Summary Report for Comments on the National Vaccine Plan

May 2009

Prepared for the Department of Health and Human Services National Vaccine Program Office

by the Oak Ridge Institute for Science and Education

The **Oak Ridge Institute for Science and Education** (ORISE) is a US Department of Energy facility focusing on scientific initiatives to research health risks from occupational hazards, assess environmental cleanup, respond to radiation medical emergencies, support national security and emergency preparedness, and educate the next generation of scientists. ORISE is managed by Oak Ridge Associated Universities.

This document was prepared for The Department of Health and Human Services by the Oak Ridge Institute for Science and Education through an interagency agreement with the US Department of Energy (DOE). ORISE is managed by Oak Ridge Associated Universities under DOE contract number DE-AC05-06OR23100.

The opinions expressed herein do not necessarily reflect the opinions of the sponsoring institutions of Oak Ridge Associated Universities.

This report was prepared as an account of work sponsored by the United States Government. Neither the United States Government nor the US Department of Energy, nor any of their employees, makes any warranty, expressed or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe on privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, mark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement or recommendation, or favor by the US Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the US Government or any agency thereof.

Table of Contents

Executive Summary 1

Introduction 4

1. Comments on Priorities for the National Vaccine Plan: 5

2. Comments on the Goals, Objectives, and Strategies for the National Vaccine Plan: 6

Goal 1 Comments: 6

Goal 2 Comments: 10

Goal 3 Comments: 14

Goal 4 Comments: 18

Goal 5 Comments: 18

3. Comments on the Indicators for the National Vaccine Plan 22

Goal 1 Indicators: 23

Goal 2 Indicators: 24

Goal 3 Indicators: 26

Goal 5 Indicators: 28

4. Comments on Stakeholders' Roles in the National Vaccine Plan 30

Conclusion 31

Executive Summary

The National Vaccine Program Office (NVPO) of the U.S. Department of Health and Human Services (HHS) is coordinating the update of the National Vaccine Plan (NVP), last issued in 1994. The 2008 draft strategic National Vaccine Plan is the initial step in updating the plan and includes goals, high level indicators of measurable outcomes, objectives, and strategies to achieve each goal. The draft plan is primarily the result of deliberation, analysis, and input from multiple Federal agencies under the coordination of the NVPO; additional input on the draft plan is currently being sought from private stakeholders and the general public.

NVPO and other agencies coordinated efforts to receive comments on the draft strategic National Vaccine Plan from private stakeholders and the public through the Federal Register. The four major areas that stakeholders were asked to comment on included:

1. Priorities for the National Vaccine Plan for a ten-year period
2. Goals, objectives, and strategies for the National Vaccine Plan for a ten-year period
3. Indicators for the National Vaccine Plan for a ten-year period
4. Stakeholders' roles in the National Vaccine Plan.

Comments on Priorities for the National Vaccine Plan

Many stakeholders commented on the priorities for the National Vaccine Plan for a ten-year period. Stakeholders suggested that a list of priorities would help but there must be flexibility to the list so that it would incorporate vaccines for specific populations and rapid emerging threats. Comments can be classified as being related to safety, immunization coverage, new vaccine development, supply, and financial and non-financial barriers to access.

Comments on the Goals, Objectives, and Strategies for the National Vaccine Plan

1. General comments were made for Goal 1 from stakeholders that contain the need for more combination vaccines, new and current vaccine development processes, alternative forms of vaccine delivery systems and vaccines for specific groups of people (e.g. immunocompromised). Additional research comments were related to infrastructure, the appropriate benefactor, and vaccine preventable disease targets.

2. Stakeholders agreed that the inclusion of Goal 2 was necessary to assure that the U.S. system continues to meet vaccine safety needs. Stakeholders want the Plan to note that vaccine safety is not entirely focused on development but also the administration of the vaccines. Specific Goal 2 comments were related to Electronic Medical Records (EMR), adverse events, the Vaccine Safety Datalink Project (VSD), and various recommended word and phrasing clarifications.

3. Stakeholders considered communication and education on vaccines and their safety critical elements in Goal 3 of the National Vaccine Plan. Specific comments were related to creating an advisory council for innovation; using non-traditional vaccine providers and specific tactics for information dissemination; the importance of government,

4. Goal 4 summary comments yet to come…

5. Many stakeholders mentioned that Goal 5 was unclear and did not consider it to be within the scope of the U.S. National Vaccine Plan. Some considered the objectives and strategies to be too general. More specific and evidence-based objectives and strategies were recommended. Another commented that the U.S. should focus on internal issues that are under our direct control. For those stakeholders that deemed it relevant to the Plan they did not sense that it was a priority. Specific Goal 5 comments were related to identification of global health stakeholders, addressing global health infrastructure and assuring global standards to vaccine quality.

Comments on the Indicators for the National Vaccine Plan

1. Comments on existing Goal 1 Indicators referred to language clarification or adding a time element. Many stakeholders commented that testing vaccine candidates' clinical trials within the timeframe of six months was not feasible and unrealistic. There were many suggestions regarding the evidence-based list for Indicator 1. Recommendations included creating a Master List of Vaccine Preventable Disease targets and associated development projects and publishing list summaries and analyses. In conjunction with the master list, a suggestion to develop a "threat matrix" to outline all of the vaccine preventable diseases that are threats to our society was mentioned by a stakeholder. When creating this list, stakeholders recommended that the agency that is prioritizing this list must coordinate and align with the agency that is responsible for addressing reimbursement issues. Suggested additions to Goal 1 Indicators were related to funding, affordability and maternal immunizations.

2. Some comments on Goal 2 Indicators were related to clarifying language and changing timeframes. There were comments related to the importance of Indicator 1 and Indicator 4. There was some disagreement with Indicator 2 and use of signal detection for evaluation. It was recommended that Indicator 4 be strategic and transparent. Additions to Goal 2 Indicators were related to use of single dose manufacturer-prefilled delivery systems, assessments of current vaccine administration practices, development of accreditation standards, adverse event reporting, conduct of controlled and randomized studies and prevention of counterfeit products.

3. Comments for current Goal 3 Indicators were related to a need to clearly and consistently state timeframes. Some suggested a five-year timeframe as adequate time to show progress and improvements. One comment for Indicator 3 specified a need for culturally appropriate education materials with varying levels of information. It was also suggested that Goal 3 Indicators focus on the general public's knowledge of vaccine benefits and not have such as heavy emphasis on adverse events and risks. Recommended additions for Goal 3 Indicators were related to measuring new vaccine product information availability and accessibility, older vaccine availability following emergence of new

4. Goal 4 Indicator summary comments yet to come…

5. Stakeholders mentioned that the indicators under Goal 5 did not mirror the objectives. It seemed unclear how the indicators were chosen and how the Plan will lead to successful implementation of the indicators. They suggested, "the indicators be designed collaboratively with global governmental and non-governmental stakeholder input to ensure alignment, enhance output and reduce uncoordinated or duplicative efforts." In addition, stakeholders recommended that indicators 1-3 align with strategies already in place through the global partners and stakeholders (e.g. Millennium Development Goal, The Global Alliance for Vaccines and Immunization (GAVI), United Nations International Children's Emergency Fund (UNICEF)).

   Other comments for current Goal 5 Indicators were related to currently specified timeframes and a need for adjustment due to changed expectation of eradication (wild polio virus) or data measurement capabilities (DTP3 vaccination). Stakeholders recommended a measles elimination goal for Indicator 2. It was suggested the vaccines referenced in Indicator 4 be prioritized according to public health need. In addition, many stakeholders suggested additional diseases be added to Indicator 4 such as Human Papilloma Virus (HPV) and Haemophilus Influenza Type B (Hib). The careful evaluation of the safe injection devices referenced in Indicator 6 was recommended. Additional Goal 5 Indicators were suggested related to gathering information on immunization advisory committees (referenced in Indicator 5), developing accountability models and standards, and assessing vaccinate waste.

