

# Vaccine Safety Working Group Update

National Vaccine Advisory Committee  
September 15<sup>th</sup> , 2010

Dr. Marie McCormick & Tawny Buck  
Co-Chairs, Vaccine Safety Working Group

# Members

- Robert L. Beck
- Guthrie S. Birkhead\*
- Tawny Buck^
- Chris Carlson
- Vicky Debold
- Cornelia Dekker
- Mark Feinberg
- Steve Goodman
- Lance Gordon
- Lawrence Gostin
- Sean Hennessy
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- James O. Mason
- Marie McCormick^
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- Trish Parnell
- Andrew Pavia^
- William Raub
- L.J. Tan

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# Charge 2

“To review the current federal vaccine safety system and develop 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.”

# Work in Progress

- Materials distributed and information presented are working drafts
- Does not represent consensus
  - There have been no votes
- More information is needed
- Revisions will occur

# Working Drafts

- Introduction (distributed)
- Methods (distributed)
- Structure of the current system
- Definition of the goals for vaccine safety system
- Key functions and attributes
- Identification of opportunities for improvement in the current vaccine safety system
- Recommendations (distributed)
- Options for oversight

# Information Gathering Charge 2 Kick-Off Meeting

- July 15-16, 2009
- Invited 26 panelists to speak on:
  - Principles and policy alternatives for a robust vaccine safety system
  - Identifying innovative ways of overcoming gaps in vaccine safety science infrastructure
  - The ideal system to meet the needs of the public, public health, and healthcare professionals for confidence in vaccine safety
  - Lessons from other safety arenas
  - Enhancing the adoption and implementation of the NVAC white paper

# VSWG Subgroups

## Content Subgroups

1. Structure/Governance (Bill Raub)
2. Epidemiology/Surveillance of Adverse Events (Lance Gordon)
3. Biological Mechanisms of Adverse Events (LJ Tan)

## Process Subgroups

1. Stakeholder Engagement
2. Implementation

# Briefings

- ASTHO Public Confidence study
- Barcoding technology
- CDC Immunization Safety Office
- CISA Biospecimen Repository
- CISA Investigators
- DoD Vaccine Healthcare Centers
- DoD Milvax Drug safety systems
- FDA/CBER
- International vaccine safety systems
- Manufacturers (VSWG members)
- NIH/NIAID
- Past IOM vaccine safety review committee consideration of biological mechanisms
- Post-Licensure Immunization Safety Monitoring (PRISM)
- VSD Investigators
- VA

# Information Gathering Salt Lake City Meeting

- 29 federal and non-federal stakeholders, including 9 VSWG members
- Issues discussed:
  - Opportunities for improvement in the current vaccine safety system
  - Proposed evaluation criteria
  - Strengths and weaknesses of various enhancements or alterations to the structure and governance of the vaccine safety system

