those stakeholders. One way to accomplish this is to link the plan with other national plans, and the committee understands that an effort has begun to consider ways to coordinate with the Healthy People 2020 process.

Recommendation 2: The committee recommends that NVPO and its partners identify specific and creative strategies (not limited to funding) that federal agencies and programs could use to motivate stakeholders to implement objectives in the national vaccine plan.

Examples include

- linking various types of grant programs to the plan (e.g., in announcing vaccine-related research grants, require applicants to explain how the proposed research relates to or advances a goal or objective of the plan); and
- asking recipients of other types of federal funding, such as vaccine funding for states, federal health financing programs (Medicare and Medicaid) or health care delivery programs (Federally Qualified Health Centers), to demonstrate that their activities promote plan objectives.

4. Making Explicit What Was Important in Developing the Plan

A plan cannot and should not offer to take every possible action to achieve a goal, and it should not be simply a wide-ranging collection of planned activities or a list of desired activities. The committee believes it is important that NVPO and its planning partners explain in the draft update to the plan the process by which priorities and objectives in the plan were selected. Ideally, a plan will aim to address a well-targeted set of major strategic issues, such as considering the relative opportunity cost and cost–benefit of pursuing one type of objective compared to another. A second important aspect of the process would involve identifying cross-cutting issues that require the attention and engagement of multiple federal agencies, as well as multiple stakeholders.

Recommendation 3: The committee recommends that NVPO and its partners explain in the draft update to the National Vaccine Plan[13] what was important to include and why, and the process by which items were selected for inclusion or discarded.

Content Areas

The committee noted some important omissions in the 1994 plan and identified several emerging areas and changes in context that will require attention in a major national document on the future of vaccine development and immunization. NVPO's initial work on the update to the National Vaccine Plan identified 13 topics of interest (Orenstein, 2008). These topics include enhancing vaccine research and development, developing specific vaccines, adult immunization, adolescent immunization, childhood vaccination, financial barriers, vaccine supply, vaccine safety, vaccine injury/compensation, communication and education, surveillance, preparedness, and global health. The committee agrees that many of these topics deserve attention in the updated plan, but is not commenting on all of them here. Specific guidance is, however, offered on two topics that NVPO has already identified: vaccine finance and communication. On the pages that follow, the committee highlights these and four additional topical areas it believes are important to consider in developing the update to the plan.

1. A Flexible Immunization System Capable of Responding to Innovation in the Development and Use of Vaccines

In the last several years, the use and purpose of vaccines has broadened to include new populations, new applications (e.g., exploration of therapeutic vaccines), and new technologies (e.g., introduction of new modes of delivery or combination vaccines, research on adjuvants to extend available vaccine doses). The science, technology, and use of vaccines continue to evolve. These changes will require flexibility and adaptability in the existing mechanisms for vaccine delivery, finance, communication about vaccines, and so on.

For example, implementation of the ACIP recommendation for universal annual influenza immunization in children exceeds the current capacity of the health care system to administer the vaccine to all relevant populations. Another example is found in the introduction of an HPV vaccine as a means for cervical cancer prevention, which has presented new communication and coverage challenges.

Recommendation 4: The committee recommends that NVPO and its partners include in the update to the National Vaccine Plan mechanisms to assess the "horizon" of innovation and new developments in vaccines, and explore strategic objectives or initiatives that enable timely consideration of and decision making to address emerging opportunities and challenges.

[13] Refers to the draft (or components thereof) that will be reviewed by the IOM committee and stakeholders.

2. Vaccine Financing

The mechanisms that the nation employs to finance the purchase of vaccines, and their deployment to and administration in clinical settings are central to national planning efforts, particularly for more costly new vaccines. In light of the nation's complex approach to health care financing, which rests on a patchwork of public and private health insurance arrangements, supplemented by various federal and state direct public investments in the purchase, distribution, and administration of vaccines, the updated National Vaccine Plan needs to consider the issue of financing in a more substantive manner than the 1994 plan. This consideration may take into account that because vaccines are administered by health professionals in various practice settings, addressing the issue of financing requires more than deciding whether a particular type of vaccine will be covered, but also how administration costs will be financed and the manner in which coverage will be effectuated and payment made and even what types of professionals are authorized to administer vaccines. As one example, no mechanism currently exists for ensuring that new adult vaccines recommended by ACIP will be accounted for in existing public funding sources in a timely way to ensure use of these vaccines on the large scale needed to support national disease prevention goals.

Another recent example, which points to the importance of a national strategic focus on the intricacies of vaccine financing and how best to structure an effective payment approach, is the case of Medicare beneficiaries' experience with the varicella-zoster vaccine. Medicare vaccine coverage now spans both Medicare Part B (medical care) and Part D (outpatient prescription drugs), which employ different approaches to coverage and payment. Part B treats payment of covered vaccines as an ancillary clinical service. This means that the treating clinician can accept assignment of the benefit and bill directly for the vaccine and its administration fee.

However, Medicare Part B covers only certain specified vaccines (against hepatitis B, influenza, and pneumococcal pneumonia). The Part D prescription drug program remedies this shortcoming by entitling enrolled beneficiaries to coverage of recommended vaccines not covered under Part B (Whitman, 2008). At the same time, however, Part D is not structured to operate as a means of financing provider-administered drugs and biologics; indeed, providers are barred from billing for services. As a result, a Medicare beneficiary enrolled in Part D must go through an unusually complicated series of steps to gain access to vaccine coverage for a new and important vaccine such as the varicella-zoster vaccine. The physician must prescribe varicella-zoster vaccine before the patient's visit, and the patient then must procure the vaccine and bring it to the physician's office to be administered.

Medicaid also deserves national attention because of its importance in closing the health gap between the richest and poorest Americans. Coverage of immunizations under Medicaid is an option in the case of beneficiaries ages 21 and older. A 2003 study conducted for CDC documented that immunization coverage at ACIP recommended levels is far less than universal for non-institutionalized adults, with only 32 states offering such coverage (Stewart et al., 2003). Adult immunization objectives would be reached more widely if state Medicaid agencies had available to them more active guidance on the value of adult immunization coverage, and tools for coverage and

payment options (including the use of replacement programs for the adult immunization supply).

3. Focus on Disparities in Access to Vaccines

Access to immunization is an issue closely linked with vaccine financing. The 1994 plan did not include a focus on disparities—whether socioeconomic or ethnic disparities—in access to vaccines, and the committee believes it is important to consider this area in drafting the update to the plan.

Innovations in vaccine research and development have led to the availability of several new vaccines (e.g., HPV vaccine, meningococcal conjugate vaccine, varicella-zoster vaccine). However, the growing number and cost of new vaccines in recent years have resulted in significant financial barriers and subsequently reduced access to newer vaccines now available for both children and adults. Although VFC (Vaccines for Children) has made vaccines available to the uninsured, there are still formidable barriers to access to care (including for Medicaid patients) and to some vaccines for the underinsured.

The VFC program has been remarkably successful in ensuring access to new vaccines for children who are uninsured, Medicaid insured, or Alaskan Native or American Indian. VFC also provides vaccines to underinsured children (i.e., those enrolled in health insurance plans that do not cover the cost of all recommended vaccines), but only if they are served at Federally Qualified Health Centers or Rural Health Centers, which are not readily accessible to all children. If underinsured children are seen in a private provider's office, they must pay out-of-pocket for the cost of newer, more expensive vaccines or go to public health clinics to receive these vaccines. Of grave concern is the inability of some states to provide these vaccines even in public health clinics due to limitations in federal and state financing (Lee et al., 2007). This greatly limits timely access to new vaccines and perpetuates the personal, societal, and economic costs of these diseases.

4. Communication as a Key Component of Vaccine Policies and Practices

A growing proportion of the public (and health care professionals) are uncertain about the benefits and the safety of vaccines and recommended immunization practices (Poland and Jacobson, 2001). Such concerns have resulted in underimmunization, disease outbreaks in the United States, and sustained transmissions of vaccine-preventable disease in other countries. These facts indicate that developing communication strategies to support immunization objectives requires understanding the beliefs and values of intended audiences.

To understand all the dimensions of the public's decision making about vaccines, it is necessary to examine the gaps between what the experts perceive as risks and benefits, and what members of the public perceive to be the risks and benefits of vaccines. This work, informed by research in communication and the social sciences, is needed to (1) develop strategies to mitigate misinformation and to communicate messages relevant to the prevalent concerns, and (2) provide people with the information they need in language they understand to help them make informed decisions.