Comments on stakeholders' roles in the National Vaccine Plan

Stakeholder's were asked to identify which stakeholders should have responsibility for enacting the objectives and strategies listed in the draft Plan, state their roles in the Plan and add any new objectives and strategies they deemed necessary. Federal along with non-federal stakeholders were mentioned. Many comments reflected their concern about stakeholder's roles and responsibilities and who would monitor and manage these duties.

Conclusion

In general, all stakeholders commented that the draft Plan was a good beginning. Many agreed on the goals and objectives that are currently in the Plan. Stakeholders positively received the concept that the Plan should be "National" vs. "Federal" and ensuring that outcomes are quantifiable. Additionally, many suggested updating the Plan on a regular basis because emerging diseases are constantly changing along with vaccine safety issues. Many revisions were minor and included adding or removing particular words to address issues of interest for particular stakeholders. Numerous new strategies and indicators were added to all of the goals in the Plan. Overall, stakeholders believed that the goals, objectives, and strategies in the Plan must have a timeframe and be inclusive of all populations, situations, and stakeholders that are involved with vaccine development, distribution, administration, and education.

Introduction

The National Vaccine Program Office (NVPO) of the U.S. Department of Health and Human Services (HHS) is coordinating the update of the National Vaccine Plan (NVP), last issued in 1994. The 2008 draft strategic National Vaccine Plan is the initial step in updating the plan and includes goals, high level indicators of measurable outcomes, objectives, and strategies to achieve each goal. The draft plan is primarily the result of deliberation, analysis, and input from multiple Federal agencies under the coordination of the NVPO; additional input on the draft plan is currently being sought from private stakeholders and the general public.

The National Vaccine Plan (NVP) was developed to guide activities in pursuit of the National Vaccine Program mission and goals. The updated National Vaccine Plan is being developed to concentrate on current challenges, to continue progress towards prevention of disease as well as increase safety of vaccines.

Meaningful stakeholder involvement forms a part of the update process. NVPO, with the National Vaccine Advisory Committee (NVAC), is implementing a process to obtain input from a wide range of stakeholders. Several activities are underway to engage expert stakeholders: 1) The Institute of Medicine (IOM) is convening meetings of stakeholders professionally associated with vaccine planning issues (e.g., pharmaceutical companies, health professionals and health insurers); 2) NVAC is staying abreast of developments and will review draft versions of the updated plan; and 3) members of the federal government involved in vaccine-related issues are working with NVAC to identify expert stakeholders and develop mechanisms for gathering their input and roles in the plan.

NVPO and other agencies coordinated efforts to receive comments on the draft strategic National Vaccine Plan from private stakeholders and the general public through the Federal Register. The four major areas focused on included:

1. Priorities for the National Vaccine Plan for a ten-year period
2. Goals, objectives, and strategies for the National Vaccine Plan for a ten-year period
3. Indicators for the National Vaccine Plan for a ten-year period
4. Stakeholders' roles in the National Vaccine Plan.

This report summarizes the email comments received through the Federal Register. NVPO will use comments from NVAC, other federal agencies and the general public for the update of the 1994 National Vaccine Plan.

1. Comments on Priorities for the National Vaccine Plan:

Stakeholders were asked to recommend top priorities for vaccines and the immunization enterprise in the United States and globally. In addition, they were to explain why these priorities were important to them. Many stakeholders commented on the priorities for the National Vaccine Plan for a ten-year period. Comments can be classified as being related to safety, immunization coverage, new vaccine development, supply, and financial and non-financial barriers to access.

- *Safety* - A majority of the comments suggested the importance of safety as a priority for the updated NVP. Safety issues were addressed in regards to research, education, and training for health care providers. One stakeholder suggested a "safety first" program that would support science, ethics, law, legal remedies, medicine, public trust, policy, business practice, and funding priorities.

- *Immunization coverage* - Another major area of priority was improving immunization coverage of adolescents, adults, and the uninsured - both nationally and globally.

- *Development of combination vaccines, alternative delivery forms and new vaccines* - Stakeholders included suggestions on developing combination vaccines, alternative delivery forms of vaccines, and vaccines for those who have sexually transmitted infections, drug resistant infections, infectious disease associated cancers and compromised immune systems.

- *Financial and non-financial barriers* - Many stakeholders commented on financial and non-financial issues and barriers as a priority. Reimbursement for health care providers that provide vaccinations was seen as an overall concern. Stakeholders mentioned that funding vaccinations for adults and adolescents should be a priority in the Plan.

- *Other priorities* - Other priorities included the supply of vaccines, disease surveillance, and oversight and monitoring of manufacturing as well as implementation of goals, objective, and strategies of the Plan.

Stakeholders suggested that a list of priorities would help but there must be flexibility to the list so that it would incorporate vaccines for specific populations and rapid emerging threats. Overall, many recommended having a clear set of priorities for commonality. Also, stakeholders suggested that having a budget strategy when setting these priorities could assist in determining their order. As of now, the Plan does not include a clear distinction or list of priorities set for stakeholders and public to address. It is suggested that NVAC and the IOM develop a set of priorities to include in the updated Plan. Many agreed with the priorities mentioned in the Plan but questioned how attainable they were and who currently has the resources to coordinate and implement each activity.

(Please see comments and disposition table for all comments on the updated NVP)

2. Comments on the Goals, Objectives, and Strategies for the National Vaccine Plan:

The updated National Vaccine Plan contains five 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

The NVPO asked stakeholders to comment on the goals, objectives, and strategies in the draft Plan and suggest additions and concerns. In addition, they were to suggest if any of the goals, objectives, or strategies should be discarded or revised and, if so, why.

Goal 1 Comments:

General comments were made for Goal 1 from stakeholders that contain the need for more combination vaccines, new and current vaccine development processes, alternative forms of vaccine delivery systems and vaccines for specific groups of people (e.g. immunocompromised). Additional research comments were related to infrastructure, funding, the appropriate benefactor, and vaccine preventable disease targets.

- *General research and innovation* - Stakeholders stated that Goal 1 was very technical and suggested that there is a "need for additional research to study the current efficacy of existing vaccines and to improve the clinical data." Comments were made addressing immunology and vaccine development. One stakeholder felt "many vaccines have not been in use long enough to evaluate development of life-long immunity." In addition, the recommendation of innovation was suggested numerous times among stakeholders' comments.

- *Research infrastructure* - One stakeholder suggested "the need to address the mismatch of public health priorities and lack of commercial viability for designing and developing new vaccines." There is a need to develop better research structures. For example, there is a need to develop research teams instead of having individual researchers." As far as development and research of vaccines are concerned, an individual recommended, "public and private markets maintain a balance in order for companies to delve into new areas of vaccine research and development."

- *Funding* - Another factor stakeholders commented on was funding. Assuring adequate funding for the Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) and basic research would assist with achieving Goal 1. Many commented that funding was not addressed in the Plan and is a significant issue that will determine many activities and strategy implementation.

- *Research Benefactor* - Some recommended addressing the issue of societal versus individual benefits in the updated Plan. Comments suggested the U.S. recognize that vaccines are not one size fit all and not everyone is at equal risk for every disease.

- *Additional stakeholder for prioritizing the needs for new vaccines* - Comments on additional stakeholders that could assist with prioritizing the needs of new vaccines were mentioned. These included the National Institute for Occupational Safety and Health (NIOSH), private philanthropies, non-profits, and academic pharmacy.

- *Goal Reordering* - A few stakeholders suggested reordering the goals to increase the knowledge of the public and healthcare providers. The suggested order consists of the following: 1) Support informed vaccine decision-making by the public, providers, and policy-makers 2) Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability and death in the United States 3) Enhance the safety of vaccines and vaccination practices 4) Develop new and improved vaccines, 5) Increase global prevention of death and disease through safe and effective vaccination. One stakeholder also recommended moving Goal 4 to Goal 1 because "by tackling the underutilization of existing vaccines, we can better ensure that the effort expended in developing new vaccines is maximized."

- *Vaccine Preventable Disease Targets for Research* - Stakeholders also recommended the Food and Drug Administration and the Centers for Disease Control and Prevention (CDC) synchronize their post-licensure safety assessments.