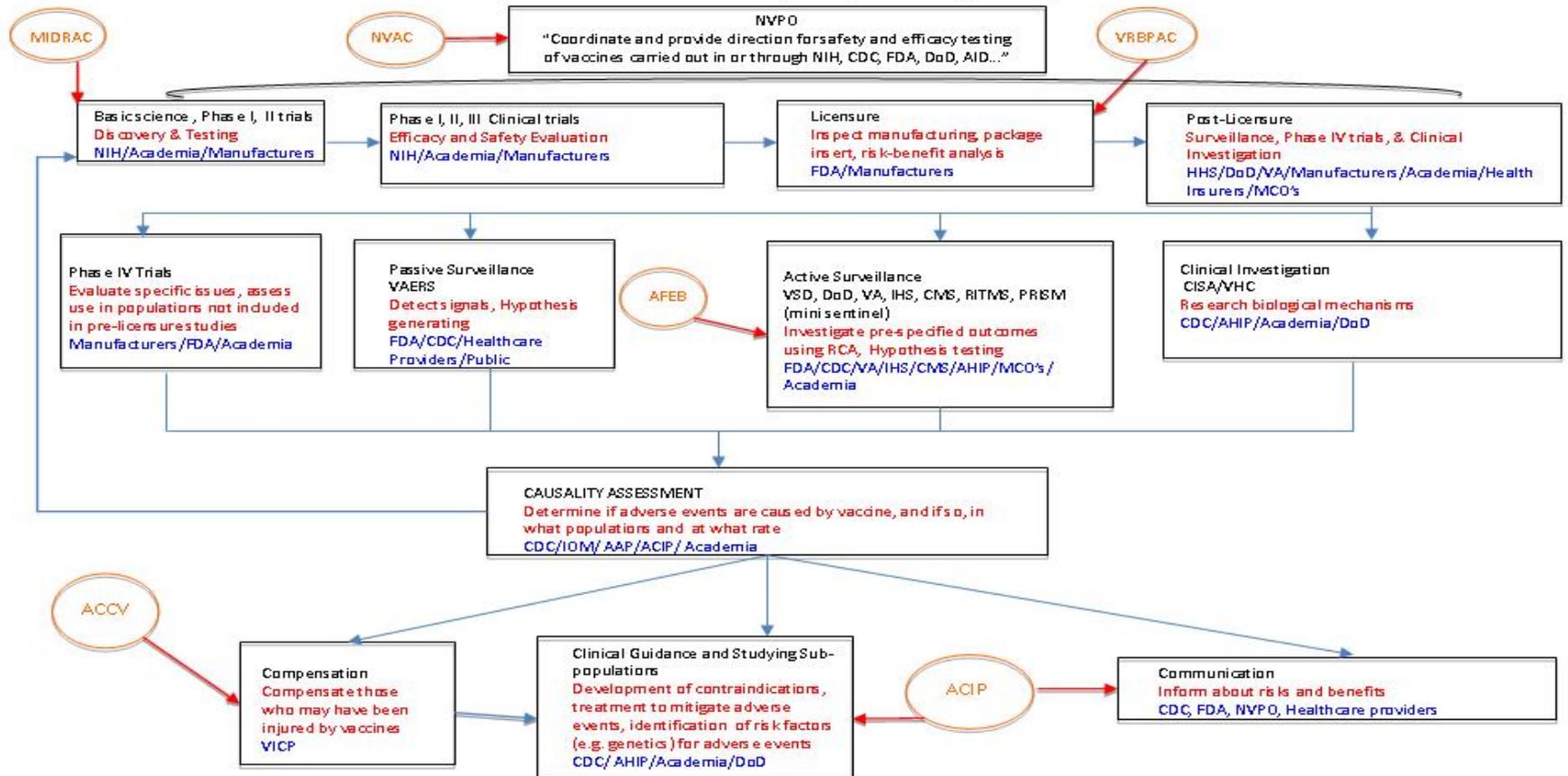
# Assessment of Safety System

## Fundamentally Sound

- US vaccine safety system one of if not the most advanced in the world
- System has many components throughout the lifecycle of a vaccine
  - Federal Government
    - Vaccine discovery (NIH)
    - Oversight before and after licensure (FDA)
    - Passive post-licensure surveillance (FDA and CDC)
    - Active post-licensure surveillance (CDC, FDA, IHS, CMS, DoD, VA)
    - Clinical investigation (CDC and NIH)
  - Industry, academia, states, providers, health plans, professional associations, advocacy organizations

# Complexity of the System

Vaccine Safety Activities & Primary Purposes by Group with Lead Role



**LEGEND**

- Indicates Advisory Committee
- Indicates primary activities
- Indicates purpose
- Indicates who has lead role
- Indicates link
- Indicates Advisory function

**Acronyms**  
 ACCV = Advisory Committee on Compensation for Vaccine Injury  
 ACIP = Advisory Committee on Immunization Practice  
 AFEB = Armed Forces Epidemiology Board  
 AHIP = America's Health Insurance Plans  
 CDC = Centers for Disease Control and Prevention  
 CISA = Clinical Immunization Safety Assessment network  
 CMS = Centers for Medicare and Medicaid Services  
 DoD = Department of Defense  
 FDA = Food and Drug Administration