Recommendation 5: The committee recommends that the update to the National Vaccine Plan include a comprehensive framework for communicating with the public and other key stakeholders such as health care providers about the benefits (both individual and community) and risks of vaccination. Communication strategies that are implemented should be evaluated for their effect on knowledge and behavior.

Such a framework could include strategies to communicate at every stage of a vaccine's lifecycle (i.e., not only at the time of FDA approval and ACIP recommendation), an emphasis on two-way communication with the public and health care providers, and strategies to incorporate the best available scientific evidence (e.g., on human behavior and decision making) and a range of communication approaches (social marketing techniques, use of targeted strategies to provide information to people who search the World Wide Web for immunization or vaccine information, etc.). Other strategies could include training key spokespersons (e.g., top scientists and others who are not communication professionals) on effectively communicating with the media regarding vaccines and immunization.

5. Vaccine Supply Issues as a Barrier to Achieving Optimal Coverage

In the year after the 2000 FDA approval of the 7-valent pneumococcal conjugate vaccine, and subsequent ACIP recommendation for universal childhood use of the vaccine, the supplier announced a shortfall in supplies (CDC, 2001). CDC published interim recommendations that called for reserving the vaccine for certain groups of children. This example illustrates one of several possible causes of inadequate vaccine supply, which also may be caused by "companies leaving the vaccine market, manufacturing or production problems, and insufficient stockpiles" (CDC, 2008).

New state-of-the-art vaccine production and inventory management techniques have greatly increased the efficiency and profitability of vaccine manufacture in the United States, but they have also exacerbated the nation's vulnerability to vaccine supply shortages. For example, "just-in-time" business practices (i.e., deliberately reducing inventory levels and delivering products only on an as-needed basis) discourage stockpiling (Wysocki and Lueck, 2006). They may create the incentive to under-produce (which could potentially lead to shortages), and they lead manufacturers to move production facilities to locations outside the country (potentially raising concerns about supply and complicating FDA oversight).

In presentations at the committee's March 2008 meeting, NVPO identified supply issues as a priority area. The committee believes strategic initiatives to consider the factors that contribute to vaccine shortages and possible solutions can be pursued as part of the update to the National Vaccine Plan.

Recommendation 6: The committee recommends that NVPO and its partners consider ways the update to the National Vaccine Plan could spur research for creative solutions to vaccine supply problems.

Exploring the costs and benefits of shifting from a just-in-time to a just-in-case approach (Wysocki and Lueck, 2006), and the use of incentives, cost-sharing contracts, accounting rule modifications, and other mechanisms to align societal public health objectives with private manufacturing choices are among many areas that warrant more research and innovation.

6. Changes in the Global Context

As noted above, it has become nearly impossible to neatly separate domestic and global vaccine issues because of porous borders and emerging infectious diseases on the one hand, and the global vaccine marketplace on the other hand.

The committee believes it is important that drafters of the update to the National Vaccine Plan pay special attention to the evolving global vaccine and immunization issues, in particular to industry views of the global marketplace as a more viable market for their vaccine products than the United States (Milstien et al., 2006). There is current tension between developing products for the U.S. market and focusing on global needs. For example, different serotypes of a disease-causing agent may be prevalent in different geographic areas, and some vaccines are developed to target serotypes found in the United States and exclude those that affect developing countries (Cutts et al., 2005; Klugman et al., 2003; Milstien et al., 2006).

CONCLUDING REMARKS

This letter report contains the committee's initial guidance to the National Vaccine Program Office and its partners as they draft the update to the National Vaccine Plan. Based on the committee's review of the 1994 plan and the process to develop it, and our knowledge about changes since 1994, we identified four process and six content areas to bring to NVPO's attention. The committee also made six recommendations. The committee underscores the preliminary nature of the guidance provided in this letter report. The committee's continuing work, including reviewing the evidence and receiving the input of national stakeholders, will form the basis for more detailed recommendations on priorities in the update to the National Vaccine Plan.

The committee thanks you for the opportunity to assist the National Vaccine Program Office as it coordinates the drafting of the update to the National Vaccine Plan.

Claire V. Broome, *Chair*
Committee on the Review of Priorities in the National Vaccine Plan

Appendix A

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Appendix B

Statement of Task

The federal government issued "Disease Prevention through Vaccine Development and Immunization, The US National Vaccine Plan" in 1994. The Institute of Medicine will convene an ad hoc committee to review the 1994 National Vaccine Plan and then provide guidance on the development of the update to the National Vaccine Plan. This will be delineated in a letter report to the National Vaccine Program Office.

The paragraph above constitutes the statement of task for the first part of the committee's work. A short description of the second part of the committee's work is provided below.

The committee will hold five meetings, each of which will involve a significant portion of time in open session with expert stakeholders to explore areas of the developing plan. Verbatim, uncorrected transcripts of the open sessions will be delivered to NVPO within a month after each meeting. Commissioned papers will be presented on less-well explored areas of the Plan. A final consensus report about priorities for the updated National Vaccine Plan will be delivered and publicly released no later than six months after the final meeting.

Appendix C

Meeting One Agenda[14]

Meeting One, March 3, 2008
Committee on Review of Priorities in the National Vaccine Plan

AGENDA

National Academy of Sciences Building
2101 Constitution Avenue NW, Washington, DC
Lecture Room

1:00 – 1:10 pm Welcome and Committee Introductions
Claire V. Broome
Committee Chair

1:10 – 1:20 pm Presentation
Anand Parekh
Acting Deputy Assistant Secretary for Health
(Science and Medicine)
Office of the Assistant Secretary for Health
Department of Health and Human Services

[14] A Website (http://www.iom.edu/vaccineplan) and listserv were created to provide information to the public about the committee's work and to facilitate communication with the committee. Materials from the committee's March 2008 meeting are available in electronic form on the website. Further, a list of materials reviewed by the committee (in the form in which they were reviewed) including all submissions of information from the public and many items not cited in this report, can be found in the study's public access file, obtained from the National Academies Public Access Records Office at (202)334-3543 or http://www8.nationalacademies.org/cp/ManageRequest.aspx?key=48905.

1:20 – 1:50 pm	Charge to the IOM Committee *CAPT Raymond A. Strikas* *Medical Officer* *U.S. Public Health Service* *National Vaccine Program Office* *Department of Health and Human Services*
1:50 – 2:05 pm	Questions from the Committee
2:05 – 3:05 pm	Key Dimensions of the National Vaccine Plan: Since 1994 and Future *Melinda Wharton* *Deputy Director* *National Center for Immunizations and Respiratory Diseases* *Centers for Disease Control and Prevention* *Norman Baylor* *Director* *Office of Vaccines Research and Review* *Center for Biologics Evaluation* *Food and Drug Administration* *Carole A. Heilman* *Director* *Division of Microbiology and Infectious Diseases* *National Institute of Allergy and Infectious Diseases* *National Institutes of Health*
3:05 – 3:20 pm	Questions from the Committee
3:20 – 3:30 pm	Break
3:30 – 4:10 pm	Key Dimensions of the National Vaccine Plan, continued *Jeffrey Kelman* *Chief Medical Officer* *Center for Beneficiary Choices* *Centers for Medicare and Medicaid Services* *Geoffrey Evans* *Director* *Division of Vaccine Injury Compensation* *Healthcare Systems Bureau* *Health Resources and Services Administration* *Jerome Donlon* *Chief Scientist Advisor & Medical Officer, Office of the Assistant Secretary for Public Health Emergency Preparedness* *Department of Health and Human Services*
4:10 – 4:30 pm	Questions from the Committee

4:30 – 4:45 pm	Relationship Between the National Vaccine Plan and Healthy People 2020 *RADM Penelope Slade Royall* *Director* *Office of Disease Prevention and Health Promotion* *Office of Public Health and Science, Office of the Secretary* *Department of Health and Human Service*
4:45 – 5:15 pm	Status of the New National Vaccine Plan Draft priorities for the National Vaccine Plan *Walter Orenstein* *Professor of Medicine and Pediatrics* *Emory University School of Medicine* *Deputy Director, Emory Vaccine Center* *Consultant to the National Vaccine Plan* Results of the first focus groups for public engagement *Richard Tardif* *Oak Ridge Institute for Science and Education (ORISE)* *Consultant to the National Vaccine Plan* Future plans for public engagement *Roger Bernier* *Centers for Disease Control and Prevention*
5:15 – 5:30 pm	Questions from the Committee
5:30 – 5:45 pm	Public Comments
5:45 pm	Adjourn

