National Vaccine Advisory Committee (NVAC)
June 7–8, 2016, Meeting Minutes

Committee Members in Attendance

Walter A. Orenstein, M.D., Chair
Richard H. Beigi, M.D., M.Sc.
Timothy Cooke, Ph.D.
Sarah Despres, J.D.
David Fleming, M.D., M.P.H.
Ann M. Ginsberg, M.D., Ph.D.
Philip Hosbach
Ruth Lynfield, M.D.
Yvonne Maldonado, M.D.
Saad Omer, M.B.B.S., M.P.H., Ph.D.
Wayne Rawlins, M.D., M.B.A.
Mitchel C. Rothholz, R.Ph., M.B.A.
Nathaniel Smith, M.D., M.P.H.
Kimberly M. Thompson, Sc.D.

NVAC Ex Officio Members

Amanda Cohn, M.D. (for Nancy Messonnier, M.D., CAPT), Centers for Disease Control and Prevention (CDC)
Andrew Ford, Ph.D. (for Barbara Mulach, Ph.D.), National Institutes of Health (NIH)
Marion Gruber, Ph.D., U.S. Food and Drug Administration (FDA, day one)
Mary Beth Hance, Centers for Medicaid and Medicare Services (CMS)
Gerald Kovacs, Ph.D. (for Richard Hatchett, M.D.), Biomedical Advanced Research and Development Authority (BARDA)
Iris Mabry-Hernandez, M.D., M.P.H., Agency for Healthcare Research and Quality (AHRQ, *by phone*)
Donna Malloy, D.V.M., M.P.H., Department of Agriculture (USDA)
CDR Valerie Marshall, M.P.H. (for Marion Gruber, Ph.D., day two), FDA
Jeffrey McCollum, D.V.M., M.P.H. (for Michael Bartholomew, M.D.), Indian Health Service (IHS)
Justin A. Mills, M.D., M.P.H., Bureau of Primary Health Care (BPHC), Health Resources and Services Administration (HRSA)
Narayan Nair, M.D., Division of Injury Compensation Programs, HRSA
COL Margaret Yacovone, M.D., M.S.P.H., Department of Defense (DoD)

NVAC Liaison Representatives

Nancy M. Bennett, M.D., M.S., Advisory Committee on Immunization Practice (ACIP)
Kimberly Martin, M.P.H. (for James S. Blumenstock), Association of State and Territorial Health Officials (ASTHO)
Scott Breidbart, M.D., M.B.A., America's Health Insurance Plans (AHIP)
Rebecca Coyle, M.S.Ed., American Immunization Registry Association (AIRA)
Claire Hannan, M.P.H. (for Kristen Ehresmann, R.N., M.P.H.), Association of Immunization Managers (AIM)
Cara Janusz, M.P.H., M.A., (for Isabella Danel, MD, MS) Pan American Health Organization (PAHO)
Rhonda Kropp, Public Health Agency of Canada (PHAC)
Tiffany Tate, M.S.H., National Association of County and City Health Officials (NACCHO)

Executive Secretary

Bruce G. Gellin, M.D., M.P.H., Deputy Assistant Secretary for Health and Director, National Vaccine Program Office (NVPO)

Day 1—June 7, 2016

Call to Order

Bruce G. Gellin, M.D., M.P.H., called the meeting to order at 9:03 a.m., and NVAC members introduced themselves.

Welcome—Jewell Mullen, M.D., M.P.H., M.A., Principal Deputy Assistant Secretary for Health, U.S. Department of Health and Human Services (HHS)

Dr. Mullen, who joined HHS recently, said she appreciated that the NVPO is doing more work at the regional level to advance immunization and strengthen community coordination. She described how her personal experiences have informed her commitment to public health. Dr. Mullen acknowledged the fiscal challenges that public health efforts face. In summarizing the agenda for this meeting, she said NVAC's expertise, leadership, and involvement are critical to developing sound, practical recommendations, particularly around prioritization of Federal and non-Federal efforts to meet the National Vaccine Plan's 2020 goals. Dr. Mullen said she was especially proud of NVAC's emphasis on adult immunization, and HHS adopted the NVAC recommendations on the issue.

This meeting represents the last for Walter A. Orenstein, M.D., and Dr. Mullen presented him with a plaque expressing the Department's deepest gratitude for his outstanding service as NVAC chair and for his many successful efforts to improve immunization and public health as a senior-level Federal public health leader. The audience responded with a standing ovation.

Dr. Mullen announced that Kimberly M. Thompson, Sc.D., will serve as the next NVAC Chair. Dr. Thompson has an impressive background that includes expertise in risk analysis, health communication, health economics, and health policy and management, with an emphasis on children's health.

Remarks

Dr. Gellin thanked Dr. Orenstein for his commitment to NVAC and presented a slide show describing Dr. Orenstein's career and legacy. He added his thanks to Dr. Orenstein for all of his hard work and dedication.

Dr. Gellin outlined key parts of the Federal Advisory Committee Act, its conflict-of-interest rules, and standards of ethical conduct for NVAC members. He noted some of the topics on the agenda for this meeting.

Chair's Report—Walter A. Orenstein, M.D., NVAC Chair

Dr. Orenstein thanked the NVPO staff, NVAC members, and the public for their roles in NVAC's success as it seeks to minimize the burden of vaccine-preventable diseases. He gave an overview of the meeting process. He noted that the public comment period is not a question-and-answer session; rather, it is an opportunity for the public to give comments that will appear in the public record. Time for public comment is limited; written comments can be sent to the NVAC for consideration by e-mail (nvpo@hhs.gov). Dr. Orenstein said the minutes of past meetings are published online.

Dr. Orenstein called for review of the February 2016 NVAC meeting minutes. NVAC members unanimously approved the minutes with no changes.