IHS = Indian Health Service  
 MIDRAC = Microbiology and Infectious Diseases Review Advisory Committee  
 NIH = National Institutes of Health  
 NVAC = National Vaccine Advisory Committee  
 NVPO = National Vaccine Program Office  
 VA = Veterans' Affairs  
 VAERS = Vaccine Adverse Events Reporting System  
 VICP = Vaccine Injury Compensation Program  
 VSD = Vaccine Safety Datalink

# Assessment of Safety System

Many successes that demonstrate what works well

- Safety profiles of vaccines used today are excellent
- Development of acellular pertussis vaccine
- Switch from OPV to IPV
- Intussusception and 1<sup>st</sup> rotavirus vaccine rapidly detected and acted upon
- H1N1 safety monitoring efforts

# Some Draft Opportunities for Improvement

- **Knowledge Base:** There are gaps and uncertainties, and critical opportunities to address them
- **Communication:** No single source for information or to solicit, receive and respond to public concerns
- **Vaccine Injury Response:** Opportunities exist to
  - improve the vaccine injury compensation program
  - enhance assistance for those who have experienced a vaccine-associated injury
- **Confidence in vaccine safety:** Public concerns about the safety of vaccines are significant and merit more attention than they have received to date
- **Leadership:** Responsibility for vaccine safety activities is distributed among several U.S. government agencies and offices, which generally pursue their respective missions independently.

# Work in Progress

- Materials distributed and information presented are working drafts
- Does not represent consensus
  - There have been no votes
- More information is still needed
- Revisions will occur

# Proposed Goals of the Vaccine Safety System

- Characterize the safety profile of vaccines and vaccination practice;
- Detect, prevent, and reduce adverse events in a timely manner;
- Develop guidance to detect and mitigate the effects of adverse events in individuals;
- Earn public confidence in the effectiveness of the vaccine safety system and in the safe use of vaccines; and
- Inform vaccine policy.

# Vaccine Safety System

## Key Functions and Attributes

### Functions

- Authority, Oversight, and Leadership
- Licensing
- Monitoring
- Research
- Causality Assessment
- Injury Compensation
- Practice
- Communications
- Engagement

### Attributes

- Accountability
- Effectiveness
- Efficiency
- Equity
- Evidence-Based Decision Making
- Initiative
- Innovativeness
- Objectivity
- Responsiveness
- Transparency

Underlined are those attributes highlighted as most important by Salt Lake City Writing Group

# Public Confidence

- Reviewed published and recent unpublished data
  - Rates of vaccine coverage and vaccine refusal
  - Parental and public attitudes towards vaccination and vaccine safety
- Identified data on public confidence of vaccines but found little data on confidence in vaccine safety system
- Substantial literature from psychology and decision-making sciences show perceptions related to risk are associated with behavior
  - Increased perception of risk leads to behaviors seeking to minimize such risks
- Assumptions were drafted & require further validation

# VSWG Working Assumptions for Public Confidence in Vaccines\*

The federal government has a primary responsibility and statutory authority for ensuring there is a robust safety system in place. Vaccine manufacturers, state governments, clinicians, and consumers all play essential roles

The general public does not separate the safety of vaccines from the infrastructure designed to ensure safety. Thus, a lack of confidence in vaccine safety is inseparable from a lack of confidence in the safety system.

It is reasonable to assume that meaningful actions taken to enhance the safety system, will lead to increased knowledge regarding vaccines, more rapid detection & prevention mechanisms, reduction of adverse events, and ultimately, safer vaccines. These enhancements, coupled with effective communication, should result in increased public confidence in vaccines.

Public confidence in vaccines/vaccine safety system has implications for the public's willingness to vaccinate. Primary care clinicians, generally the most trusted source of vaccine safety information cited by parents, are more likely to connect a robust safety system with greater confidence in the safety of vaccines.