Appendix D

1994 National Vaccine Plan
Goals, Objectives, and Anticipated Outcomes

GOALS

1. Develop new and improved vaccines	2. Ensure the optimal safety and effectiveness of vaccines and immunizations	3. Better educate the public and members of the health professions on the benefits and risks of immunizations	4. Achieve better use of existing vaccines to prevent disease, disability, and death

OBJECTIVES

1.1 Develop new and improved vaccines for priority diseases	2.1 Enhance the ability to evaluate the safety and effectiveness of vaccines	3.1 Increase public demand for immunization, especially among populations at risk of underimmunization	4.1 Ensure an adequate supply of vaccines
1.2 Ensure the Nation's capability to detect and respond effectively to new and emerging diseases in the United States and abroad	2.2 Improve the surveillance and evaluation of adverse events following vaccination	3.2 Improve the immunization practices of all health care providers	4.2 Increase immunization coverage levels for infants and children
1.3 Enhance the process of translating technologic innovations into new vaccines	2.3 Ensure the optimal use of vaccines	3.3. Increase the awareness of the benefits of immunization among special target audiences (third-party payers, employers, legislators, community leaders, hospital administrators, etc.)	4.3 Maintain immunization coverage levels for school-aged children

1.4 Ensure the Nation's capability to evaluate new vaccines, and to conduct prompt reviews of new and improved candidate vaccines	2.4 Continue to ensure fair and efficient compensation to individuals injured by vaccines	3.4 Develop more effective methods of communicating the benefits and risks of immunization to health care providers, patients, and parents/guardians	4.4 Increase immunization coverage levels among older adolescents, adults, and the elderly
1.5 Promote the improvement of existing vaccines and development of new vaccines ad vaccine-related technologies for other diseases of importance in developing countries	2.5 Promote and support the efforts of the World Health Organization to develop and harmonize international standards and improve regulatory capabilities in countries involved in vaccine production	3.5 Continue to evaluate the benefits and impact of immunization through the use of cost-effectiveness studies	4.5 Improve the surveillance of vaccine preventable diseases to assess the impact of immunization programs
			4.6 Establish registry and immunization tracking systems
			4.7 Enhance immunization coverage to strengthen national defense
			4.8 Enhance immunization coverage of international travelers who are of highest risk of acquiring vaccine-preventable diseases
			4.9 Eradicate poliomyelitis globally
			4.10 Promote better control of neonatal tetanus and measles, worldwide
			4.11 Promote the self-sustaining capacity of immunization programs in developing countries

ANTICIPATED[15] OUTCOMES

Provision of adequate resources to make possible the vigorous and comprehensive pursuit of the wide range of activities outlined in the National Vaccine Plan could result in substantial health benefits for the American people by the year 2000. These benefits are expected to be realized as the following outcomes:

[15] Also described as "predicted" outcomes in the National Vaccine Plan

- Age-appropriate immunization with all recommended vaccines will be extended to at least 90 percent of infants and children, and access to affordable vaccination services will be made available for every person in the United States.
- Diphtheria, tetanus, poliomyelitis, measles, rubella, mumps, some forms of hepatitis, pertussis (whooping cough), and bacterial meningitis (from *Haemophilus influenzae* type b) will be essentially eliminated as significant causes of death, disease, and disability in the United States.
- Educational communication networks will be in place that will inform all health care providers, communities, and families of the benefits and risks of vaccination.
- In a global context, polio will be drastically reduced, if not eliminated, and neonatal tetanus and measles will be better controlled.
- Pneumococcal pneumonia and influenza in American adults over the age of 65 will be significantly reduced.
- A nationwide system will monitor the vaccines that children receive, and will remind parents when individual infants and children should be vaccinated.
- A nationwide surveillance system will report and investigate cases of vaccine-preventable diseases.
- Vaccine safety and efficacy will be continuously monitored, and adverse events following immunization will be reported and carefully analyzed.
- Improved vaccines will replace some of the vaccines in current use.
- Some vaccines requiring multiple doses and multiple contacts with the health care system will be replaced by more cost-effective ones that will improve people's access to immunization.
- Many new vaccines will be developed, or be much closer to licensure, for diseases for which effective vaccines do not now exist.
- New mechanisms for the more rapid assessment of vaccines proposed for licensure will be in place.
- A reliable supply of all recommended vaccines and a capability to respond to emergencies and emergent threats to public health will be achieved and sustained.
- Information on the cost and benefits of the National Vaccine Plan will be made available on an ongoing basis to the American people.

Appendix E

History of Public Engagement at the National Vaccine Program Office

The committee has followed with great interest and appreciation the efforts of the National Vaccine Program Office (NVPO) and its National Vaccine Advisory Committee (NVAC) to engage the general public on the National Vaccine Plan and on the research agenda of the Immunization Safety Office (ISO). The activities conducted in 2008 and 2009 followed an occasional series of notable public engagement activities on vaccine policy issues spearheaded by the Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), and NVPO over the past decade and a half.

In 2002, working through NVPO, the U.S. Public Health Service agencies and the Johnson Foundation in Wisconsin jointly sponsored the Wingspread Public Engagement Planning Group, which was facilitated by the Keystone Group (Keystone Center, 2003). The purpose of this group was to explore whether and how to enhance public engagement in government decision making on vaccine policy issues. The Wingspread Public Engagement Planning Group considered the recommendations of its Steering Committee and finalized its best judgment on how to enhance public engagement, which is captured in the proposal to create the Vaccine Policy Analysis Collaborative (VPACE), a 3-year demonstration project designed to conduct dialogue and collaborative deliberations on selected vaccine issues with representative segments of the general public and stakeholder groups (Hamlin, 2004).

In 2004, CDC convened a Blue Ribbon Panel of health and safety science professionals, as well as consumer advocates, to provide their independent assessments of CDC immunization safety activities, including the organizational placement of ISO (CDC, 2005).

Also in 2004, the NVAC's Working Group on Public Participation convened a meeting to consider options for enhancing public participation in vaccine policy deliberations and to evaluate the proposal from the Wingspread Public Engagement Planning Group for VPACE.

In July 2005, the Public Engagement Pilot Project on Pandemic Influenza (PEPPPI) process was initiated to discuss and rank goals for a pandemic influenza vaccination program and to pilot-test a new model for engaging citizens on vaccine-related policy decisions. PEPPPI was sponsored by a network of 14 public and private organizations throughout the United States. The project provided "proof of principle" that a large and diverse group of citizens and stakeholders could be recruited successfully to deliberate thoughtfully, interact respectfully, and reach a productive agreement on the topic of immunizations (Bernier, 2006). The principal conclusions reached in the pilot project received serious consideration at the national level and were reflected in the national Pandemic Influenza Plan released in November 2005 (Bernier and Marcuse, 2005).

More recently, beginning in April 2008, NVAC (supported by NVPO) has been involved in two major public engagement activities: (1) a review of the draft ISO research agenda to identify gaps and help set priorities and (2) engagement with the public and other stakeholders to obtain input on the draft National Vaccine Plan. As part of the NVAC-NVPO process for the ISO agenda, one stakeholder and three public engagement workshops (convened in Alabama, Oregon, and Indiana) have been held; stakeholder and public comments have been solicited via the *Federal Register* and other outreach; and an NVAC vaccine safety writing group developed a list of research gaps and criteria for prioritizing items in the ISO research agenda, which was used as a basis for discussion at a stakeholder meeting in March 2009 (HHS, 2009b). The public engagement activities were coordinated by the Keystone Center, and the committee was greatly impressed by the systematic process that NVPO-NVAC and Keystone used.

For the draft National Vaccine Plan, NVPO has solicited feedback via the *Federal Register*; through vaccine-related meetings in which NVPO staff discussed the plan; and at an NVAC meeting in February 2009 to discuss the plan and comments on the draft plan received by NVPO. NVPO also held three public engagement activities in March and April 2009 in Saint Louis, Missouri; Syracuse, New York; and Columbus, Ohio (HHS, 2009a).