Goal 1 Objective and Strategy Comments: ***(All comments below are verbatim from stakeholders)***

Objective 1.1: Prioritize the needs for developing new vaccines.

Suggested priorities:

- Need broad consensus and support
- Support NVPO commission appropriate body (e.g. IOM) to include all stakeholders
- Cornerstone of the goal
- Linkage to benefits of development of priority vaccines (e.g. addressing barriers such as regulatory approval, streamline ACIP recommendations, reimbursement)

Strategy 1.1.1

- Is there any indication of how a consensus will be reached/tiered with such a large group of stakeholders?
- Further articulate how NVPO will coordinate with key stakeholders in the development of certain objectives where considerable pre-existing stakeholder activity exists.
- In strategy 1.1.1, a qualification should be added as it relates to a prioritization that "considers the leading causes of morbidity and mortality from infectious diseases..This qualification should note that not only current causes, but future potential causes of morbidity and mortality should be considered in ongoing disease prioritization.

Strategy 1.1.2

- Biodefense specific diseases referenced in 1.2, but not here – should be for consistency. Surveillance for diseases for which there is no vaccine only, or also for diseases with a vaccine that can be improved/modified based on disease pattern changes?

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

- Wording needs to be revised throughout Objective 2 because certain words or phrases could have negative connotations or be misinterpreted. For example, one participant suggested that "optimize" be used instead of "enhance". One facilitator suggested that the NVP could spell out certain terminology in the IP (e.g. what does "improve" mean) to further clarify the intention.
- Need to address the gap in research to study the efficacy of current vaccines and to improve the clinical data.
- This needs to be clearer with regard to which development is done for diseases without a current vaccine and diseases that need a newer/better vaccine.
- Need to address ACIP recommendations. ACIP recommendations are a critical component in the decision making process for manufacturers.

Strategy 1.2.1

- It is essential to understand that significant differences may exist between vaccines used for the same indication from different manufacturers (e.g. acellular pertussis vaccines produced by different manufacturers may differ even in the number of component antigens).
- Vaccine Burden: As we expand the number of vaccines required the burden on the consumer is significant and it is becoming increasingly difficult to convince families to justify the number of 'needles' we are ordering for routine infant/toddler vaccine series. The continued development of combination vaccines makes the number of vaccines delivered more palatable.

Strategy 1.2.3

- If these are in priority order, this should move up, since this research should be done before the research in 1.2.2

Strategy 1.2.4

- This is prioritization and should be in 1.1.1, not part of 1.2. Delivery is specifically addressed in 1.3.1, should be taken out of here.
- **(Revised):** Develop a process that identifies current vaccines and vaccine delivery systems 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.
- Add "vaccine packaging and presentation"

- Disagreement about the inclusion of safety as an improved performance character. This language implies that FDA approved vaccines are not safe.

Strategy 1.3.1

- **(Revised):** Develop and evaluate *new and improved* alternate delivery methods to *enhance* the protective immune response, safety, effectiveness, and/or efficiency (e.g. *increased* number of doses *from available antigen mass, rapidity of administration) of vaccination.*
- Delivery systems other than injection (Ex: Nasal).

Strategy 1.3.2

- **(Revised):** Expand knowledge of the mechanisms by which induction of protective immunity can be stimulated by *vaccination into or onto the skin or* mucosal surfaces and other *target tissues for* administration. Include studies to identify and mitigate host factors that may have an impact on the effectiveness of *vaccination* by these routes.
- Does this include genetic classification? If so, that should be specifically addressed, so people are aware that it will be done.

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

- Reorder strategies in a more logical sense and aligned with regulatory timeline.
- Clarify language- e.g., having a process for manufacturing clinical grade material i.e., contract manufacturing.
- The relevant DOD organization for this is the Chemical-Biological Medical Systems Office- a component of the Joint Program Executive Office for Chemical and Biological Defense. The Defense Threat Reduction Agency (DTRA) does not have authority for advanced development and licensure issues.

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

- This section needs clarity. There needs to be a distinction between innate and adaptive immune responses. There also needs to be a consensus amongst the various agencies on how they define items such as adjuvants.

Strategy 1.5.1

- HHS should consider broadening this expansion of research to study genetic variances in immunological response based on ethnicity and race.

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

- Link this section to safety as a whole and clarify that pre-licensure safety should also inform post-licensure safety (i.e., hand off of safety information)

- The four strategies presented here seem to start to address indicator #4, in terms of rapid clinical testing of a vaccine, but don't' fully address the idea of timeliness. It does not sync well with the listed indicators.

The following objective **additions** were recommended:

- The objective of developing a process to identify vaccines benefiting from improved performance characteristics would be useful for industry to determine whether or not to invest in such programs.
- Address the regulatory barriers of adjuvant containing vaccines.
- An objective about assessing individual immunological characteristics and tailoring vaccines to match them.

The following strategy **additions** were recommended:

- **Strategy 1.2.5 (new):** Support the use of single-dose manufacturer-prefilled delivery systems for current and new vaccine candidates in order to enhance vaccine performance (effectiveness, safety, number of doses, and/or delivery characteristics) and conduct and support studies to bring them to licensure.
- **Strategy 1.3.3 (new):** Suggests adding a strategy to support increased funding for novel vaccine delivery methods.
- **Strategy 1.4.9 (new):** The US Government should provide additional resources to the FDA to permit more frequent communication (e.g., early feedback, consultation during review) and more transparent review (e.g., more consultation and consistent expectations during review) with vaccine sponsors.
- **Strategy 1.6.6 (new):** Identify current and future vaccine trials where the route of administration and the single dose manufacturer-prefilled delivery system should be considered in the early phase trial design. *Rationale: It is critical to incorporate single dose manufacturer-prefilled delivery systems earlier in the vaccine development process in order to create opportunities for increased success – reducing the need to address delivery integration issues later and capitalizing on the potential enhancement alternate delivery systems may contribute to a given vaccine candidate.*
- **Strategy (new):** There should be something on cost effectiveness and cost utilization types of studies.
- **Strategy (new):** A strategy should be included that promotes the establishment of clear regulatory guidance on the use of novel adjuvants in vaccines. Newer adjuvants represent an important advance in vaccinology; however, a lack of clear regulatory guidance on their acceptability for various populations and situations will constrain additional innovation utilizing these tools.

(Please see comments and disposition table for all comments on the updated NVP.)

Goal 2 Comments:

Stakeholders agreed that the inclusion of Goal 2 was necessary to assure that the U.S. system continues to meet vaccine safety needs. Although some cautioned that this might lead to the misperception that current vaccines are not safe, overall, they deemed it essential to the Plan. Stakeholders want the Plan to note that vaccine safety is not entirely focused on development but

also the administration of the vaccines. Specific Goal 2 comments were related to Electronic Medical Records (EMR), adverse events, the Vaccine Safety Datalink Project (VSD), and various recommended word and phrasing clarifications.

- *Electronic Medical Records* - Stakeholders also recommended the U.S. government support EMR standards to enhance the ability to conduct safety studies and accurate vaccination records.

- *Adverse events* - It is essential to stakeholders that adverse events are addressed in a timely manner in order to maintain the public trust in vaccines and immunization.

- *Vaccine Safety Datalink Project* - Stakeholders found Goal 2 lacked information about VSD. They believe that it is a critical tool for early detection of vaccine safety concerns and should be included in the Plan.

- *Word and phrasing clarifications* - One stakeholder suggested that the title of Goal 2 is misleading because "the safety profile of a given vaccine is an inherent characteristic that cannot be enhanced." Another preferred the language of Goal 2 from the 1994 Plan stating, "Ensure the safety and effectiveness of vaccines and immunization." Furthermore, stakeholders commented that the Plan should contain a clearer definition of benefits and risks of vaccines as well as better communication about "safety signals." They charge the NVAC to clarify that safety signals represent a need for further information rather than proof of causation in the Plan.

Goal 2 Objective and Strategy Comments: ***(All comments below are verbatim from stakeholders)***

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

- This will be accomplished through holding the producers accountable for their product. Until that is done, this goal will not be met.
- The four strategies in this section address vaccine safety from a product quality standpoint, and not the basic risks associated with vaccines – this difference between both types of vaccine safety should be spelled out more clearly.