Dr. Orenstein gave a brief history of NVAC and welcomed the incoming chair, Dr. Thompson. He also called out Dr. Gellin and Jennifer Gordon, Ph.D., of NVPO and his assistant Katy Seib, MSPH in particular for their hard work and support of him and NVAC.

Dr. Orenstein summarized the meeting agenda. Most of the presentations can be found online at http://www.hhs.gov/nvpo/nvac/meetings/pastmeetings/index.html. The next two NVAC meetings are tentatively scheduled for September 7–8, 2016, and February 7–8, 2017.

Pinpointing Challenges to Vaccine Innovation: Analysis from McKinsey and Company—Tara Azimi and Michael Conway, McKinsey and Company

McKinsey and Company has been working to understand whether the vaccine industry is innovating to meet unmet needs, said Ms. Azimi. Collaborating with NVPO and industry leaders, McKinsey is evaluating the challenges to innovation and possible solutions. Ms. Azimi described the global unmet need to address vaccine-preventable diseases and those diseases likely to respond to vaccines. Improving vaccine delivery systems could increase pediatric uptake of vaccines, given the extensive immunization schedule, as well as adult uptake.

On the surface, the vaccine product pipeline appears robust, and a higher proportion of vaccines in development are late-stage vaccine candidates compared with 10 years ago. Over the past 10 years, the number of new vaccines on the market has increased globally. The industry is expected to continue growing at least through 2020. However, a closer look reveals that sales of new products peaked in 2011, and most of the industry growth comes from sales of existing vaccines and the expansion of global markets. Biotech firms and emerging markets are driving early-stage vaccine research, but it is not clear whether the large, multinational pharmaceutical companies have the absorptive capacity to identify promising candidates and take them to market.

Ms. Azimi pointed out that vaccine candidates are more likely than biologics to be abandoned early in the research process. One hypothesis is that researchers are learning more quickly about potential candidate viability and so can weed out candidates faster. Another hypothesis is that the high cost of moving from Phase II to Phase III research is prohibitive.

Mr. Conway described the factors affecting the declining profitability of vaccines for large pharmaceutical companies. The success rate for vaccine development is going down and as a result, so is the return on investment (ROI). The time from Phase I to launch is also increasing. Shortages, recalls, and other manufacturing challenges damage profitability. In selecting investments, companies take into account the likelihood that a vaccine would be recommended, for example by the Advisory Committee on Immunization Practices (ACIP), which strongly influences uptake in the U.S. pediatric population. Technical feasibility—such as the population's natural immunity or the fast-changing nature of a pathogen—influences candidate selection.

Mr. Conway offered profiles of vaccines according to their commercial potential and technical feasibility, pointing out that those likely to have a strong ROI in high-income countries (especially for nosocomial infections) are also needed in low-income countries. The commercial value of incremental improvements is uncertain, which tempers enthusiasm for investment. A number of companies are addressing emerging threats, but the commercial potential is limited. Companies are very interested in potential blockbusters, such as a universal influenza or respiratory syncytial virus (RSV) vaccine, but they have proven to be technically very

challenging. For vaccines most applicable in low-income countries, companies see moderate commercial potential but low-to-moderate technical feasibility.

Potential solutions for boosting innovation for vaccines in high-income countries and for nosocomial infections include clarifying the market demand. Mr. Conway said publishing target product profiles (TPPs) or an ACIP "advance" recommendation would spur development. For example, if a vaccine for *Clostridium difficile* were available, would ACIP be likely to make a general recommendation for its use in people over 65 years or would the recommendation only apply to certain risk groups)? Innovation in incremental improvements could be sparked by a clearer picture of market signals and the likely value of an improved product. More specific guidance on formulation, presentation, and delivery innovations would also be helpful. If buyers are not willing to signal what they want, said Mr. Conway, suppliers probably are not going to step up to produce it.

For emerging threats, debates are underway about the use of economic incentives to push investments. The U.S. Government (USG) has already invested in flexible manufacturing platforms, which reduces economic barriers for companies. Both of these tactics contribute to innovation.

Better data-sharing and transparency about technical challenges could motivate development around potential blockbuster vaccines. For vaccines for low-income countries, greater clarity about the value of longer-term product innovations, through TPPs and pricing signals, for example, would be helpful. The uncertainty of demand (e.g., the slow uptake of dengue virus vaccine) translates into less investment and innovation.

Discussion

Timothy Cooke, Ph.D., said investors are currently much more enthusiastic about supporting advances in oncology than infectious disease. Therapeutics for infectious disease are a more popular investment than prophylactic vaccines. When immunization platforms are developed, there is tremendous pressure to apply the research to oncology rather than infectious disease. He felt that the decline in profitability of vaccine manufacturing means that investors will be less likely to support small biotech firms doing vaccine research. It may be difficult for ACIP to make advance recommendations, and even then, companies must gamble on how much more they will invest after FDA approval. Dr. Cooke added that funding to help biotech firms get products beyond Phase II testing is critical.

Ann M. Ginsberg, M.D., Ph.D., said that for vaccines for low-income countries, such as tuberculosis, the barrier is not so much uncertainty about demand as about ROI. The real barrier is lack of funders and investment. Governments, foundations, and biopharmaceutical companies need to see the value of developing such vaccines, and they need incentives to invest, said Dr. Ginsberg. With sufficient funding, the science is feasible and achievable.

Philip Hosbach agreed that lack of funding is part of the problem. Another is that some manufacturers globally are developing vaccines but not innovating. Some large manufacturers are finding vaccine development is not yielding a good ROI given the difficulty of moving products forward. Mr. Hosbach pointed out that UNICEF'S purchase of vaccines tends to attract manufacturers that make only a single product. Finally, the regulatory hurdles and compliance issues across countries are a substantial barrier. Mr. Hosbach called for harmonization, noting that companies currently have to navigate each country's unique requirements.