NVAC, with the support of NVPO, is also beginning work on a review of the current federal vaccine safety system and development of "a White Paper describing the infrastructure needs for a federal vaccine safety system to fully characterize the safety profile of vaccines in a timely manner, reduce adverse events whenever possible, and maintain and improve public confidence in vaccine safety" (HHS, 2009b). The committee praises CDC and ISO for going substantially beyond the recommendation of the 2005

Institute of Medicine committee that public input be obtained on the Vaccine Safety Datalink (VSD) research plan. CDC and ISO have opened the entire ISO agenda to public viewing and wide input, facilitated by NVAC and NVPO.

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Appendix F

Agendas of Stakeholder Meetings Held by the Committee on Review of Priorities in the National Vaccine Plan (July 2008-June 2009)

FIRST NATIONAL STAKEHOLDER MEETING
VACCINE SUPPLY AND USE

Thursday, July 24, 2008
University of Chicago Gleacher Center, Room 300
Chicago, Illinois

8:15 – 8:30 am	**Welcome and Committee Introductions** *Claire V. Broome* *Institute of Medicine (IOM) Committee Chair*
8:30 – 9:45 am	**Childhood immunization schedule** *Melinda Wharton* *Deputy Director* *National Center for Immunizations and Respiratory Diseases (NCIRD)* *Centers for Disease Control and Prevention (CDC)*

Alternative venues for immunization (adolescent and adult)
Gina Mootrey
Associate Director for Adult Immunization
Immunization Services Division
National Center for Immunization and Respiratory Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention

Incentives and requirements (across the lifespan)
Lance Rodewald
Director
Immunization Services Division
National Center for Immunization and Respiratory Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention

Surveillance and monitoring
Anne Schuchat
RADM, U.S. Public Health Service (PHS)
Director, National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

9:45 – 10:00 am **Committee questions**

10:00 – 10:45 am **Panel: Surveillance and information systems**
Mike Garcia
Vice President and Chief Operations Officer
Scientific Technologies Corporation

Christine Hahn
Idaho State Epidemiologist
Department of Health and Welfare

Discussant:
Emily Peterson
Coordinator, Immunization Information Systems
Minnesota Department of Health

10:45 – 11:15 am **Committee questions and discussion**

11:15 – 11:45 am	**Achieving better use of vaccines** *Gregory A. Poland* *Director* *Vaccine Research Group* *Mayo Clinic*
11:45 am – 12:00 pm	**Committee questions and discussion**
12:00 – 1:00 pm	Lunch
1:00 – 2:00 pm	**Panel: Access to immunization services** *Jeffrey Duchin* *Chief, Communicable Disease Control* *Epidemiology and Immunization Section* *Public Health—Seattle & King County* *Mitchel Rothholtz* *Chief of Staff* *American Pharmacists Association* *Carl Toren* *Medical Director* *Chicago Family Health Center* Discussants: *Lyle J. Fagnan* *Director,* *Oregon Rural Practice-Based Research Network* *Associate Professor of Family Medicine* *Oregon Health and Science University* *Representative, American Academy of Family Practice* *Cheryl A. Peterson* *Senior Policy Fellow* *Department of Nursing Practice and Policy* *American Nurses Association*
2:00 – 2:30 pm	**Committee questions and discussion**

2:30 – 3:10 pm	**Vaccine finance: Overview of stakeholder input and NVAC working group draft white paper** *Walter Orenstein* *National Vaccine Advisory Committee (NVAC)* *Vaccine Finance Working Group* *Associate Director, Emory Vaccine Center* *Director, Emory Program for Vaccine Policy and Development* *Emory University* Discussants: *Ann Clemency Kohler* *Executive Director* *National Association of State Medicaid Directors* *Alan Rosenberg* *Vice President* *Wellpoint, Inc.* *Representative, America's Health Insurance Plans*
3:10 – 3:30 pm	**Committee questions and discussion**
3:30 – 3:45 pm	Break
3:45 – 4:15 pm	**Panel: Provider knowledge and practice** *George Isham* *Chief Health Officer* *Health Partners* *Allison Kempe* *Professor of Pediatrics* *Director, Primary Care Research Fellowship* *Director, Children's Outcomes Research Program* *University of Colorado at Denver* *Health Sciences Center* *Julie Morita* *Medical Director* *Immunization Program* *Chicago Department of Public Health*

Discussants:
Lyle J. Fagnan
Director, Oregon Rural Practice-Based Research Network
Associate Professor of Family Medicine
Oregon Health and Science University
Representative, American Academy of Family Practice

Wayne Hachey
Director, Preventive Medicine and Surveillance
Office of the Assistant Secretary of Defense (Health Affairs) Force Health Protection and Readiness
Department of Defense

4:15 – 4:45 pm **Committee questions and discussion**

4:45 – 5:45 pm **Panel: Vaccine supply**
Norman W. Baylor
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

Laurel Wood
Manager
Immunization Program
Alaska Department of Health and Social Services
Chair
Association of Immunization Managers

Discussants:
Marguerite D. Baxter
Vice President and Head, Global Public Affairs
Novartis Vaccines and Diagnostics, Inc.

Isabelle Claxton
Director
Public Policy and Advocacy
GSK Vaccines

John D. Grabenstein
Senior Director, Adult Vaccine Medical Affairs
Merck Vaccines & Infectious Diseases

Gregory S. Wallace
Chief, Vaccine Supply & Assurance Branch
Immunization Services Division
National Center for Immunization & Respiratory Diseases
Centers for Disease Control and Prevention

5:45 – 6:15 pm **Committee questions and discussion**

6:15 – 6:30 pm **Public comment**

SECOND NATIONAL STAKEHOLDER MEETING
DEVELOPMENT OF NEW AND IMPROVED VACCINES

Monday, December 1, 2008
Huntington Room, Arnold and Mabel Beckman Center
100 Academy Drive
Irvine, California

Please note:
Panelist titles and affiliations are provided at the end of the agenda.
(*) denotes panelists who will give a formal presentation
(†) denotes panelists who contributed to the draft National Vaccine Plan

8:30 am **Welcome and Committee Introductions**
Claire V. Broome
Institute of Medicine (IOM)
Committee Chair

8:45 – 10:15 am **Panel 1: Encouraging scientific innovation (new vaccines, better vaccines)**
Moderator: Milagritos Tapia (IOM committee member)

	Panelists: *Philip Dormitzer (Novartis)* *Kathryn Edwards (Vanderbilt University)* *Emil Gotschlich (Rockefeller University)* *Harry Greenberg (Stanford University)* *Diane Griffin (Johns Hopkins University)* *Ed Mocarski* (MedImmune)* *Barbara Mulach† (National Institutes of Health [NIH]/National Institute of Allergy and Infectious Diseases [NIAID])* *Stanley Plotkin* (Sanofi)* *Robin Robinson† (HHS/BARDA)* *Rebecca Sheets† (NIH/NIAID) (via video)* *Justin Wright (BD Medical-Pharmaceutical Systems)*
10:15 – 10:30 am	Break
10:30 – 11:15 am	**Panel 1 continued**
11:15 am – 12:30 pm	**Panel 2: Financing vaccine research and development** *Moderator: Claire V. Broome (IOM Committee Chair)* Panelists: *Harry B. Greenberg (Stanford University)* *Karl D. Handelsman (CMEA Ventures)* *David C. Kaslow (Merck)* *Leighton Read* (Alloy Ventures)* *Jeffrey Ulmer (Novartis)*
12:30 – 1:30 pm	Lunch
1:30 – 3:00 pm	**Panel 3: Addressing public needs and priorities** *Moderator: Edgar Marcuse (IOM committee member)* Panelists: *Philip R. Dormitzer (Novartis)* *Kathryn Edwards (Vanderbilt University)* *David C. Kaslow (Merck)* *Edward Mocarski (MedImmune)*

	Stanley A. Plotkin (Sanofi)* *Robin Robinson† (HHS/BARDA)*
3:00 – 3:15 pm	Break
3:15 – 4:30 pm	**Panel 4: Regulatory and other issues in developing and licensing novel processes, new technologies, etc.** *Moderator: Arthur Reingold (IOM committee member)* Panelists: *Karl D. Handelsman (CMEA Ventures)* *David C. Kaslow (Merck)* *Karen Midthun (FDA/CBER)* *Leighton Read (Alloy Ventures)* *Rebecca Sheets† (NIH/NIAID) (via video)* *Jeffrey Ulmer (Novartis)*
4:30 – 5:30 pm	**Closing dialogue** *Moderator: Claire V. Broome (IOM committee chair)* *Question to all stakeholders at the meeting: What criteria would you use to determine what objectives should receive the greatest level of attention in the National Vaccine Plan?* *Final observations about the day's discussions* *All panelists and audience members*
5:30 pm	Adjourn