Strategy 2.2.1

- **(Revised):** Improve the effectiveness and timeliness of AEFI signal identification and assessment through coordinated use of national passive and active surveillance systems, *including IIS.*

Strategy 2.2.3

- Providing active surveillance to healthcare providers could facilitate Strategy 2.2.3, to assess lay public and professional questions and concerns about vaccine safety. In addition, we suggest expanding the term "lay public" to include community vaccine groups, particularly those who oppose vaccination.

Strategy 2.2.4

- Suggest move to objective. A consistent framework for signal management that is based on risk benefit evaluation would ensure the appropriate signals are expediently evaluated without prematurely driving a vaccine off the market. It would also improve consumer confidence in the process of AEFI evaluation.

Strategy 2.3.1

- **(Revised):** "Increase the size of the VSD population to facilitate timely and rigorously conducted epidemiological studies of vaccine adverse events."
- Increase the size of VSD or develop a new active surveillance system?

Strategy 2.3.3

- **(Revised):** Enhance capacity to monitor immunization safety in the event of a mass vaccination *campaign by quickly aggregating the data in a state, local or regional IIS.*

Strategy 2.4.1

- **(Revised):** As appropriate, develop algorithms and assess the evidence on an individual level for a causal relationship between certain **vaccine delivery systems**, vaccines and specific AEFI. *Rationale: Recent studies have shown that vaccine delivery systems have an impact on vaccine administration, including risk of error.5 Inserting "vaccine delivery systems" in this strategy broadens the scope of the evaluation to include this known contributing factor.*

Objective 2.7: Improve cross-cutting scientific capabilities to enhance vaccine safety and the vaccination safety system

- New systems, such as electronic health records, may allow for better data transmission and integration

Objective 2.8: Enhance integration and collaboration of vaccine safety activities.

- **(Revise):** Objective 2.8 is important, but vague. We recommend rewording this to emphasize the importance of federal collaboration as follows: "Enhance timely and collaborative efforts among the federal agencies involved in vaccine safety."
- Include additional partners and stakeholders: design engineers, academia, sociologists, risk communication, medical technology industry and others that are involved in the vaccine delivery system.

The following objective **additions** were recommended:

- One objective might be to overcome potential coding biases related to healthcare provider behavior (e.g., when reimbursement rates may influence code selection)
  .

The following strategy **additions** were recommended:

- **Strategy 2.1.5 (new):** Develop a process by which single dose manufacturer-prefilled delivery systems are incorporated into the vaccine development process to ensure compatibility, optimal product quality, and patient safety. *Rationale: Creating a standard process for integrating single dose manufacturer-prefilled delivery systems earlier in the vaccine development process allows for optimal matching of candidates to delivery system and leveraging of its associated advantage profile.*
- **Strategy 2.2.5 (new):** Increase support for the VSD project to rapidly detect and confirm signals for vaccine adverse events.
- **Strategy 2.6.4 (new):** Expand the use of single dose manufacturer-prefilled delivery systems to enhance AEFI reporting measures through vaccine traceability and reduce AEFIs related to the preparation of the vaccine for administration and the administration process.
- **Strategy 2.6.5 (new):** Assess current vaccine administration practices and associated errors in order to identify opportunities for improvement. *Rationale: Recent studies have shown substantial errors directly associated with the administration of vaccines. Vaccine delivery systems have an impact on vaccine administration, including risk of error.5 For this reason, the NVP should include more specific strategies that acknowledge "vaccine delivery system" as a potential contributing factor to the incidence of AEFI. Moreover, single dose manufacturer-prefilled delivery systems present opportunities for improving the traceability of vaccines and vaccinations, providing a clear mechanism for tracking quality improvement in vaccine administration.*
- **Strategy 2.7.3 (new):** Identify and support research that examines single dose manufacturer-prefilled delivery systems as a means of engineering safety into vaccine administration across all settings. *Rationale: Studies have shown that by nature of their design, single dose manufacturer-prefilled delivery systems may mitigate considerable error potential by eliminating several of the steps associated with conventional syringe and vial administration.*
- **Strategy 2.8.3 (new):** Assure there is independent and timely review of vaccine safety concerns to determine whether selected temporally related adverse events are causally related, and, if so, to determine risk factors for such events, and formulate a vaccine safety research agenda.
- **Strategy 2.8.4 (new):** Review the approaches used to provide independent oversight of safety issues associated with other federally-sponsored programs including transportation, blood products, and environmental concerns to identify opportunities to enhance public confidence in the vaccine safety system.
- **Strategy (new):** Establish an independent group of experts to review major vaccine safety concerns including evaluation of the evidence that a vaccine or vaccines were causing particular adverse events and recommendations for future actions including further research.

(Please see comments and disposition table for all comments on the updated NVP.)

Goal 3 Comments:

Stakeholders considered communication and education on vaccines and their safety critical elements in Goal 3 of the National Vaccine Plan. Specific comments were related to creating an advisory council for innovation; using non-traditional vaccine providers and specific tactics for information dissemination; the importance of government, healthcare and public health professional education; informed-decision-making; cultural competence; alignment of objectives with *Healthy People 2010;* and addressing public trust and confidence.

- *Advisory Council for Innovation* - One suggestion from a stakeholder included developing an "Immunization Innovation Council" comprised of scientists, laypersons, and engineers to provide important advice and council to all.

- *Role of Non-traditional Vaccine Providers* - When commenting on Goal 3, stakeholders believed that non-traditional vaccine providers needed to be recognized for their role in immunization rates. One also suggested the modification of Goal 3 to include "payors" in the list of stakeholders.

- *Information Dissemination* - Disseminating the information about vaccines in a timely manner was also a main suggestion by stakeholders. An important resource that stakeholders considered a great communication tool was the Vaccine Adverse Event Reporting System (VAERS). It was mentioned that if VAERS were capable of communicating vaccine-related issues to health professionals, it would assist in information being disseminated in a timely fashion. One stakeholder stated, "using the NPI number registry [perhaps mandatory email accounts] for health professional safety service announcements," as a suggestion. In addition, stakeholders mentioned the Plan did not identify how dissemination of vaccine information would be implemented among hard to reach populations.

- *Government, Public Health and Healthcare Professional Education* - Stakeholders also indentified healthcare workers as an area to increase education and immunization. They referred to providers' lack of education and information about vaccines. They suggested that healthcare workers be immunized and that there be some type of monitoring of assessment for this requirement. A number of stakeholders stated that issues related to public health and governmental authorities' disconnection from patients and delivery of vaccines and politicians ignorance of public health needs were not acknowledged within the Plan and must be addressed. Stakeholders consider these issues to impact the Plan and believe they should be included.

- *Informed Decision-Making* - One omission that a stakeholder believed was not addressed in Goal 3 was the principle of informed decision-making by patients or parents. They commented, "Sections of our public input provide recommendations for additional components of informed decision-making, which should be included in the final NVP."

- *Vaccine Misinformation* - Another topic that stakeholders recommended addressing in the Plan was the misinformation about vaccines and anti-vaccine groups.

- *Alignment with Healthy People 2010* - Stakeholders recommended that Goal 3 indicators align with the Health People 2020 objectives that have a target percentage increased based on a best practice to strengthen their outcome.

- *Culturally Competence* - For the education and communication of the Plan to be successful, stakeholders suggested that all materials be culturally competent for varied populations. Some stakeholders mentioned the lack of specific strategies that address at-risk populations.

- *Public Trust and Confidence* - Stakeholders also commented that having specific objectives to increase public trust and confidence would help strengthen the Plan.

Goal 3 Objective and Strategy Comments: ***(All comments below are verbatim from stakeholders)***

Strategy 3.1.3

- Implies that no educational strategies exist or they are ineffective. We recommend the following wording: "Identify and review current educational strategies and, when appropriate, develop and test new interventions that would enable public audiences and policy makers to read, understand and use information about vaccine benefits and risks when making immunization decisions."