\* Further validation of working assumptions will be garnered from planned engagement activities

# Draft Recommendations - Overview

To date the VSWG has drafted recommendations structured within three areas:

- Leadership, Coordination and Oversight;
- Tools and Resources;
- Research, Causality Assessment, and Identification subpopulation/ characterization/managing adverse events.

Each recommendation area outlines action steps within the area.

# Draft Recommendation #1

Providing authoritative leadership, coordination and oversight

The VSWG recommends the Department strengthen leadership, coordination, and oversight of the vaccine safety system.

# Draft Recommendation #1- Action Steps

- 1.1 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 to the Secretary of HHS would achieve the needed organizational authority, including the critical authority through the Secretary to allocate resources.
  - The Secretary of should affirm the commitment of the Executive Branch to fulfilling the letter and spirit of the National Childhood Vaccine Injury Act (NCVIA) of 1986.

# Draft Recommendation #1- Action Steps

- 1.2 Expand the scope of the Federal Immunization Safety Task Force (ISTF).
- 1.3 The ASH, NVPO, and the NVP-participating agencies, under the direction of the ASH and reporting directly to the Secretary, should develop and maintain a unified program of public information about vaccines and the vaccine safety system that can serve as a resource to the public and health professionals.

# Draft Recommendation #1- Action Steps

- 1.4 Assign NVAC a broader and stronger role with regard to review and evaluation of the NVP and the plans and accomplishments of the vaccine safety system.
  - Create a standing Subcommittee on Vaccine Safety which would track the implementation of these and other related NVAC safety recommendations, lead reviews of agencies' plans and progress, and address emerging vaccine safety issues as they arise
- 1.5 The ASH, NVPO, and the NVP-participating agencies, should develop and maintain an ongoing and meaningful program of stakeholder engagement around vaccine safety.
- 1.6 Establish a temporary expert committee to look at the feasibility of and mechanisms/structure for providing/ensuring responsible access by researchers to preclinical, clinical, and post-licensure data.

# Draft Recommendation #2

Ensuring adequate resourcing

**The VSWG recommends the Department enhance the tools and resources available to the vaccine safety system.** There are a number of steps that will help develop a dynamic, up to date and evolving system for vaccine safety science and surveillance but they are dependent on adequate and stable resources.

# Draft Recommendation #2- Action Steps

- 2.1 Identify resources for vaccine safety activities commensurate with existing needs and opportunities.
- 2.2 Create funding and scientific review pathways specific for intramural and extramural vaccine safety research, and encourage researchers to apply the most powerful emerging scientific tools to detect, understand and if possible prevent adverse events associated with immunization.

# Draft Recommendation #2- Action Steps

- 2.3 Leverage existing infrastructure and investments for vaccine safety research, such as CISA, the National Children's Study, and others.
- 2.4 Develop training programs for scientists in vaccine safety research and medical professionals, including epidemiology and pathophysiology of adverse events following immunization.
- 2.5 Facilitate a community of vaccine safety researchers that crosses the boundaries to ensure continuity of research from different arenas, entities, and disciplines.

# Draft Recommendation #2–Action Steps

- 2.6 Engage vaccine manufacturers to capitalize on their expertise, large preclinical and clinical databases, specimen repositories and scientific resources to inform further vaccine safety studies.
  
- 2.7 Complete planning and implement recommendations for the enhancement of a National Vaccine Safety Biospecimen Repository linking biological samples to clinical data for unusual AEFI.

# Draft Recommendation #2–Action Steps

- 2.8 Facilitate the expansion of the population under active surveillance to the FDA Amendments Act (FDAAA) requirements of 100 million by 2012.
- 2.9 Create a routine system of barcode labeling of vaccine vials and pre-filled syringes that is coordinated, ideally with international standards.
- 2.10 Improve methods to evaluate and follow individuals who experience adverse events that are reported to VAERS.