PANELIST TITLES AND AFFILIATIONS

Philip Dormitzer
Senior Director and Senior Project Leader (viral vaccine research)
Novartis Vaccines and Diagnostics

Kathryn Edwards
Sarah Sell Professor of Pediatrics
Director, Division of Pediatric Clinical Research
Vanderbilt University School of Medicine

Emil Gotschlich
R. Gwin Follis-Chevron Professor
Laboratory of Bacterial Pathogenesis and Immunology
Rockefeller University

Harry B. Greenberg
Senior Associate Dean for Research and Training
Stanford University School of Medicine
Professor of Medicine (Gastroenterology & Hepatology) Microbiology and Immunology, and Staff Physician VA Palo Alto Health Care System

Diane Griffin
Professor
Alfred and Jill Sommer Professor and Chair in Molecular Microbiology and Immunology
Johns Hopkins Bloomberg School of Public Health

Karl D. Handelsman
Managing Director
CMEA Ventures

David C. Kaslow
Vice President, Infectious Diseases and Vaccines Franchise
Merck Research Laboratories

Karen Midthun
Deputy Director, Center for Biologics Evaluation and Research
Food and Drug Administration

Edward S. Mocarski, Jr.*
Distinguished Fellow, MedImmune Vaccines
MedImmune, AstraZeneca
Professor Emeritus Stanford University
Robert W. Woodruff Professor in the Department of Microbiology and Immunology
Emory Vaccine Center, Emory University

Barbara Mulach†
Director, Office of Scientific Coordination and Program Operations
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases
National Institutes of Health

Stanley Plotkin*
Executive Advisor to CEO, Sanofi Pasteur
Emeritus Professor of Pediatrics, University of Pennsylvania

Leighton Read*
General Partner
Alloy Ventures

Robin Robinson†
Director, Biomedical Advanced Research Development Authority
U.S. Department of Health and Human Services

CAPT Rebecca Sheets†
Vaccine Scientific and Regulatory Specialist
National Institute of Allergy and Infectious Diseases
National Institutes of Health

Jeffrey Ulmer
Global Head, External Research
Novartis Vaccines and Diagnostics

Justin Wright
Manager, Bio-Analytical Sciences
BD Medical-Pharmaceutical Systems

THIRD NATIONAL STAKEHOLDER MEETING
INFORMED VACCINE DECISION MAKING

Monday, February 2, 2009
Keck Center of the National Academies
500 Fifth Street, N.W.
Washington, DC

Please note:
Panelist titles and affiliations are provided at the end of the agenda.
(*) denotes panelists who will provide brief introductory comments at the beginning of a panel
(†) denotes panelists who contributed to the draft National Vaccine Plan

8:30 am

Welcome and Overview of the Agenda and the Day's Proceedings
Committee Introductions
Claire V. Broome
Institute of Medicine (IOM)
Committee Chair

8:45 am

Panel 1: Who and what informs personal decision making about immunization?
Moderator: Edgar Marcuse, IOM committee member

Topics of discussion may include

- Science, values, social norms, credibility of sources, ease of access, access to and comprehension of information, behavioral factors (e.g., risk aversion), opinions of formal or informal community leaders
- Factors for and against using certain sources of information
- Preferred sources and information needs of diverse populations (age, ethnicity, etc.)
- Health care providers, their knowledge, and their role

Panelists:
Louis Z. Cooper (Columbia University)
Vicky Debold (National Vaccine Information Center [NVIC])
Julie Downs (Carnegie Mellon)
Lynda Flowers (AARP)
Samuel L. Katz (Duke University)
Julie Leask (University of Sydney)
Anita Manning (Freelance Journalist)
Mairi Breen Rothman (American College of Nurse-Midwives)
Kristine Sheedy[†] (CDC/NCIRD)

Questions and comments from the audience

10:30 am

Break

10:45 am

Panel 2: The science of communication and good practices in communicating about vaccines and immunization
Moderator: Élaine Chatigny, IOM committee member

Topics of discussion may include
- Evidence from social and behavioral sciences
- Gaps in the available research

Panelists:
Julie Downs (Carnegie Mellon)
Julie Leask (University of Sydney)*
Martin G. Myers (NNii)
Rebecca Parkin (George Washington University)
Kristine Sheedy (CDC/NCIRD)

Questions and comments from the audience

12:30 pm

Lunch

1:30 pm

Panel 3: Ethical, legal, and policy issues in communicating about immunization
Moderator: Sara Rosenbaum, IOM committee member

Topics of discussion may include
- Communicating in the context of policies requiring immunization (e.g., for school entry, for healthcare workforce)
- How ethical questions and standards influence communication about immunization

Panelists:
Barbara Loe Fisher (NVIC)
Ross Silverman (Southern Illinois University)
Christina Tan (N.J. Department of Health)
L.J. Tan (American Medical Association [AMA])

Questions and comments from the audience

3:15 pm	Break
3:30 pm	**Panel 4: Communicating to encourage immunization** *Moderator: Richard Mandsager, IOM committee member* Topics of discussion may include • Strengthening the communication activities of public health agencies • Lessons to be learned (in general, and from the day's discussions) • Interactions between public health agencies and the media • Meeting public needs and expectations • Health care providers, their knowledge, and their role Panelists: *Louis Z. Cooper (Columbia University)* *Samuel L. Katz (Duke University)* *Nancy Lee* (Social Marketing Services, Inc.)* *Martin G. Myers (NNii)* *Rebecca Parkin (George Washington University)* *Glen Nowak (CDC/OEC)* *Kristine Sheedy* (CDC/NCIRD)* *Dean Sidelinger* (San Diego County Public Health Services)* *Christina Tan (N.J. Department of Health)* *L.J. Tan (AMA)*
5:30 pm	Adjourn

PANELIST TITLES AND AFFILIATIONS

Louis Z. Cooper
Professor Emeritus, Pediatrics
College of Physicians and Surgeons
Columbia University

Vicky Debold
Director of Patient Safety
National Vaccine Information Center

Julie Downs
Research Scientist
Department of Social and Decision Sciences
Carnegie Mellon University

Lynda Flowers
Strategic Policy Advisor
AARP Public Policy Institute

Samuel L. Katz
Wilburt C. Davison Professor Emeritus of Pediatrics
Duke University

Julie Leask
Senior Research Fellow
National Centre for Immunisation Research and Surveillance
Conjoint Senior Lecturer
Faculty of Medicine
University of Sydney

Nancy Lee
President
Social Marketing Services, Inc.

Barbara Loe Fisher
President and Co-Founder
National Vaccine Information Center

Anita Manning
Freelance Journalist

Martin G. Myers
Executive Director
National Network for Immunization Information (NNii)
Professor of Pediatrics, Preventive Medicine, and Community Health
Associate Director for Public Health Policy and Education
Sealy Center for Vaccine Development
University of Texas Medical Branch

Glen Nowak
Director
Division of Media Relations
Office of Enterprise Communication
Centers for Disease Control and Prevention

Rebecca Parkin
Associate Dean, Research and Public Health Practice
Professor
Department of Environmental and Occupational Health, and
Department of Epidemiology and Biostatistics
School of Public Health and Health Services
George Washington University

Mairi Breen Rothman
Professional Services Consultant
American College of Nurse-Midwives

Kristine Sheedy
Associate Director
Office of Communication Science
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Dean Sidelinger
Deputy Public Health Officer
Public Health Services Administration
San Diego County

Ross Silverman
Chair, Medical Humanities
Professor, Medical Humanities and Psychiatry
School of Medicine
Professor, Medical Jurisprudence
School of Law
Director, Program in Law and Health Policy
Southern Illinois University

Christina Tan
State Epidemiologist
New Jersey Department of Health and Senior Services

L.J. Tan
Director, Medicine and Public Health
American Medical Association

FOURTH NATIONAL STAKEHOLDER MEETING
THE SAFETY OF VACCINES AND VACCINATION PRACTICES

Tuesday, April 14, 2009
Keck Center of the National Academies, Room 100
500 Fifth Street, N.W.
Washington, DC

Please note:
Panelist titles and affiliations are provided at the end of the agenda.