Strategy 3.1.5

- Does this reference only under immunization due to vaccine refusal, or also financial barriers? These need to be differentiated.

Strategy 3.1.6

- Add "**availability**". Accessibility to health facilities does not equate with availability of product and vaccination services. "**Acceptability**" could be added, as well, as services may be available but not utilized.

Strategy 3.1.7

- Only discusses collecting information on the direct and indirect costs of vaccination. Why not benefits and costs averted?

Strategy 3.2.3

- Health literacy at all levels is not sufficiently explained. The AAP recommends more specific details because health literacy is such an important issue to ensure the proper delivery of vaccines to all populations.

Strategy 3.4.2

- Currently, web-based information is only available in English. In order to reach as many audience groups as possible and to make dissemination of information as convenient as

Strategy 3.4.3

- In recent years ECBT has achieved much success in reaching our target population using social networking technologies and will be investigating the use of mobile technologies. We urge others to investigate this means of communicating with today's generation of parents as well.

Strategy 3.5.2

- **(Revised):** Develop, disseminate, and evaluate broad-based education of key groups…on the benefits, risks, and economics of vaccines, the basis of immunization recommendations, vaccine policy development, and on the standards of immunization practice **and administration**. *Rationale: The addition of the word administration" is appropriate given that "practice" suggests decision-making standards to determine whom and when, while "administration" suggests how.*

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.

- Consider adding communication skills to this objective. Further, it may be useful to cross-reference the HHS Office of Minority Health's national standards for culturally and linguistically appropriate services in health care.

Strategy 3.6.1

- Expand and implement training and education of immunization providers at all levels of their education on the proper use **and administration of vaccines**, the proper storage, and handling of vaccines… *Rationale: The addition of the word "administration" is appropriate given that "practice" suggests decision-making standards to determine whom and when, while "administration" suggests how. Well-documented errors in administration5 suggest this is a critical area for focusing retraining efforts and an opportunity to utilize vaccine delivery systems that greatly reduce or eliminate the risk of error.*
- In collaboration with the major medical associations, CDC should establish on-line training modules for physicians and office staff (nurses) on a wide variety of vaccine related topics (vaccine safety, vaccine delivery, vaccine management, assessment techniques, surveillance, etc. As an incentive, award CMEs and CEUs for successful completion.
- **(Revised):** 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, on the standards of immunization practice, *and the use of IIS as a decision-support tool.*

Strategy 3.6.2

- **(Revised):** Develop and implement educational strategies for providers on vaccine-preventable diseases, including diagnosis, modes of transmission, prevention and control, reporting requirements, *and the use of IIS as a decision-support tool.*

Strategy 3.7.3

- Should reference the Vaccine Information Sheet (VIS) and indicate the need for research on obstacles and contributing factors to VIS utilization as well as the impact of the VIS on vaccine administration.
- **(Revised):** Develop evidence-based tools *and use IIS to assis*t individuals, parents, and providers in synthesizing relevant vaccine-related information to make informed decisions regarding vaccination.

The following objective **additions** were recommended:

- To develop an effective response to manage the influence of the anti-vaccination lobby by improving knowledge of the attitudes, methodology, the reach and impact of this group.
- Given the success of the United Kingdom in assessing public attitudes and perceptions about immunizations, shouldn't there be an objective about developing a comparable system in the United States?

The following strategy **additions** were recommended:

- A strategy to refute vaccine disinformation and respond to anti-vaccine strategies that have the potential to compromise the public health.
- The rationale for requiring vaccinations should be a stated strategy.
- **Strategy 3.1.8 (new):** add a strategy for studying factors obstructing utilization of programs even among those accepting of vaccine science and develop initiatives that will communicate with the public about existing immunization programs and the eligibility requirements of those programs. Increased knowledge about existing federal and state programs may serve as a positive influence on decision-making about vaccines and may increase rates of program utilization.
- **Strategy 3.1.8 (new) 2:** Enhance efforts to understand why individuals decline vaccines. Use information to enhance objectives in future communications efforts.
- **Strategy 3.1.9 (new):** add a strategy to conduct research into how to promote a sense of community contribution among individuals, e.g. the public health aspect of immunization, as another positive influence on decision-making about vaccines.
- **Strategy 3.3.4 (new):** Elicit private and public sector collaboration to facilitate the dissemination of research findings and general information regarding vaccine safety (e.g. formulation and delivery) and effectiveness. *Rationale: Private manufacturers and other entities invest significantly in the research and development of their vaccines and vaccine delivery systems. They stand ready to act in partnership with government to improve vaccine delivery and supply. Private and public collaboration allows for effective*

- **Strategy 3.3.4 (new) 2:** Enhance communication of value and benefit of vaccines; demonstrate the medical benefit provided by vaccines.
- **Strategy 3.3.4 (new) 3: P**roactively encouraging responsible journalism and providing guidance to journalists regarding reliable and unreliable sources of vaccine information.
- **Strategy 3.3.5 (new):** Enhance communication on vaccine development.
- **Strategy 3.4.6 (new):** Educate to improve knowledge of vaccines and vaccine-preventable diseases and understanding of basis for immunization recommendations.
- **Strategy 3.5.4 (new):** A strategy should be added to this objective to inform policy-makers about the economics of vaccine manufacture, on the need to recapitalize manufacturing equipment for existing vaccines from time to time to meet evolving stringent expectations of regulators. An analogy can be found in the utility industry that periodically needs to replace capital equipment.
- **Strategy 3.6.5 (new):** Educate to improve knowledge of vaccines and vaccine-preventable diseases, understanding of basis for immunization recommendations, and immunization practices of all health care providers.
- **Strategy 3.7.4 (new):** Add an indicator/strategy to address disparities and barriers related to accessing vaccines. This goal does not seem to address any barriers to immunizations such as cost, location, culture. Identifying the barriers will be useful in the other strategies that address the development of educational strategies related to increasing immunization.
- **Strategy (new):** I think making Important Information Forms shorter, more readable and less intimidating could be an important strategy.
- **Strategy (new):** Consider including a strategy to enhance access to information and education among minority, low-income populations at risk for under-immunization.

(Please see comments and disposition table for all comments on the updated NVP)

Goal 4 Comments:

Ray to contribute

(Please see comments and disposition table for all comments on the updated NVP)

Goal 5 Comments:

Many stakeholders mentioned that Goal 5 was unclear and did not consider it to be within the scope of the U.S. National Vaccine Plan. Some considered the objectives and strategies to be too general. More specific and evidence-based objectives and strategies were recommended. Another commented that the U.S. should focus on internal issues that are under our direct control. For those stakeholders that deemed it relevant to the Plan they did not sense that it was a priority. Specific Goal 5 comments were related to identification of global health stakeholders, addressing global health infrastructure and assuring global standards to vaccine quality.

- *Global health stakeholders and infrastructure* - Some stakeholders believed the Plan should incorporate the recognition the U.S. commitment to global health and the

- *Quality* - Several stakeholders wanted to ensure that the NVAC would not rely on a single solution approach to global standards and norms to assure vaccine quality. They fear that this would raise barriers to the licensure and production of vaccines particularly if (European Medicines Agency (EMEA) and CBER guidelines form the basis of these standards and norms.

Goal 5 Objective and Strategy Comments: ***(All comments below are verbatim from stakeholders)***

Objective 5.1: Improve global surveillance for VPDs and strengthen health information systems to monitor vaccine coverage, effectiveness, and safety.

- Recommend that vaccine industry be included in the implementation phase of this objective

Strategy 5.1.6

- **(Revised):** "Improve the measurement of immunization coverage to assure it accurately reflects population immunity levels induced by vaccination and improve the use of such information at district and local levels."

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.

- Add "safely, effectively, **efficiently and equitably"**
- Suggest specific strategies that address, injection safety, cold chain and logistics issues.

Strategy 5.2.1

- Vaccine distribution" doesn't quite do justice to "vaccine forecasting, ordering, storage, and distribution"

Strategy 5.2.2

- Add "..safe injection and Disposal.."
- **(Revised):** 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, **safety boxes. and final waste treatment systems.**

Objective 5.3: Support introduction and availability of new and under-utilized vaccines to prevent diseases of public health importance.