# Draft Recommendation #3

Advancing basic, clinical and epidemiological research

**The VSWG recommends the Department enhance research to strengthen the scientific basis for vaccine safety**, including understand the biological mechanisms for adverse events following immunization (AEFI), surveillance and epidemiological studies to detect unexpected AEFI and explore associations between vaccines and AEFI, consider the aforementioned information as well as other relevant information to determine if the vaccine causes the AEFI, and in such cases identify and characterize subpopulations at increased risk for AEFI and protocols for managing AEFI.

# Draft Recommendation #3-Action Steps

- 3.1 Sponsor a study to characterize the extent to which vaccine administration errors occur and implement strategies for reducing them as appropriate for quality improvement and patient safety.
- 3.2 Coordinate the development, implementation and periodic update of a National Vaccine Safety Scientific Agenda.
- 3.3 Develop and regularly review a national agenda to enhance post-licensure surveillance.
- 3.4 Expand approaches to assure ascertainment of public concerns and perceptions regarding the safety of vaccines and adverse events.

# Draft Recommendation #3-Action Steps

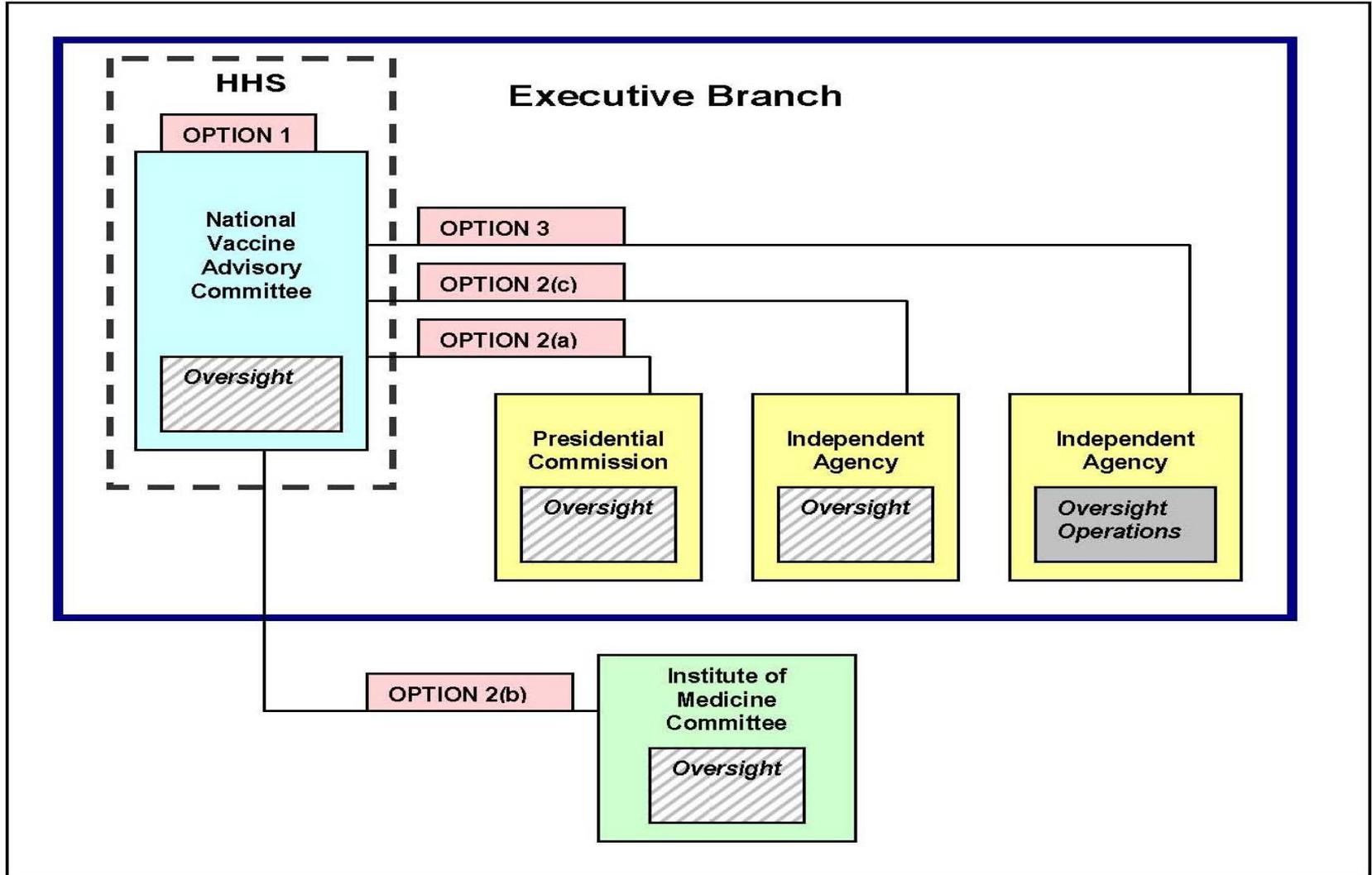
- 3.5 Sponsor a standing independent panel (or a mechanism for such a panel) to assess the causal relationship between vaccines and suspected adverse events, such as the IOM.
- 3.6 Promulgate consistent, accepted and effective guidance on reporting and clinically managing AEFIs.