Saad Omer, M.B.B.S., M.P.H., Ph.D., pointed out that a lot of innovation in the United States is funded by taxpayers; he asked whether McKinsey evaluated the role of USG funding in innovation (e.g., through Small Business Innovation Research grants) and whether taxpayers are getting a reasonable ROI. If there is evidence of ROI for taxpayers, can an argument be made for increasing public investment in early-stage research? With blockbuster vaccines, Dr. Omer wondered whether more public or foundation funding would help get vaccines past the so-called valley of death (i.e., from Phase II to Phase III trials). Ms. Azimi said McKinsey did not look at the ROI for taxpayers but would do so. She said that without clearer market signals or a good business case, it is very hard to get additional funding from any source.

Dr. Thompson asked for more information on GAVI's impact on new product launches and revenues. She also asked for more analysis of whether good vaccine candidates are not moving forward—that is, whether there are potential products sitting on a shelf because there is no market.

Dr. Thompson further noted that the competition around new products still exists, especially competition to be the first to market. Sometimes the reality behind poor profitability is that another company made a better product. Dr. Thompson observed that TPPs and advance recommendations are sticky issues. With new delivery technologies, it bears repeating that the market is seeking cost savings for the vaccine delivery system, but supporting development would mean transferring funds from those sources paying for vaccine delivery, and there is no mechanism for that, which explains the lack of incentives for investing in new delivery systems. Dr. Thompson hoped McKinsey would make stronger, clearer statements about its findings and recommendations. Mr. Conway said he would look more closely at the role of revenue from GAVI and other sources of capital.

Dr. Orenstein focused on "pull" investments—such as government actions intended to spur funding from other sources. For example, the NVPO's and the National Academy of Medicine's Strategic Multi-Attribute Ranking Tool (SMART) for vaccines or some other process could be used to develop a list of priorities. Dr. Orenstein asked which is more important for the United States—push or pull mechanisms? Mr. Conway replied that when there is a credible market and a pathway to the market, a pull mechanism may work. When uncertainties abound and the pathway is unclear, push mechanisms are more important.

In response to the discussion about "advance" recommendations from ACIP, Nancy M. Bennett, M.D., M.S., said the ACIP looks at three, straightforward factors when recommending vaccines: efficacy, safety, and burden of disease. Cost-effectiveness is weighed but is secondary to the other factors. She emphasized that the deliberations are evidence-based and asked how ACIP could articulate its criteria more clearly. Mr. Conway said that, for example, ACIP could describe how a vaccine for a nosocomial infection might be used, posing some potential scenarios. Ms. Azimi said business leaders should be thinking about the role of recommendations earlier in the development process.

David Fleming, M.D., M.P.H., asked what proportion of the problem could be solved with new delivery systems and where investments on new solutions should be made. Ms. Azimi said at least three avenues should be addressed: infrastructure and data systems (especially for adult immunizations and in retail settings), product innovation (e.g., products likely to increase adult uptake), and commercial models that increase adult uptake.

Yvonne Maldonado, M.D., suggested and Ms. Azimi agreed that more collaboration between biotech firms and large multinational companies could help spur innovation. In response to Dr.

Cooke, Ms. Azimi said that companies have finite resources to invest, which affects their absorptive capacity. The market is growing, but businesses are facing real challenges that affect the capacity to move vaccine research forward.

Dr. Orenstein asked about BARDA's role in addressing emerging threats. Gerald Kovacs, Ph.D., responded that biotech and pharmaceutical companies are steering away from innovation because of the risks involved. For Zika virus, BARDA is supporting several vaccine platforms, and Dr. Kovacs hoped that would spur interest among biotech and pharmaceutical companies to move forward with their own, more innovative platforms. He noted that a lot of the innovation that BARDA supports comes by way of the National Institute of Allergy and Infectious Diseases (NIAID).

Mr. Hosbach called for revisiting the idea of creating facilities with flexible manufacturing capability, which would reduce capital investment costs. When a manufacturer has a lot of capital tied up for years to produce a single vaccine, other opportunities could fall to the wayside. The cost of developing new production facilities is significant, said Mr. Hosbach.

Dr. Orenstein said that if the Assistant Secretary for Health (ASH) charges NVAC with looking more closely at overcoming barriers to vaccine innovation, NVAC should form a working group to delve into the issue.

Dr. Gellin asked whether McKinsey sees any threat to maintaining the current vaccine supply mechanisms. Ms. Azimi said commitment to vaccine development and public health remains strong among business leaders. The industry will likely be watching closely the results of the launch of a new herpes zoster vaccine, which is an incremental improvement. Nosocomial vaccine launches on the horizon will also serve as use cases. Ms. Azimi did not think there was any immediate concern about more companies leaving the market. Mr. Conway said the U.S. vaccine market is stable. However, in the developing world, he predicted that shortages may occur once again because of low profitability.

Ms. Azimi said McKinsey will publish its findings with the next few months. She appreciated the feedback from NVAC.

Identifying and Overcoming Scientific Challenges to Vaccine Innovation—Wayne Koff, Ph.D., The Human Vaccines Project

The old way of developing new vaccines is not working anymore to address the major diseases of the 21st century, said Dr. Koff. Some of the barriers are pathogen-specific: insufficient understanding of the antigens required and the lack of correlates of protection against a range of diseases. Others are issues across vaccinology:

- Limitations of animal models
- Limited understanding of human immune responses to vaccines
- Population-specific issues (e.g., in infants, the elderly, and the developing world)

However, tremendous advances in technology over the past decade offer new opportunities for vaccine research. Antigen discoveries have resulted in reverse vaccinology, mass spectrometry immunopeptidomics, novel platforms for rapid screening (e.g., messenger RNA), and structural vaccinology. For example, researchers were able to look at the genome of meningitis B, identify a relatively small number of surface-exposed proteins, and target vaccine candidates accordingly.