- Availability" is only part of the challenge. Add "availability and **use**."
- **(Revised):** Support introduction and availability of new and under-utilized vaccines *and delivery technologies* to prevent diseases of public health importance.

Strategy 5.3.1

- It is likely that some vaccines will be tailor made either for specific regions or countries and will be clinically tested and licensed directly in developing country settings (eg clade specific HIV vaccine, conjugate pneumococcal vaccines with regional compositions). Such vaccines may be produced either by the major pharmaceutical manufacturers or, increasingly, by developing country vaccine manufacturers. Vaccines from either source may not be subject to clinical evaluation nor licensing in a developed country.
- **(Revised):** Collaborate with global organizations and partners to accelerate the clinical testing and licensure, where appropriate, in developing countries of vaccines *and delivery methods* already licensed in developed countries.

Strategy 5.3.2

- **(Revised):** Strengthen country capacity to make informed decisions on introduction of new vaccines *and safer and improved delivery technologies* based on evaluation of epidemiology, financial sustainability, safety, and programmatic considerations.

Strategy 5.3.3

- **(Revised):** Support the integration of new and under-utilized vaccines into each GAVI-eligible country's multi-year national plan of action and provide training and logistical support necessary to successfully incorporate new vaccines *and delivery methods* into routine programs.

- **(Revised):** Support the integration of new and under-utilized vaccine into each GA VI-eligible country's multi-year national plan of action and provide training and logistical support necessary to successfully incorporate **safe delivery of** new vaccines into routine programs.

Strategy 5.3.4

- This should be with the global safety strategies such as those in 5.1.7
- **(Revised):** Conduct post-licensure evaluations of the impact of new vaccines *and delivery techniques* on immunization programs, disease patterns, and the occurrence of AEFI.

The following objective **additions** were recommended:

- Suggest an objective to support the challenges of low-middle income countries be added.

- An objective should be added to develop a process to more accurately estimate vaccine demand for different country markets, as this is directly linked to a goal of assurance of adequate and sustainable vaccine supply.

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.

- While economic studies are important tools to support decision-makers, the assessment of the value of vaccination programs must include more than economic studies. This is not articulated in the strategies supporting this objective.

<u>Strategy 5.5.4</u>

- **(Revised):** here you could add "effective vaccines PRESENTED AND PACKAGED FOR SMOOTH INTRODUCTION INTO EXSTING VACCINATION PROGRAMS…"
- Insert ", in accordance with current Good Manufacturing Practices" at end of sentence (to mimic Strategy 5.5.2).
- **(Revised):** Provide technical assistance to developing country vaccine manufacturers to support development and production of safe and effective vaccines and related **safe injection and waste management** technologies.

<u>Strategy 5.6.5</u>

- **(Revised):** Work with global partners to secure and maintain adequate stockpiles/strategic reserves of vaccines **and vaccine delivery systems** to maintain uninterrupted supply, for emergency response to outbreaks, and for special purposes. *Rationale: To have an adequate supply of vaccines without an accompanying adequate supply of the required delivery system will lead to an insufficient response capacity. The addition of "vaccine delivery systems" to this strategy demonstrates the Nation's understanding that vaccines and vaccine delivery systems are two separate components of the NVP. Moreover, the need to add "vaccine delivery systems" in the context of stockpiling for pandemics or bioterror events is even more critical due to the ability of novel delivery systems – such as single dose manufacturer-prefilled delivery systems – to minimize waste, save time, increase cost efficiency, optimize efficacy and reduce risks inherent in nonintegrated delivery systems.*
- **(Revised):** Build and strengthen bilateral and multilateral partnerships and other collaborative efforts to support availability, access, sustainable financing, and use of current, underutilized, and new vaccines **and their delivery systems.**

<u>Strategy 5.6.5</u>

- One could argue that Activity 5.6.7 (develop a global advocacy agenda) could be an explicit objective, since many of the activities that would emerge from the agenda – resource mobilization, political will, public awareness – will be critical to the success of the other Goal 5 objectives and activities. Assuming that the global agenda will remain an activity rather than a full objective, you may make the point that this component is a

The following strategy **additions** were recommended:

- **Strategy 5.2.5 (new):** Reduce access barriers to vaccination and enable wider distribution of vaccines to countries by simplifying training for administration through providing ready-to-use delivery systems, removing steps to assemble, and assuring dose accuracy. *Rationale: Manufacturer-prefilled delivery systems, in easy-to-use self-storage units, simplify administration and, as is the case with prefilled syringes, minimize waste, reduce the risk of error and save time – all critical considerations, especially in formerly underserved populations*.
- **Strategy 5.3.5 (new):** Support the introduction of the new meningococcal A conjugate vaccine in African meningitis belt countries. (important for USAID and CDC support).
- **Strategy 5.3.5 (new) 2:** Evaluate standard metrics that may be used in assessing whether new and improved vaccines represent a cost-effective investment." One might look at cost per disability-adjusted life year (DALY) averted as a potential standard, or years of potential life lost, or other measures.
- **Strategy 5.3.5 (new) 3:** Collaborate with global organizations and partners and vaccine producers early in the design and manufacturing processes, so that vaccines will be presented and packaged for smooth introduction into low- and middle-income country immunization programs.
- **Strategy 5.3.5 (new) 4:** Evaluate standard metrics to be used in assessing whether new and improved vaccines represent a cost-effective investment.
- **Strategy 5.3.5 (new) 5:** Support the introduction of the new meningococcal A conjugate vaccine in African meningitis belt countries. (Important for USAID and CDC support).
- **Strategy 5.3.6 (new):** Collect critical data on health burden, expected impact of vaccines on that burden, and relevant costs in enough countries to assure globally-derived estimates are accurate and assist individual country decision makers in making evidence-based policy decisions."
- **Strategy 5.5.5 (new):** Suggest a new strategy to expand regional registration capabilities to support countries that do not have country specific registration resources.
- **Strategy (new):** Continued support of HIV vaccine development should be an explicit strategy, and one which also applies to Goal 5, given the long time horizon of this plan.

(Please see comments and disposition table for all comments on the updated NVP.)

3. Comments on the Indicators for the National Vaccine Plan

The NVPO asked stakeholders to comment on the existing indicators, suggest target estimates, and add new indicators for the National Vaccine Plan. In addition, stakeholders were asked to comment on indicators that do not address their concerns.

Goal 1 Indicators:

Comments on existing Goal 1 Indicators referred to language clarification or adding a time element. Many stakeholders commented that testing vaccine candidates' clinical trials within the timeframe of six months was not feasible and unrealistic. There were many suggestions regarding the evidence-based list for Indicator 1. Recommendations included creating a Master List of Vaccine Preventable Disease targets and associated development projects and publishing list summaries and analyses. In conjunction with the master list, a suggestion to develop a "threat matrix" to outline all of the vaccine preventable diseases that are threats to our society was mentioned by a stakeholder. When creating this list, stakeholders recommended that the agency that is prioritizing this list must coordinate and align with the agency that is responsible for addressing reimbursement issues. Suggested additions to Goal 1 Indicators were related to funding, affordability and maternal immunizations.

Indicator #1

- Need clarification on how this indicator will be executed. The short and long-term ramifications need to carefully analyzed by all stakeholders before publishing this type of list. The list must be flexible and transparent.

Indicator #2

- This indicator sends the wrong message. It sends the message that these are aspiration priorities.
- A time element should be added.
- It was suggested to delete Indicator 2.
- Identify **4** candidate vaccines from those targets identified in the 1 year process above.
- As you can imagine, identifying X candidates and advance Y priority vaccines, will be quite difficult.

Indicator 3

- The meaning of "delivery strategies" should be clarified with examples.
- Advance X new delivery strategies *and methods* that will improve effectiveness, feasibility, acceptability, safety, or ease of administration of new or improved vaccines into clinical trials.
- Advance the same **4** along the R&D and advanced clinical trials pathways.