# Oversight and Organizational Options -under consideration-

The VSWG defines **Oversight** as monitoring, evaluating, and reporting on particular programs or activities. **Oversight** does not include authority to assign tasks to, assume any of the operational responsibilities of, or overrule decisions by the agencies that are responsible for those programs or activities.

- Option 1:** Do not create an entity outside HHS to supplement NVAC oversight of the vaccine safety system.
- Option 2:** Reinforce NVAC's oversight role by creating an entity that is independent of and external to HHS to provide a supplementary level of oversight for the vaccine safety system.
- Option 2a.* Establish a Presidential Commission
  - Option 2b.* Establish a Committee of the IOM
  - Option 2c.* Create an independent agency within the Executive Branch
- Option 3:** Create an independent agency within the Executive Branch to operate aspects of the vaccine safety system, (i.e. VAERS, etc).

# Oversight and Operational Options -under consideration-



# Evaluation of oversight and operational options under consideration

- Each option is being evaluated through the lens of the previously defined functions (leadership, monitoring, communications, etc.) of a vaccine safety system
- Consideration will be given to how each option would affect, positively or negatively, the 10 attributes (objectivity, transparency, efficiency etc.) of the system
- Consideration will also be given to feedback from NVAC, stakeholders, and the public.
- Data will be synthesized to summarize the overall pros/cons.

# Public and Stakeholder Input

- Completed
  - Kick off meeting (July 15-16, 2009)
  - Salt Lake City meeting (April 11-13, 2010)
- Planned\*
  - Open Stakeholder meeting (Fall, 2010)
  - Solicit public and stakeholder written comments on draft report (Fall, 2010)
  - Other strategies under discussion (Keystone Presentation, timeline TBD)

\*Subject to change

# Draft Data needs moving forward

- To understand how stakeholders:
  - View the vaccine safety system needs
  - Preferences for governance and structure options
  - Priorities for system enhancements
  - Provide guidance on a participatory approach for on-going dialogue re: vaccine safety issues (developed by the Immunization Task Force)
- To understand the following about public views:
  - To what extent there is a problem regarding public confidence as it pertains to the safety infrastructure and how it links to behavior (testing the VSWG's assumptions)
  - Views on what are the most important system functions, priority attributes, and trade-offs among different priorities.
- To understand the following implications of the oversight options:
  - Administrative feasibility
  - Fiscal feasibility
  - Political feasibility
- Others?

# Next Steps

- Feedback from the NVAC
  - Working Assumptions
  - Data needs
  - How to fill those data needs
  - Draft recommendations
  - 3 Oversight Options
- Fill in the data needs
- Update report based on this information
- NVAC vote at February NVAC meeting