In the area of correlates of protection, human challenge models have advanced the field by allowing researchers to test a wide range of vaccines (accelerating malaria vaccine research, for example). Better understanding of the immune system has led to novel adjuvants. Human immune monitoring may be the greatest advance in the science, said Dr. Koff. Researchers can now look closely at a single cell and look outside the blood to other tissues; these human monitoring approaches together form a systems approach to vaccinology. Next-generation sequencing allows researchers to predict which individuals will respond better to which vaccines. To understand the immune system, scientists will have to generate enormous amounts of data, and data science is beginning to make it possible to gather, store, and analyze very large data sets.

The Human Vaccine Project was created to harness advances to accelerate development of vaccines and immunotherapies. Decoding the human immune system is key to transformational advances in infectious disease, cancer, allergies, and autoimmune diseases. The consortium's primary goals are to decipher the human immunome and to elucidate the rules of immunogenicity. The effort will look at large data sets from around the world, representing thousands of immunomes, and analyze the immunomes at the molecular, structural, and functional level to find common elements that can inform vaccine development. Identifying the rules of immunogenicity means understanding how one elicits a specific antibody response. Dr. Koff envisioned carrying out a number of small vaccine trials of experimental immunogens as a step toward this goal.

The Human Vaccine Project consortium will include large vaccine manufacturing companies, biotech firms, nonprofit foundations, academic scientists, and industry partners in artificial intelligence and machine learning. It will also engage partners in developing countries to support studies in heterogenous populations. The consortium plans to seek diverse funding sources. Dr. Koff projected the effort would take about a decade and cost between $1 billion and $2 billion. The initial discussions and fact-finding around this effort revealed that while there are other research efforts underway, the Human Vaccine Project represents a large-scale problem-solving initiative with a level of integration unlike any other.

Success would have a huge impact not only on thinking about vaccines but also by creating resources on which the next generation of scientists will build. The Human Vaccine Project could accelerate development of vaccines for infectious diseases that are global killers and for cancer. It could also improve the effectiveness of existing vaccines, Dr. Koff concluded.

Discussion

Dr. Orenstein pointed out that Dr. Koff's presentation emphasizes that the challenges are not solely financial. Dr. Koff said key policy issues affecting the Human Vaccine Project are regulatory considerations and interactions with institutional review boards (IRBs). The project received a grant to explore with regulators, IRBs, and communities how to approach small vaccine trials with experimental antigens. In that context, Dr. Koff said, it is important that all those involved have a common understanding about experimental immunogens and experimental medicine trials.

Furthermore, Dr. Koff noted, the Human Vaccine Project will generate a lot of data, so data protection policies are needed. One goal is to make as much information open-source as possible. Questions about big data and privacy have been discussed since the Human Genome

Project mapped the genome. Dr. Koff said this effort will likely result in a map of the human immunome.

Dr. Thompson asked how researchers would structure their work to assess both cross-sectional and dynamic interactions (across and within individuals). Dr. Koff said there are plans to enroll a cohort for at least a decade. In a subset of individuals, the immunome will be deciphered, and researchers can look at their immune systems' responses to vaccines. Scaling up to the number of participants needed for this project requires a lot of funding, Dr. Koff observed, but he was confident that it will be obtained. Dr. Maldonado pointed out that existing data sets may help address the cross-sectional issues. In addition to population variability, Dr. Maldonado noted the need to account for variations in environmental exposures. Dr. Koff agreed that there are many other data repositories that may be available for use, including many outside the United States. Some companies have biospecimens stored from previous vaccine studies. Dr. Omer suggested and Dr. Koff agreed that NVAC could assist by recommending that HHS convene domestic and international experts to identify the existing repositories and other data sources, including data generated as a result of Federal funding or regulatory requirements.

Dr. Omer noted that HHS' Office for Human Research Protections (OHRP) developed new paradigms for research on stored samples for the Human Genome Project that addressed IRB concerns and human subject protections. Dr. Koff said such input from the OHRP and similar international agencies would be very helpful. Dr. Orenstein felt NVAC should take the lead in understanding current systems and how they can be modified to overcome technical and financial challenges to progress.

Maternal Immunization Working Group (MIWG) Update—Richard Beigi, M.D., and Saad Omer, M.B.B.S., M.P.H., Ph.D., NVAC Members

Dr. Beigi said the MIWG was charged with identifying barriers and opportunities for developing vaccines for pregnant women and making recommendations to overcome the barriers. He presented the MIWG's draft recommendations in four categories: ethical issues, policy issues, preclinical and clinical research, and provider education and support.

Ethical Issues

- The ASH should work with the OHRP and other relevant stakeholders and agencies to revise the current exclusionary climate of research in pregnancy. Such areas of focus include but are not limited to:
    - IRB guidance on interpretation on minimal risk
    - Code of Federal Regulations language surrounding research in pregnancy
    - Collaboration with bioethics experts, regulatory agencies and the scientific community to optimize the design of studies to minimize the risk of interventions for research in pregnancy
    - Clarification that pregnant women should be classified as a scientifically complex population rather than a vulnerable population for the purposes of ethical review
- The ASH should work with OHRP and the stakeholder community to develop policy and regulatory guidelines that would promote inclusion of pregnant women in clinical trials when scientifically appropriate.