Indicator #4

- Add ….to test potential vaccine candidates and *delivery strategies*…
- Clarify what event the 6-month interval is based on.
- Advance **4** delivery strategies to improve effectiveness, etc. of new or improved vaccines.
- Do you really think we will have candidates to be tested within 6 months of identification of the need for a vaccine – perhaps for influenza when we are using a technology we have, only changing the antigen slightly. I may be out of touch but to have a vaccine for human clinical trials within 6 months of identification of the pathogen and need for a vaccine does not seem realistic.

The following indicator **additions for Goal 1** were recommended:

- Addition of an indicator to support increase in basic funding.
- An indicator should be added (under one of the goals of this plan) to ensure that the development of vaccines which may have the effect of benefiting unborn children is not discouraged (e.g., by including those claiming injury due to exposure in utero as covered claimants under the National Childhood Vaccine Injury Act, which would also have the effect of allowing such individuals to seek compensation under the VICP).
- Within X year(s), develop appropriate incentives to improve the affordability and cost-effectiveness of vaccines.
- Participants felt strongly about maternal immunizations and felt there should be an indicator addressing (e.g., hold workshop to discuss barriers to developing these vaccines).

Goal 2 Indicators:

Some comments on Goal 2 Indicators were related to clarifying language and changing timeframes. There were comments related to the importance of Indicator 1 and Indicator 4. There was some disagreement with Indicator 2 and use of signal detection for evaluation. It was recommended that Indicator 4 be strategic and transparent. Additions to Goal 2 Indicators were related to use of single dose manufacturer-prefilled delivery systems, assessments of current vaccine administration practices, development of accreditation standards, adverse event reporting, conduct of controlled and randomized studies and prevention of counterfeit products.

Indicator #1

- Dissemination is very important
- The first indicator, first sub-bullet suggests that safety assessments be conducted and disseminated within one year after vaccine recommendations are published in CDC's *Morbidity and Mortality Weekly Report*. VSD rapid cycle studies are critically important to assess causal relationships regarding vaccine safety. However, these studies generally take about two years to have sufficient power to detect reasonably elevated relative risks. Therefore, we recommend this time window be extended from one year to two years.
- Indicator needs to be targeted, consider performing assessments at several stages.
- Will this be a general indicator, or will vaccine-specific values be given, since different recommendations may lead to widely different timeframes for a fixed number of doses.

Indicator #2

- Signal detection does not equal evaluation
- This indicator should focus on the International Conference on Harmonization (ICH) end-to-end (E2E) risk management plan (RMP) for each vaccine (which addresses known risks, potential risks, unknown risks).
- Should also include specific dissemination programs for any research conducted of AEFI signs in healthcare workers and other at risk worker populations that are being encouraged to be vaccinated.

Indicator #3

- We suggest NVPO consider tailoring the indicator.

- The percentages may need to vary for each of the specified cohorts.
- Will the results of this active surveillance be periodically reported, like the research into mechanisms of AEFI will be, according to indicator 4?
- I think that the indicator that x% of infants, children, adolescents, adults and pregnant women will be under active surveillance for AEFIs is inappropriate. This either will lead to 'fishing/dredging' exercises or will not necessarily be adequate to the challenge. There needs to be a capacity to put in place adequately powered studies in various populations in response to signals that have been generated elsewhere.
- This sounds great, but active surveillance, really?? I've looked downstream in the document and don't see mention of how this might be accomplished. It seems that some idea of how this would be done would be worth mentioning.

Indicator #4

- The Department of Veterans Affairs is missing from the list of groups of Research Entities suggested to receive annual report results. Since VA funding was a critical part of the support that allowed for a study of the benefits and side effects of zoster vaccine, this seems to be a significant oversight.
- There was consensus among the group that it was a very important new field of science, although there was caution against being unrealistic or over-promising. There was also support shown for reducing administration errors. The group did not propose values for Xs in the indicators.
- Strategies must be developed for how to deal with this topic, which garners enormous scientific and public interest, but scientifically poses challenges. The process should be transparent of what the studies are, what the methods are, and who is doing the research.
- With current vaccine fears and biases, continued research is needed to explore host factors related to adverse effects and failures at different stages in life, e.g., infancy, adolescence, pregnancy, elderly, etc. as well as those associated with workplace exposures, genomic characteristics and/or biomarkers immune responses/indicators.

The following indicator **additions for Goal 2** were recommended:

- **Goal 2 Indicators (new):** By X year, vaccine administration adverse events will be reduced by X% through the use of single dose manufacturer-prefilled delivery systems. *Rationale: Indicators that include assessment and surveillance are a laudable, and necessary first step; setting target reductions in adverse events following immunization stands to keep the Nation on track for improving vaccine safety.*
- **Goal 2 Indicators (new):** Conduct and disseminate the results of active and passive surveillance-based assessments of current vaccine administration practices in various settings (e.g., healthcare facilities, convenient care centers and community centers). *Rationale: Recent studies have shown that drug delivery systems have an impact on vaccine administration, including reducing risk of error that may contribute to adverse events.6,7,15 A better understanding of how healthcare providers actually administer vaccines in practice (as opposed to in training) and especially in the context of emergency settings promises to reveal opportunities for improvement in training and in the engineering of, and access to, vaccine delivery systems designed to mitigate error by reducing steps required for administration.*

- **Goal 2 Indicators (new):** Conduct or support research that examines single dose, manufacturer-prefilled delivery systems as a means of engineering safety into vaccine administration across all settings. *Rationale: Manufacturer-prefilled delivery systems eliminate several of the steps associated with conventional syringe-and- vial administration. Simplified administration may reduce the risk of error associated with conventional nonintegrated delivery systems.*
- **Goal 2 Indicators (new):** By year X develop accreditation standards for various categories of immunization providers;
- **Goal 2 Indicators (new):** Y% of immunization providers with appropriate level of accreditation by the year X.
- **Goal 2 Indicators (new):** AE report quality: An indicator should be added to increase the proportion of adverse event reports that include the vaccine's lot number, concomitant medications, underlying disease states, and other clinical details that would improve interpretation of vaccine safety data.
- **Goal 2 Indicators (new):** An indicator should be added to enhance the ability to conduct controlled, randomized database studies. The US Government should enable more HMOs to establish electronic medical records (EMRs), to permit high-quality collaborative research. With more uniformity and compatibility (to allow concatenation), vaccine safety research would be enhanced.
- **Goal 2 Indicators (new):** The US Government should add an indicator to monitor effectiveness of its efforts to detect and prevent distribution of counterfeit products.
- **Goal 2 Indicators (new):** Another indicator under safety could be that X% of all vaccines should be monitored in Immunization Information systems.

Goal 3 Indicators:

Comments for current Goal 3 Indicators were related to a need to clearly and consistently state timeframes. Some suggested a five-year timeframe as adequate time to show progress and improvements. One comment for Indicator 3 specified a need for culturally appropriate education materials with varying levels of information. It was also suggested that Goal 3 Indicators focus on the general public's knowledge of vaccine benefits and not have such as heavy emphasis on adverse events and risks. Recommended additions for Goal 3 Indicators were related to measuring new vaccine product information availability and accessibility, older vaccine availability following emergence of new vaccines, drivers and barriers to immunization uptake, number of "conscientious objectors," and point-of-care informatics-based decision support for clinicians.

Indicator #1

- The document should clearly state the initial time point to be used to calculate the "within X days" interval. The standard should be set carefully, to allow for scenarios where poorly understood situations would have to be reported before adequate guidance to the public could accompany it.
- How do you measure "enhance communication"?
- Too fast is as much of a problem is too slow and in the past trying to get information out fast has resulted in confusion – as part of a local public health agency we have at times

- In the first bulleted indicator, we would suggest including communication about vaccine quality and safety as well as vaccine safety concerns. This will help ensure the plan is proactive as well as reactive.