8:30 am — **Welcome and Overview of the Agenda and the Day's Proceedings**
Committee Introductions
Claire V. Broome,
Institute of Medicine (IOM)
Committee Chair

8:45 am — **Panel 1: Identifying vaccine safety concerns**
Moderator: Grace Lee, IOM committee member

Topics of discussion may include

- Assessing safety in pre-licensure clinical trials (Phase I-III)
- Safety objectives pre-licensure versus post-licensure
- Gaps in the detection of safety signals and how to address them
- Vaccine Adverse Events Reporting System
- Active surveillance capabilities of the Vaccine Safety Datalink

Participants:
Robert Ball, FDA
Louis Z. Cooper, Columbia University
Adrian Dana, Merck
Vicky Debold, NVIC
Susan Ellenberg, University of Pennsylvania
Neal Halsey, Johns Hopkins University

Florence Houn, Celgene
Phillip Krause, FDA
Lanie Friedman Ross, University of Chicago
Thomas M. Vernon, Sanofi Pasteur
Melinda Wharton, CDC/Immunization Safety Office (ISO)

Questions and comments from the audience

10:30 am Break

10:45 am **Panel 2: Studying vaccine safety**
Moderator: Art Reingold, IOM committee member

Topics for discussion may include

- What triggers switching from surveillance to evaluation of a safety signal
- Evaluating safety signals, assessing potential causality of an observed adverse event
- Approaches and methodological, ethical, and practical advantages and challenges
- Assessing the relationship between immunization and diagnostic categories (e.g., demyelinating diseases, rheumatologic diseases)
- Vaccine Safety Datalink and Clinical Immunization Safety Assessment network challenges and opportunities
- Enhancing timeliness of conducting and completing studies (tools such as rapid cycle analysis)
- Gaps in vaccine safety science

Participants:
Robert Ball, FDA
Sean Hennessy, University of Pennsylvania
John Iskander, CDC/ISO
Samuel L. Katz, Duke University
Tracy Lieu, Harvard University
Andy Pavia, University of Utah, NVAC Vaccine Safety WG
Lanie Friedman Ross, University of Chicago

Kenneth J. Rothman, RTI International
Patricia Saddier, Merck
Brian Strom, University of Pennsylvania
Melinda Wharton, CDC/ISO

Questions and comments from the audience

12:30 pm Lunch

1:30 pm **Update from the National Vaccine Advisory Committee Safety Working Group**
Andy Pavia, NVAC working group chair

1:45 pm **Panel 3: Basic science (in vivo, in vitro, and human clinical models)**
Moderator: Claire V. Broom, IOM Committee Chair

Topics for discussion may include

- Current research on host risk factors, gaps
- Genetic contributions to immune response
- Adequacy of animal models for studying vaccine responses
- Exploring the role of adjuvants in adverse reactions to vaccines
- Gaps in understanding of immune system (immune response to vaccines, the immature immune system, etc.)

Participants:
George Curlin, NIH/NIAID
Kathy Edwards, Vanderbilt University
Charles Hackett, NIH/NIAID
Neal Halsey, Johns Hopkins University
Ruth Karron, Johns Hopkins University
Phillip Krause, FDA

Questions and comments from the audience

3:15 pm Break

3:30 pm	**Panel 4: Policy issues related to vaccine safety and compensation for vaccine injuries** *Moderator: Sara Rosenbaum, IOM committee member* Topics for discussion may include • Vaccine safety as conceived in the 1986 act that established the Vaccine Injury Compensation Program • Implications of recent decisions of the U.S. Court of Federal Claims Participants: *Louis Z. Cooper, Columbia University* *Barbara Loe Fisher, NVIC* *Anthony Robbins, Tufts University* *Jeff Sconyers, Seattle Children's Hospital, outgoing chair ACCV* *Tim Westmoreland, Georgetown University* **Questions and comments from the audience**
5:15 pm	Closing comments
5:30 pm	Adjourn

PANELIST TITLES AND AFFILIATIONS

Robert Ball
Chief, Vaccine Safety Branch
Division of Epidemiology
Food and Drug Administration

George Curlin
Medical Officer
Office of the Director
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases
National Institutes of Health

Louis Z. Cooper
Professor Emeritus, Pediatrics
College of Physicians and Surgeons
Columbia University

Adrian Dana
Senior Director
Clinical Risk Management and Safety Surveillance
Merck Research Labs

Vicky Debold
Director of Patient Safety
National Vaccine Information Center

Kathryn Edwards
Sarah Sell Professor of Pediatrics
Director, Division of Pediatric Clinical Research
Vanderbilt University School of Medicine

Susan Ellenberg
Professor of Biostatistics
Associate Dean for Clinical Research
University of Pennsylvania School of Medicine

Barbara Loe Fisher
President and Co-founder
National Vaccine Information Center

Charles Hackett
Deputy Director
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
National Institutes of Health

Neal Halsey
Professor
Department of International Health, Disease Prevention & Control
Department of Pediatrics
Johns Hopkins University

Sean Hennessy
Senior Scholar, Epidemiology
Center for Clinical Epidemiology and Biostatistics
Assistant Professor of Epidemiology, University of Pennsylvania School of Medicine
Assistant Professor of Pharmacology, Department of Pharmacology
Director of Ambulatory Drug Use and Effects, University of Pennsylvania Medical Center

Florence Houn
Vice President, Regulatory Affairs
Celgene Corporation

John Iskander
Associate Director for Immunization Safety
Centers for Disease Control and Prevention

Ruth Karron
Director, Center for Immunization Research
Director, Johns Hopkins Vaccine Initiative
Johns Hopkins University

Samuel L. Katz
Wilburt C. Davison Professor Emeritus of Pediatrics
Duke University

Phillip Krause
Laboratory Chief
Lead Research Investigator
Center for Biologics Evaluation and Research
Food and Drug Administration

Tracy Lieu
Professor
Director of Faculty Development
Director, Center for Child Health Care Studies
Department of Ambulatory Care and Prevention
Harvard Pilgrim Health Care and Harvard Medical School

Andy Pavia
Professor, Division of Infectious Diseases
University of Utah School of Medicine
Chair, Vaccine Safety Working Group, National Vaccine Advisory Committee

Anthony Robbins
Professor
Department of Public Health and Family Medicine
Tufts University

Lanie Friedman Ross
Carolyn and Matthew Bucksbaum Professor of Clinical Ethics
Professor, Departments of Pediatrics, Medicine, and Surgery
Associate Director, MacLean Center for Clinical Medical Ethics
University of Chicago

Kenneth J. Rothman
Distinguished Fellow in Epidemiology
Vice President, Epidemiology Research
RTI International

Patricia Saddier
Senior Director, Epidemiology Department
Merck Research Laboratories

Jeff Sconyers
Senior Vice President and General Counsel
Seattle Children's Hospital
Chair, Advisory Commission on Childhood Vaccines

Brian Strom
George S. Pepper Professor of Public Health and Preventive Medicine
Departments of Biostatistics and Epidemiology
University of Pennsylvania

Thomas M. Vernon
Consultant with Sanofi Pasteur
Former VP, Merck Vaccine Division
Former Executive Director, Colorado Department of Health

Tim Westmoreland
Visiting Professor of Law
Georgetown University

Melinda Wharton
Deputy Director
National Center for Immunizations and Respiratory Diseases
Centers for Disease Control and Prevention

Some federal agencies contributed to the development of the draft strategic National Vaccine Plan

FIFTH NATIONAL STAKEHOLDER MEETING VACCINES AND GLOBAL HEALTH

Thursday, June 4, 2009
The Seattle Public Library
1000 Fourth Avenue
Seattle, Washington

Please note:
Complete participant affiliations are provided at the end of the agenda.