Policy Issues

- The ASH should continue to support maternal immunization as an important public health strategy to encourage manufacturer investment in the development of new and

currently licensed vaccines for additional indications for use specifically in pregnant women.
- The ASH should advocate to the HHS Secretary to resolve the uncertainties around coverage under the Vaccine Injury Compensation Program (VICP) for vaccines administered to pregnant women that are not recommended for use in children by CDC and for liability protections for live-born infants born to mothers vaccinated during pregnancy.

Preclinical and Clinical Research Issues

- The ASH should prioritize increased support for preclinical and early clinical research to develop vaccines for pregnant women:
    - The ASH should work with Federal and non-Federal stakeholders to create or promote mechanisms that support investigator-initiated and other types of research that foster innovation and expand the field of vaccines for pregnant women.
- The ASH should emphasize the need for a better understanding of the public health burden of diseases preventable by maternal immunization.
- The ASH should work with CDC and other relevant Federal agencies to support evaluation of the maternal and neonatal outcomes of vaccines administered during pregnancy with respect to the 1) safety of vaccines, 2) effectiveness of vaccines to reduce maternal and infant morbidity and mortality caused by vaccine-preventable diseases, and 3) better understanding of the potential risks and benefits of maternal immunization.
- The ASH should support continuing evaluation of vaccines in pregnant women and infants born to vaccinated mothers while advocating for the adoption of standardized approaches to data collection, analysis, and safety evaluation.
- The ASH should support the adoption and utilization of standardized definitions of possible maternal and neonatal outcomes to evaluate the safety and effectiveness of vaccines administered during pregnancy.
- The ASH should convene stakeholders and other Federal agencies to work on the expansion of pharmacovigilance systems that readily link maternal and fetal electronic health records (EHRs) and safety surveillance systems.

Provider Education and Support Issues

- The ASH should encourage professional societies to continue to advocate for clinical research to be conducted in pregnant women.
- The ASH should work with relevant stakeholders to increase awareness among obstetric providers and pregnant women about the importance of vaccine research during pregnancy.
- The ASH should work with professional societies to educate obstetricians and other obstetric providers on vaccination and interpretation of new regulations regarding labeling (e.g., the Pregnancy and Lactation Labeling Rule) so they can make informed decisions and counsel their patients more effectively.

Discussion

Dr. Orenstein asked whether there is a need for further liability protection for clinical trials of an unlicensed product that involve pregnant women. He noted that the VICP applies to licensed vaccines in use. Dr. Omer said there were broad concerns raised about liability during trials and after licensure. The VICP was called out in the recommendations as an example of an existing

framework. Clarification of certain terms and definitions (e.g., definition of minimal risk) would address some preclinical and other concerns. Dr. Orenstein suggested the issue of liability protections for clinical trials and the need for preclinical protections be clarified in the recommendations.

Wayne Rawlins, M.D., M.B.A., cautioned against underestimating the challenges of conducting research among pregnant women. He also noted the importance of communicating information not only to practitioners but also to pregnant women, specifically information about effectiveness and safety. Practitioners should acknowledge to patients what is not known.

Dr. Fleming raised the question of what constitutes an appropriate threshold for safety in clinical trials involving pregnant women. Dr. Omer said the recommendations ask for more clarity, but it may also be appropriate to ask what constitutes an acceptable risk (and in what contexts). The risk-benefit calculation varies by context, he pointed out. Dr. Fleming agreed, saying that a company trying to develop a vaccine would want to know the regulatory standards to which the product would be held.

Ruth Lynfield, M.D., asked whether providers of women's health who are not obstetrician-gynecologists are familiar with vaccine recommendations and what can be done to educate them further. Dr. Omer said there are champions for maternal immunization among all the major women's health practitioner groups, and there is emerging evidence on how to communicate about vaccines in the antenatal setting. Awareness is increasing, and physicians' willingness to recommend vaccination is increasing.

Mr. Hosbach asked how to gather baseline data so that the effects of vaccine can be distinguished from other events. Dr. Omer said the evaluation of risks and benefits should cover the underlying risk. He said the issue could be further discussed in a subrecommendation that addresses platforms. Dr. Beigi noted that there are few data on outcomes, especially internationally. More research involving pregnant women will yield more data about the baseline. Some research among pregnant women includes placebos so that the trial has pregnant control subjects. Dr. Beigi stressed that studies should be conducted with experienced obstetric researchers who can distinguish complications of pregnancy from adverse effects of treatment.

Dr. Gellin suggested identifying within the document those recommendations for domestic policies that may also have international reach.

Dr. Thompson asked whether more research on the placenta should be recommended. Dr. Omer said the recommendations speak broadly in favor of supporting investigator-initiated and directed research. Some examples could be provided. Dr. Beigi suggested the background text reference some current initiatives, such as research on placenta supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Dr. Orenstein recommended that the background text explain how new labeling guidelines regarding pregnant and lactating women influence the field and give some examples. The report should show an FDA-accepted label before and after the change in guidelines and explain the impact of the new guidelines.

Sarah Despres, J.D., suggested the document reiterate that the Advisory Commission on Childhood Vaccines (ACCV) has made the same recommendation regarding VICP, as has NVAC previously. It should also note that the technical clarification is consistent with the intent

of the legislation that created VICP, which was to provide compensation and liability protection for the development of vaccines for children.

Dr. Bennett asked about plans or mechanisms to get more input from women who would be affected. Dr. Omer said the MIWG had input from consumer advocates, but NVPO may be able to facilitate more engagement from individuals.

> **Action Item**
> NVAC members will review the recommendations further and provide additional comments. The MIWG will incorporate comments and prepare final draft recommendations as well as a final report for NVAC approval at its September meeting. The draft report will be sent in advance of the meeting so that NVAC members have opportunity to comment.