Indicator #2

- An alternative could be X___ % of the public will report that they are satisfied with how their health care provider **communicates with them** about the benefits and risks of vaccines by Y (year).
- If providers were compensated adequately for the cost of vaccines and administration they would be more able to spend time answering questions – initial evaluation should be setting a baseline unless one exists
- This is a passive indicator that essentially depends upon the "consumer" knowing about product availability. It seems that a more critical component is making sure providers are discussing the availability of the vaccine, noting the fact that there is a national recommendation for vaccination, and answering questions about vaccination.

Indicator #3

- The US Government should play an active role in providing additional culturally-appropriate educational materials (with varying levels of information content) on the benefits of vaccination in general and that of specific vaccines to the public.
- Good quality information needs to be available by Google search or on YouTube – take advantage of information sources people are using and this will be successful.

Indicator 5

- For consistency, indicators 2 – 5 should start with "By Y (year)" – having it at the end of the sentence may cause the timeline to get lost.

Indicator 6&7

- Last two indicators – "all" is tough to achieve.
- The measureable indicator on training programs for all health professional schools should include content on best practices for work-related exposure prevention as well as work-site vaccination programs for vaccine-preventable diseases and assessment of their knowledge of programs.
- We recommend that education about the vaccine supply chain be incorporated into this training to help HCWs understand how vaccine reaches them and to eliminate confusion or frustration on their part that may negatively impact their desire and/or ability to immunize.

The following indicator **additions for Goal 3** were recommended:

- **Goal 3 Indicators (new):** X % of health care providers will report they are satisfied with the availability of new vaccine product information and accessibility.

- **Goal 3 Indicators (new):** X% of health care providers will report they are satisfied with availability of older, effective and less costly single antigen vaccines when newer more costly combination vaccines emerge.
- **Goal 3 Indicators (new):** X% of key decision and policy makers will report they have access to costs of newly emerging vaccines along with efficacy and risk.
- **Goal 3 Indicators (new):** By year X, map drivers and barriers to immunization uptake across geographical and social spectrums, and identify and develop measures to achieve consistent national immunization coverage;
- **Goal 3 Indicators (new):** Reduce the proportion of the population who are conscientious objectors by Y% in X years.
- **Goal 3 Indicators (new):** One of the critical areas for information development is point-of-care informatics-based decision support to enable clinicians to rapidly find detailed vaccine information. Global searches of vast web sites are not the answer. This applies to Goal 3 and can be an indicator.
- **Goal 3 Indicators (new):** x % of the public will report receipt of official health care messages via media sources (i.e. text, email, social networking, television, Internet).

Goal 5 Indicators:

Stakeholders mentioned that the indicators under Goal 5 did not mirror the objectives. It seemed unclear how the indicators were chosen and how the Plan will lead to successful implementation of the indicators. They suggested, "the indicators be designed collaboratively with global governmental and non-governmental stakeholder input to ensure alignment, enhance output and reduce uncoordinated or duplicative efforts." In addition, stakeholders recommended that indicators 1-3 align with strategies already in place through the global partners and stakeholders (e.g. Millennium Development Goal, The Global Alliance for Vaccines and Immunization (GAVI), United Nations International Children's Emergency Fund (UNICEF)).

Other comments for current Goal 5 Indicators were related to currently specified timeframes and a need for adjustment due to changed expectation of eradication (wild polio virus) or data measurement capabilities (DTP3 vaccination). Stakeholders recommended a measles elimination goal for Indicator 2. It was suggested the vaccines referenced in Indicator 4 be prioritized according to public health need. In addition, many stakeholders suggested additional diseases be added to Indicator 4 such as Human Papilloma Virus (HPV) and Haemophilus Influenza Type B (Hib). The careful evaluation of the safe injection devices referenced in Indicator 6 was recommended. Additional Goal 5 Indicators were suggested related to gathering information on immunization advisory committees (referenced in Indicator 5), developing accountability models and standards, and assessing vaccinate waste.

Indicator #1

- The first indicator seeks to set a year by which wild polio virus will be eradicated. The global community now acknowledges the effort will take longer than expected. As no fixed target year is broadly accepted elsewhere, it is problematic for a date to appear in a U.S. plan.

Indicator #2

- Mortality from measles will be reduced by X% by Y (year) compared with an X (year) baseline" could be reviewed. Indeed, in the next 10 yr, we anticipate that all regions will have moved towards a 'measles elimination' goal (zero incidence vs zero mortality)
- This is the only indicator that uses a % difference from a baseline value – can it just reference a specific reduction as all other indicators do?

Indicator #3

- 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)" : we already remove the second part from our list of indicators in WHO since it is difficult to have data to measure both in a reliable manner.

Indicator #4

- Suggests tailoring to specifically reference conjugate meningococcal vaccine.
- The list should be prioritized based on public health need. A mechanism should be provided to augment this list, perhaps by linking it to other vaccines provided via Expanded Programme on Immunization (EPI) or an Accelerated Development and Introduction Plan (ADIP)- or GAVI-like process.
- I think that influenza vaccine should be added (I was recently appointed as a member of the WHO Strategic Advisory Group of Experts and have now become aware that the topic of influenza vaccine has moved up on the list of vaccines to be considered for global introduction).

Indicator #5

- Suggests establishing a metric of X countries establishing immunization advisory committees, and requiring this metric to incorporate assessment submetrics. Suggests adding an objective which would gather information on advisory committees.

Indicator #6

- The benefits and risks of individual devices such as those named need to be carefully analyzed, including assessment of practicality of their use, to avoid unintended consequences.
- **(Revised):** X countries enhance injection safety by Y (year) through the use of auto-disable syringes or other safe<u>r</u> injection devices (e.g., needle<u>-</u>free delivery) for all <u>vaccinations</u>.
- As it relates to the last indicator (X countries enhance injection safety by Y year), promoting the use of auto-disable syringes and other safety injection approaches should be balanced with the cost implications and resulting impact on affordability, which constrains overall utilization of vaccines. This consideration should be factored into the final language of the indicator.
- **(Revised):** 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), **safety boxes. and sufficient capacity to treat resulting shams and other infectious waste** for all immunizations.

The following indicator **additions for Goal 5** were recommended:

- Within X years, collaborate with international funding organizations to develop accountability models and standards to improve efficiency and effectiveness of immunization program delivery in developing countries.
- Assess vaccine wastage due to storage conditions assess vaccine wastage due to excessive heat or cold and reduce wastage by X percent.

4. Comments on Stakeholders' Roles in the National Vaccine Plan

Stakeholder's were asked to identify which stakeholders should have responsibility for enacting the objectives and strategies listed in the draft Plan, state their roles in the Plan and add any new objectives and strategies they deemed necessary. Federal along with non-federal stakeholders were mentioned. Many comments reflected their concern about stakeholder's roles and responsibilities and who would monitor and manage these duties.

Federal Stakeholders - The addition of the National Institute for Occupational Safety and Health (NIOSH) along with Occupational Safety and Health Administration (OSHA) were mentioned among the comments. Some suggested including professional medical societies at the state level to better represent health professions and the health care settings at the local and national level. Organizations such as Infection Control Societies and the Association of Homes and Services for the Aging were a few mentioned.

Non-Federal Stakeholders - Comments suggested a list of non-federal stakeholders to be included for influencing the draft of the Plan. Industries and organizations include the medical technology industry, childcare facilities, community organizations, academia, pharmacists, insurance companies, and churches. These stakeholders contribute to vaccine administration and education and are valuable to the Plan.

Stakeholders commented that vaccine manufacturers should address the high cost of new combination vaccines and elimination of suitable less expensive vaccines.

Conclusion

In general, all stakeholders commented that the draft Plan was a good beginning. Many agreed on the goals and objectives that are currently in the Plan. Stakeholders positively received the concept that the Plan should be "National" vs. "Federal" and ensuring that outcomes are quantifiable. Additionally, many suggested updating the Plan on a regular basis because emerging diseases are constantly changing along with vaccine safety issues. Many revisions were minor and included adding or removing particular words to address issues of interest for particular stakeholders. Numerous new strategies and indicators were added to all of the goals in the Plan. Overall, stakeholders believed that the goals, objectives, and strategies in the Plan must have a timeframe and be inclusive of all populations, situations, and stakeholders that are involved with vaccine development, distribution, administration, and education.