8:30 am	**Welcome, Overview, and Committee Introductions** *Claire V. Broome, IOM Committee Chair*
8:45 am	**Panel 1: Development of new vaccines and those needed for global use** *Moderator: Claire Broome, IOM Committee Chair*

Topics of discussion may include

- Setting priorities
- Scientific challenges
- Regulatory issues
- Implementation issues
- Advocacy or policy communication issues
- Role of non-Western vaccine companies as vaccine developers and suppliers for both developed and developing nations

Discussants:
Norman Baylor, CBER/FDA (by phone)
Brent Burkholder, NCIRD/CDC
Thomas Cherian, World Health Organization (WHO)
Mark Feinberg, Merck
John Ferguson, Novartis Vaccines & Diagnostics
Orin Levine, Johns Hopkins University
Adel Mahmoud, Princeton University (by phone)
Margaret McCluskey, U.S. Agency for International Development (USAID)
Regina Rabinovich, Gates Foundation
Jerald Sadoff, Aeras Global TB Vaccine Foundation
Theodore Tsai, Novartis
Justin Wright, BD Medical-Pharmaceutical Systems

10:30 am Break

10:45 am **Panel 2: Immunization program issues: Infrastructure, communication, impact of eradication or elimination**
Moderator: Milagritos Tapia, IOM committee member

Topics of discussion may include

- Quality and safety of administration, storage, inventory management, cold chain, other infrastructure issues
- Impact of health systems "reform"
- Are vaccines reaching those at highest risk of disease?
- Innovative approaches to target high-risk or hard-to-reach groups
- Implications of target populations with high proportion of HIV infected

Discussants:
Brent Burkholder, NCIRD/CDC
Thomas Cherian, WHO
Rod Hausser, BD Medical-Pharmaceutical Systems

Orin Levine, Johns Hopkins University
Margaret McCluskey, USAID
Robert Steinglass, John Snow Inc.
Linda Venczel, Gates Foundation

12:30 pm — Lunch

1:30 pm — **Panel 3: Surveillance of safety, effectiveness, coverage, disease**
Moderator: Art Reingold, IOM committee member

Topics of discussion may include
- Immunization program monitoring and evaluation
- Coverage measurement versus disease impact
- Challenges of safety monitoring (e.g., yellow fever vaccine in Africa)

Discussants:
Brent Burkholder, NCIRD/CDC
John Ferguson, Novartis Vaccines & Diagnostics
David Fleming, Director & Health Officer, WA
Kathy Neuzil, Program for Appropriate Technology in Health (PATH)
Robert Steinglass, John Snow Inc.
Linda Venczel, Gates Foundation

3:15 pm — Break

3:30 pm — **Panel 4: Financing vaccine development and purchase**
Moderator: David Paltiel, IOM committee member

Topics of discussion may include
- Financing new vaccine development
- Financing purchase of expensive new vaccines (e.g., pneumococcal conjugate, human papilloma virus)
- Sustainable support for new vaccines by developing countries

- Experience with novel financing approaches—International Financing Facility for Immunization (IFFIm), Advance Market Commitment (AMC), Gates (pros and cons)
- Prioritizing support for optimal use of existing vaccines versus development of new vaccines

Discussants:
Brent Burkholder, NCIRD/CDC
Orin Levine, Johns Hopkins University
Melinda F. Moree, Global Health Services
Regina Rabinovich, Gates Foundation
Jerald Sadoff, Aeras Global TB Vaccine Foundation

5:30 pm Adjourn

PANELIST TITLES AND AFFILIATIONS

Jon Kim Andrus
Professor, Department of Global Health Director, Global Health MPH Program
George Washington University

Norman Baylor
Director, Office of Vaccines Research and Review
Center for Biologics Evaluation and Research
Food and Drug Administration

Brent Burkholder
Director, Global Immunization Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Thomas Cherian
Coordinator
Expanded Programme on Immunization
Department of Immunization, Vaccines and Biologicals
World Health Organization

Mark Feinberg
Vice President, Medical Affairs and Policy
Merck Vaccines and Infectious Diseases
Merck & Co., Inc.

John Ferguson
Vice President and Global Head
Pharmacovigilance & Medical Safety
Novartis Vaccines & Diagnostics

David Fleming
Director and Health Officer
Department of Public Health
Seattle/King County

Rod Hausser
Director
Business Development and Operations
BD Medical-Pharmaceutical Systems

Orin Levine
Executive Director, PneumoADIP
Associate Professor, International Health
Johns Hopkins University

Adel Mahmoud
Woodrow Wilson School of Public and International Affairs
Department of Molecular Biology
Princeton University

Margaret McCluskey
Senior Technical Advisor, HIV Vaccines
GH/Office of HIV & AIDS
U.S. Agency for International Development

Melinda F. Moree
Vice President, Global Health Services

Kathy Neuzil
Director, Influenza Vaccine Project
Clinical Director, Rotavirus Vaccine Program
PATH

Regina Rabinovich
Director, Infectious Diseases Development
Global Health Program
The Bill & Melinda Gates Foundation

Jerald Sadoff
President and Chief Executive Officer
Aeras Global TB Vaccine Foundation

Robert Steinglass
Technical Director, IMMUNIZATIONBasics Project
John Snow Inc.

Theodore Tsai
Senior Vice President, Scientific Affairs
Novartis

Linda Venczel
Vaccine-Preventable Diseases
Integrated Health Systems Development
The Bill & Melinda Gates Foundation

Justin Wright
Manager, Bio-Analytical Sciences
BD Medical-Pharmaceutical Systems

Appendix G

Acronyms

ACIP	Advisory Committee on Immunization Practices
AE	adverse event
AHIP	America's Health Insurance Plans
AMC	Advance Market Commitment
ARRA	American Recovery and Reinvestment Act
ASPR	Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
BLA	Biological License Application
BRFSS	Behavioral Risk Factor Surveillance System
CAVD	Collaboration for AIDS Vaccine Discovery
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CISA	Clinical Immunization Safety Assessment
CMS	Centers for Medicare & Medicaid Services
DALY	disability-adjusted life year
DoD	Department of Defense
DTaP/DTP	diphtheria, pertussis (whooping cough), and tetanus vaccine
EHR	electronic health record
EMEA	European Medicines Agency
EMR	electronic medical record

FDA	Food and Drug Administration
FE(L)TP	Field Epidemiology Training Program/Field Epidemiology and Laboratory Training Program
FTE	full-time equivalent/employee
GAVI	Global Alliance for Vaccines and Immunisation
HEDIS	Healthcare Effectiveness Data and Information Set
HHS	Department of Health and Human Services
Hib	*Haemophilus influenzae* type B
HIT	health information technology
HPV	human papilloma virus
HRSA	Health Resources and Services Administration
IAVG	Interagency Vaccine Group
IAVI	International AIDS Vaccine Initiative
IFFIm	International Financing Facility for Immunization
IIS	immunization information systems
IOM	Institute of Medicine
IPV	inactivated polio vaccine
ISO	Immunization Safety Office
IT	information technology
MCO	managed care organization
MMR	measles, mumps, and rubella vaccine
MMRV	measles, mumps, rubella, and chickenpox vaccine
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NCQA	National Committee for Quality Assurance
NCVIA	National Childhood Vaccine Injury Act
NDA	New Drug Application
NHIN	National Health Information Network
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health
NIS	National Immunization Survey
NVAC	National Vaccine Advisory Committee
NVIC	National Vaccine Information Center
NVP	National Vaccine Plan
NVPO	National Vaccine Program Office
ONCHIT	Office of the National Coordinator for Health Information Technology
OPHS	Office of Public Health and Science
OPV	oral polio vaccine
PAHO	Pan American Health Organization
PATH	Program for Appropriate Technology in Health

PDP	product development partnership
PEPPPI	Public Engagement Pilot Project on Pandemic Influenza
PHS	Public Health Service
PRISM	Post-Licensure Rapid Immunization Safety Monitoring
RRV-TV	Tetravalent Rhesus-based Rotavirus Vaccine
RVP	Rotavirus Vaccine Program
SARS	severe acute respiratory syndrome
SCHIP	State Children's Health Insurance Program
SIVR	Strategic Issues in Vaccine Research
TB	tuberculosis
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
VA	Department of Veterans Affairs
VAERS	Vaccine Adverse Event Reporting System
VFC	Vaccines for Children
VHC	Vaccine Healthcare Center
VICP	Vaccine Injury Compensation Program
VPACE	Vaccine Policy Analysis Collaborative
VPD	vaccine-preventable disease
VSD	Vaccine Safety Datalink
WHO	World Health Organization

Appendix H

Committee Biographies

Claire V. Broome, M.D. (*Chair*), is currently an adjunct professor in the Department of Global Health at the Rollins School of Public Health, Emory University. Previously she held several positions at the Centers for Disease Control and Prevention (CDC) including senior adviser, Integrated Health Information Systems (2000-2006); deputy director (1994-1999); acting director (1998); acting director, National Center for Injury Prevention and Control (1991-1993); associate director for science (1990-1994); and chief, Bacterial Special Pathogens Branch, National Center for Infectious Diseases (1981-1990). Dr. Broome has served as an adviser for the following institutions: World Health Organization; World Bank; Global Alliance for Vaccines and Immunization; The Bill & Melinda Gates Foundation; Burroughs Wellcome Fund; the Wellcome Trust; U.S. Agency for International Development (USAID); the U.S. Food and Drug Administration (FDA) (member, Vaccines and Related Biologicals Advisory Committee); and the National Institutes of Health (NIH). Dr. Broome's research experience includes developing and implementing research programs in bacterial disease epidemiology, observational epidemiology for vaccine evaluation, and public health surveillance methodology. She also has informatics experience, including leading the development and implementation of the National Electronic Disease Surveillance System. Dr. Broome has received numerous honors and awards including Infectious Disease Society of America's Squibb Award for Excellence of Achievement in Infectious Diseases; American Public Health Association Epidemiology Section's John Snow Award; U.S. Public Health Service (PHS) Distinguished Service Medal; Surgeon General's Medallion; Charles Shepard Award 1986; and Langmuir award

coauthor in 1981, 1983, 1988, 1989, 1993; she is a member of the Institute of Medicine. Dr. Broome received her B.A. from Harvard University and her M.D. from Harvard Medical School; she specialized in internal medicine at the University of California, San Francisco. She was a CDC Epidemic Intelligence Service (EIS) officer and completed a fellowship in infectious diseases at Massachusetts General Hospital.