Improving Access to and Financing of Vaccines across the Lifespan

Introduction—CAPT Angela Shen, Sc.D., M.P.H., NVPO

CAPT Shen said the Third Immunization Congress built on discussions of previous congresses and NVAC meetings. She noted that financial barriers vary depending on the perspective of the commenter. Providers face challenges with purchasing and managing vaccine inventory and related supplies and with receiving payment for vaccine and vaccination services. While the Affordable Care Act (ACA) generally ensures first-dollar coverage (no copays or cost-sharing) for most vaccines, some adults remain uninsured or have insurance coverage that is not subject to ACA requirements.

The Congress sought to better understand barriers and challenges, primarily from the perspective of providers and payers, so that key barriers to access for routinely recommended vaccines could be addressed. Among the topics of discussion were coding challenges and the possible need for a national coding standard, particularly as payers move toward value-based payment systems; the cost of vaccinating adults; and the financial feasibility of providing vaccines to adults under value-based payment models. A provider panel stressed that providers should not lose money providing immunization services, and providers can take steps to lower their purchase prices.

Overview of the Third Immunization Congress: Financing Vaccines across the Lifespan—James Appleby, R.Ph., M.P.H., Gerontological Society of America (GSA)

Mr. Appleby explained that the GSA represents people in various disciplines who research aging, provide care for older adults, or educate the next generation of researchers or providers. The participation of the GSA ensured that the Congress truly addressed the whole lifespan.

Mr. Appleby reiterated that the ACA increased access to care but financial barriers to vaccination remain. For example, Medicare and some Medicaid beneficiaries do not have first-dollar coverage. The health care system's move from volume to value is a great concept, said Mr. Appelby, but raises challenges, because the value of care may not manifest for many years and is difficult to measure and demonstrate. In addition, immunization rates fall short of Healthy People 2020 goals. Mr. Appleby outlined key conclusions and areas of need identified by the Congress:

Diagnosis and Research

- Ascertain populations for which ACIP-recommended vaccines are not covered.

- Better understand the impact of alternative payment models (e.g., should vaccines be exempt from value-based purchasing models?)
- Better understand existing supports for providers (e.g., vaccine purchasing groups).
- Evaluate the full costs of vaccine delivery to understand whether payment is adequate.

Managing a Vaccine Practice and Helping Providers

- Develop a business case for adult vaccination.
- Establish a national coding standard to simplify and streamline coding across payers and standardize its use without payer-specific modifications.
- Showcase innovative best practices.
- Increase information-sharing about mitigating costs and running operations.
- Address the wide variability among payment plans (e.g., payment for administration of single-antigen vs. multiple-antigen vaccine).

Public Programs: VFC and Medicare

- Clarify Vaccines for Children (VFC) policies: Address the perception that delivery of non-VFC vaccines is faster than VFC vaccines; improve and better align payment; and spell out eligibility (e.g., across State borders).
- Consider what should be covered through Medicare Part D.

Surveillance and Health Information

- Gather more data on adult vaccination (e.g., cost-effectiveness and benefits of investment) to distinguish vaccine failures from failure to vaccinate.
- Improve data on the global and societal costs of adult vaccine-preventable diseases.
- Address vaccine registries (e.g., linking reimbursement to entry of information into a registry) across the life course.

The key takeaways of the Congress can be summarized as follows:

- Develop the business case for vaccinating adults and disseminate it widely to encourage providers to supply vaccines to older patients.
- Sort out coding issues, which are confusing and can put practices at risk.
- Examine whether the current payment system is adequate and what alternatives exist.
- Ensure appropriate, ongoing surveillance so that data can be gathered to demonstrate the effectiveness of vaccines.

Mr. Appleby concluded that it is important to distinguish the very-hard-to-do (e.g., convince every American of the need for adult vaccination) from the hard-to-do. He said NVAC could help by addressing coding, surveillance, and reimbursement and creating a business case for adult vaccination.

Financial Barriers in Adult Immunizations from the Family Physician Perspective—David G. Cope, M.D., American Academy of Family Physicians (AAFP)

Dr. Cope detailed some provider barriers, most notably the concern that physicians will lose money with adult vaccinations because of the hidden costs of storage, handling, documentation, etc., and reimbursement rates that only cover vaccine acquisition costs. He noted that even when prices are negotiated online with manufacturers, there is no guarantee that the prices will stay fixed. Providers must also take into account spoilage (e.g., from a power outage or errors).

Coding is burdensome and complicated, and the variations in payments among providers make it difficult to tell patients whether a vaccine is covered.

More consistency would help overcome these barriers—such as reliable suppliers and uniform coverage guidelines (e.g., that follow ACIP guidelines). Developing a common database seems feasible, said Dr. Cope. He suggested that State registries could link to a national registry, and interoperability between registries and EHRs would be even better. Dr. Cope said physicians want to do the right thing, but they do not want to lose money doing it.

Vaccine Financing Challenges: The Pediatric Perspective—Geoffrey Simon, M.D., American Academy of Pediatrics (AAP)

Dr. Simon echoed concerns raised by previous speakers. He said payers vary in their interpretation of even standard codes, and the inconsistency results in unnecessary costs and burden to providers. Payers vary in their payment rates for products and administration fees (e.g., some do not accept the codes for additional components in multi-antigen vaccines, although the codes were intended to incentivize use of combination vaccines to improve vaccination rates). Providers face infrastructure and storage issues, although CDC is working with VFC providers to address these. Program administration and eligibility pose a challenge, because it is not always easy to distinguish Medicaid from State children's health insurance plan (CHIP) beneficiaries, which differ in eligibility for VFC.

To move forward, Dr. Simon called for a national coding standard across public and private payers. The National Coding Initiative should evaluate coding issues and ensure clarity. Changes in coding requirements necessitate changes in billing processes and software, which are costly and burdensome. Also, consideration should be given to creating a carve-out for immunizations in value-based payment models so that the models recognize the costs of storage and the work of administration. Further review of State Medicaid payments is needed to address the low rates and the wide variability across States. For VFC, said Dr. Simon, efforts should focus on clarifying program eligibility and requirements and better aligning payment with the private sector.

Remarks from the American College of Physicians (ACP)—C. Michael Soppet, M.D., ACP

Dr. Soppet said that in 2014, Medicare vaccine reimbursement exceeded the cost of the product by $6 to $25 per dose, and the reimbursement rate for administration was approximately $25 for the first dose and half that for subsequent doses. The ROI ranged from 19 percent to 207 percent. Dr. Soppet pointed out that providers were very savvy purchasers of vaccine who were able to buy products below the average wholesale prices, but those discounts have since disappeared, especially for high-dose formulations such as quadrivalent influenza vaccine.

In contrast, in 2016, payment for the vaccine exceeded cost by $0 to $4 per dose, and administration payment rates dropped slightly. As a result, the ROI now ranges from 3 percent to negative 1 percent (i.e., a loss), largely because some vaccines are so expensive.

Dr. Soppet said the ACP advocates for a learning system so that practices that are not currently stocking vaccines can do so at no risk, perhaps in concert with distributors or manufacturers. For example, just as some hospitals currently use automated medication dispensing systems, a similar mechanism could be created to store and dispense vaccines. It could have battery backup to protect against power outages and biometric identification so that every barcoded dose is identified and matched to a particular patient. The distributors or manufacturers could manage the system, and providers would only need to determine which patients need vaccines.

Finally, the ACP calls for disbanding Medicare Part D, because it conflicts with the goals of adult vaccination. At the least, Part D should be on hold until it can be made to function more like Part B, said Dr. Soppet.

Perspective of the American College of Obstetricians and Gynecologists (ACOG)—Debra Hawks, M.P.H., ACOG

Ms. Hawks explained that ACOG surveys, focus groups, and expert input from obstetrician-gynecologists (ob-gyns) reveal that cost is the biggest barrier for ob-gyns. For example, a single three-dose series of HPV vaccine costs the practice $400, and that does not take into account related storage, personnel, or administrative costs. A practice with a large vaccine inventory is one power outage or unclosed refrigerator door away from financial disaster, said Ms. Hawks.

Payment is a major barrier for ob-gyns to provide vaccination. The typical profit margin is 5-10 percent, which translates to breaking even for a medical practice. Payment rates can take as much as 6–12 months to catch up with product price increases. Strategies to enhance payment often involve substantial administrative burden, but administration services come with high overhead but low returns. Ob-gyns must track paperwork diligently to ensure that, at a minimum, the costs of the goods purchased are covered by payers.

Often, ob-gyns cannot compete with retail pharmacies that can offer lower-cost vaccinations and greater convenience. The challenge is compounded for high-cost vaccines and those that are not eligible for first-dollar coverage. Lastly, said Ms. Hawks, unlike pediatricians, ob-gyns and other providers who see adults primarily do not have a high volume of demand for vaccine services.

AHIP Perspective—Scott Breidbart, M.D., M.B.A., AHIP

Dr. Breidbart said all of the presenters agreed on the need to increase awareness about the importance of vaccines and foster an expectation that adult vaccines be covered and delivered in the same manner as childhood vaccines. In response, health insurers are implementing value-based incentive payments that reward preventive care and helping providers adopt more efficient practices so they can make a profit on the vaccines they give. Insurers promote vaccine safety and effectiveness and work with various populations to decrease disparities.

Dr. Breidbart agreed with the need for a payment system that ensures that efficient providers can give vaccines. He acknowledged that it may not be possible for ob-gyns to be efficient vaccine providers, especially if they work in standalone practices that do not include internists or pediatricians. He also pointed out that other clinical services also involve overhead costs that must be factored in, regardless of expense.

Vaccines are so important that they must be considered an integral part of delivering care, Dr. Breidbart concluded. He called for collaboration to improve coverage, increase awareness, and make the case that adult vaccines are as important as childhood vaccines.

DISCUSSION

Dr. Orenstein asked how health plans decide reimbursement, and Dr. Breidbart said a lot of factors go into the calculation. The standard payment for oncology drugs, for example, is calculated as the average sales price plus 6 percent. However, the formula may incentivize providers to choose more expensive drugs. There is always some negotiation, said Dr. Breidbart, but reimbursements are usually based on CMS rates.

Dr. Fleming asked if any research has evaluated the relative contribution of each of the various barriers to the overall problem, in which settings they exist, and how they impact coverage. He asked presenters to name two or three barriers to address that would make the biggest improvements in U.S. adult immunization rates. Mr. Appleby said that removing any of the barriers would make vaccination easier for providers, but he suggested focusing on coding, which is a solvable, targeted issue that requires the most will to address.

Ms. Hawks said the importance of the barriers varies among providers. An ACOG survey found that solo practitioners reported more barriers to receiving payment than those in group practices. Dr. Cope recommended targeting consistent, equitable payment, which encompasses coding. Dr. Soppet called for a single code for adult vaccine administration. He also suggested creating two systems at first—a simplified version of the current billing system and a learning system for small practices that cannot purchase and store all the vaccine they need up front. Dr. Soppet added that practices need stable markets.