Élaine Chatigny is director general, Communications, at the Public Health Agency of Canada. She is responsible for risk communications, crisis communications, strategic communication planning, media relations, social marketing, and a host of other communication functions. Her previous position with the government of Canada was director, Public Affairs, with the Communications, Marketing, and Consultation Directorate at Health Canada. In her 8 years with the government of Canada, Ms. Chatigny has established Crisis and Emergency Communications and Risk Communications Units. She was also responsible for the development of Health Canada's and the Public Health Agency of Canada's *Risk Communications Framework and Handbook*, which is unique to the government of Canada. Ms. Chatigny has been an external adviser to the World Health Organization on pandemic influenza communications planning and co-chair of the Communicators' Network of the Global Health Security Initiative (G7 plus Mexico); she is the founder of a federal, provincial, and territorial communications working group on pandemic influenza, which reports to Canada's Pandemic Influenza Committee. Prior to joining the federal government, Ms. Chatigny worked 14 years with the Canadian Broadcasting Corporation as a journalist and a manager.

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Grace M. Lee, M.D., M.P.H., is an assistant professor of population medicine and pediatrics at the Harvard Medical School, Harvard Pilgrim Health Care Institute, and Children's Hospital Boston. Dr. Lee's research focuses on vaccine economics, vaccine safety, infectious disease epidemiology, and infection control and prevention. She is currently principal investigator or coinvestigator on Agency for Healthcare Research and Quality (AHRQ)-, NIH-, and CDC-funded studies. Several key research projects include conducting active surveillance of H1N1 and seasonal influenza vaccine safety in the United States, understanding gaps in the vaccine financing and delivery system, modeling the cost-effectiveness of vaccines and interventions to reduce health care–associated infections, and evaluating the impact of Medicare's policy of nonpayment for health care–associated infections in hospital settings. Dr. Lee joined the faculty at Harvard Medical School, Harvard Pilgrim Health Care Institute, and Children's Hospital Boston in 2003 after completing an AHRQ postdoctoral fellowship. She received her M.D. at the University of Pennsylvania School of Medicine and M.P.H. at Harvard School of Public Health. She completed her pediatric residency and

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Richard Mandsager, M.D., is chief executive at Providence Alaska Medical Center and was the executive director of the Children's Hospital at Providence in Anchorage from October 2006 to August 2009. From 2004 to 2006, he was the director of public health for the State of Alaska. During his tenure, legislative support and funding were achieved for purchase, implementation, and operation of an immunization registry. Prior to that, he was medical director of the Pediatric Service Center of Alaska Native Medical Center (ANMC) in Anchorage. While he was in that position the ANMC achieved more than a 90 percent immunization rate for children. His prior experience includes serving as staff pediatrician for Southcentral Foundation, where he revised and improved protocols for medical care for children and adolescents. Dr. Mandsager has also served as the past director for the Alaska Native Medical Center and service unit director for the Anchorage Service Unit. He led and facilitated completion of the ANMC hospital campus, which was the largest project in the history of the Indian Health Service and the first joint construction project of the Indian Health Service and the Centers for Disease Control and Prevention in Atlanta. He retired from the Commissioned Corps of the U.S. Public Health Service with the rank of an assistant surgeon general.

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David B. Reuben, M.D., is director, Multicampus Program in Geriatrics Medicine and Gerontology (MPGMG), and chief, Division of Geriatrics, at the University of California at Los Angeles (UCLA) Center for Health Sciences. He is the Archstone Foundation Chair and Professor at the David Geffen School of Medicine at UCLA. He is also director of the UCLA Claude D. Pepper Older Americans Independence Center. Dr. Reuben sustains professional interests in clinical care, education, research, and administrative aspects of geriatrics. He maintains a clinical primary care practice of frail older persons and attends on inpatient and geriatric psychiatry units at UCLA. He has won seven awards for excellence in teaching. Dr. Reuben's current research interests include redesigning the office visit to improve healthcare quality and measurement of how older adults function. In 2000, Dr. Reuben was given the Dennis H. Jahnigen Memorial Award for outstanding contributions to education in the field of geriatrics, and in 2008,

he received the Joseph T. Freeman Award from the Gerontological Society of America. Dr. Reuben was part of the team that received the 2008 John M. Eisenberg Patient Safety and Quality Award for Research—Joint Commission and National Quality Forum, for Assessing Care of the Vulnerable Elderly (ACOVE). He is a past president of the American Geriatrics Society and the Association of Directors of Geriatric Academic Programs. Dr. Reuben is currently chair-elect of the Board of Directors of the American Board of Internal Medicine and sits on its Executive Committee. He is lead author of the widely distributed book *Geriatrics at Your Fingertips*. Dr. Reuben produced *Freda Sandrich: Center Stage*, a short documentary that was a finalist for a FREDDIE award. His play about decision making at the end of life, *Reprieves*, had its first reading in Los Angeles in 2007 and has had two subsequent commissioned readings, by the California Healthcare Foundation in 2008 and by the Friends of the Semel Institute in 2009. His second play is about Lyndon Johnson and the Civil Rights Act of 1957. Dr. Reuben has served on four past IOM committees.

Sara Rosenbaum, J.D., is chair of the Department of Health Policy and Harold and Jane Hirsh Professor of Health Law and Policy at the George Washington University. She also holds an appointment as professor of health care sciences at George Washington's School of Medicine and Law. As a scholar, an educator, and a national leader, Professor Rosenbaum has dedicated her career to promoting more equitable and effective health care policies in this country, particularly in the areas of Medicaid and Medicare, managed care, employee health benefits, maternal and child health, health services for medically underserved populations, and civil rights in health care systems. Her commitment to strengthening access to care for low-income, minority, and medically underserved populations has had a transforming effect on the lives of many Americans, particularly children. In addition to her responsibilities as chair of the Department of Health Policy, which she founded and developed, Professor Rosenbaum directs the Hirsh Health Law and Policy Program. As a mentor, she is drawn to young people interested in improving health care for the poor. Professor Rosenbaum has been named one of the nation's 500 most influential health policy makers by McGraw Hill. Among other honors, she has received the Investigator Award in Health Policy from the Robert Wood Johnson Foundation and has been recognized by the Department of Health and Human Services for distinguished national service on behalf of Medicaid beneficiaries. As a member of the White House Domestic Policy Council under President Clinton, she directed the drafting of the Health Security Act and oversaw the development of the Vaccines for Children Program. Professor Rosenbaum received her B.A. from Wesleyan University and her J.D. from Boston University School of Law.

Milagritos D. Tapia, M.D., is assistant professor of pediatrics and medicine at the University of Maryland. She is interested in the utility of oral fluid as a proxy for serum measurement of antibody responses. She has found that there is an excellent correlation between the serum and oral fluid measurements of antibodies against measles, meningococcus, and tetanus. She also spends a great deal of her time working at the Center for Vaccine Development field site in Bamako, Mali, in West Africa. There, she has been studying the epidemiology of invasive bacterial infections, the incidence of group A streptococcal pharyngitis, and the prevalence of rheumatic heart disease in the pediatric population. She was coinvestigator on several multicenter vaccine trials including an efficacy trial of rotavirus vaccine in Malian infants and safety and immunogenicity trials of conjugate meningococcal A vaccine in Malian toddlers and adults.