Dr. Thompson asked if having national standards for interoperability between EHRs and immunization information systems (IIS) would be helpful. She also asked whether the financial calculations presented take into account the costs of interfacing with IISs and EHRs, which adds cost and burden to providers. Mr. Appleby said the current registry approach is good for pediatricians, but there is no cultural expectation for a similar approach for adults. The GSA believes there is enormous value to interoperability between EHRs and IISs, and the technology exists (as seen with prescription monitoring programs used to flag opioid use). There should be a mechanism that consumers can use to get their information as well, said Mr. Appleby. Dr. Cope said interoperable IIS and EHRs are a very high priority. Patients often cannot recall which vaccines they had, when, or where. Ms. Hawks added that there should be one system for the whole life course. Some States limit recordkeeping at age 18, so the patient must start a new record as an adult. Dr. Soppet said there is an opportunity to leverage current requirements for quality and practice improvement around advancing health care information by focusing on reporting adult immunizations.

In response to Dr. Thompson, Dr. Simon said the AAP's business case did include the costs of submitting data to IIS, which involved some manual administration and eventually the interface with EHR. He hoped the Medicare Access and CHIP Reauthorization Act would eliminate the need to do both. The heterogeneity of systems is a significant barrier, as is the variation in laws and regulations across States. Dr. Simon said the AAP determined that the biggest concern around a national IIS is data integrity. At the Congress, there was discussion about universal access by providers to separate state databases by means of a unique personal identifier code. That approach may be easier than creating a national database, which could take decades, said Dr. Simon.

Mitchel C. Rothholz, R.Ph., M.B.A., pointed out that the barriers fall into two categories: what it costs providers to give service (across all providers) and the impact of policies and procedures, such as coding. With the new focus on quality, he asked, is there recognition of the costs of improving quality and are there enough incentives for practices to invest in mechanisms that measure quality? He further asked presenters how their members are measuring the impact of immunizations and whether practices are taking a team/community-wide approach or focusing on individual practices.

Dr. Soppet said small practices are moving away from immunization, although some are pursuing partnerships or contracts to manage them. The ACP is trying to develop tools to help

small practices. Dr. Cope said his practice has merged with others to create a very large group but still faces the same problems around economies of scale.

Dr. Simon said pediatricians are affected by policies aimed at adults. Regarding the team approach, he said the AAP is working on defining what it means to be a good neighbor within the medical neighborhood in terms of supporting the medical home and outlining the appropriate scope of practice in various settings.

Dr. Rawlins underscored several important points. First, private and public payers pay very differently. Second, coding consistency will be critical, but financial success is easier for those who work in groups, who can focus more on volume, and who address efficient management. Third, engaging low-cost, high-quality providers to create an immunization neighborhood, such as retail pharmacies, is an important concept in team-based care. Fourth, information technology (IT) systems should not just be interoperable but should also help with clinical decision support and inventory management.

Dr. Cope agreed that engaging third parties as partners in immunization helps everyone, but to make that approach work, shared databases are needed to identify who has received which vaccines. Dr. Soppet pointed out that practitioners can see when a patient has filled a prescription but not whether a patient has received a recommended vaccine. Ms. Hawks said recordkeeping is critical, especially for quality assessment and measurement. Dr. Breidbart said the situation should improve as insurers have more data exchange capacity with primary care providers. Insurers can give providers data on whether a prescription was filled or a referral obtained, so they could also give information about vaccination.

Rebecca Coyle, M.S.Ed., cautioned that tracking adult histories is hard because there is no central repository. To ensure a complete history, someone has to take ownership and responsibility for collecting adult patient data. Dr. Cope pointed out that entering data is the most onerous part of patient care. Interoperability between IISs and EHRs could alleviate some of that work. Dr. Soppet added that new patients usually do not know their vaccination history. He pointed out that Alabama has a good pediatric registry, and even school nurses have access to it, but tracking becomes problematic if patients get vaccinated at a retail pharmacy.

There is no easy way for adults to get EHR data into a State registry, said Dr. Soppet. With fewer than 100 IIS systems in the country, there should be a way to facilitate information exchange. Dr. Soppet proposed using new approaches to digital patient identification to speed up data entry and improve accuracy. Mr. Appleby expressed optimism that with momentum, the field could move forward on the idea of universal provider access to immunization records. Ms. Hawks noted that ob-gyns face challenges getting a complete medical history from a prenatal patient.

CAPT Shen asked for verification that despite national coding standards, payment varies across private players. Dr. Simon said payers vary in their interpretations of codes (e.g., the number of units covered and the use of coding edits). The AAP has identified inconsistencies related to payments and claims processing across payers through data collection. Dr. Rawlins agreed that plans may have different interpretations of codes, especially around modifiers, that affect reimbursement. Dr. Breidbart said that if there are areas where the correct coding is not clear and there are discrepancies among plans, he would support an effort to make sure that all the coding is straightforward and accepted everywhere.

Mary Beth Hance explained that the statutory language of VFC prohibits the use of certain codes, so combination vaccines are paid at the same rate as single-antigen vaccines. The Office of General Counsel has reviewed the issue many times, and there is no flexibility in the statute. Dr. Simon called for some creative thinking around financing mechanisms or billing approaches that would support the goal of ensuring children are vaccinated. Ms. Hance said CMS updated the VFC fee schedule for the first time in 2012, raising the cap on payments. Many States pay above the cap.

Asked for clarification around eligibility for VFC, Ms. Hance said States have the flexibility to provide CHIP coverage through Medicaid expansion, a standalone CHIP, or a combination of both. Those covered by Medicaid expansion qualify for VFC, just as those in traditional Medicaid programs do. Those in standalone CHIPs or combination programs can get vaccines without cost-sharing but not through VFC. States can buy vaccine on their own or work through CDC for purchasing, but it is the responsibility of the provider to give vaccines purchased for VFC only to children eligible for VFC. Finally, Ms. Hance said CMS is working with States to improve identification cards so it is easier for providers to determine which program a child is in.

Dr. Orenstein concluded the session by noting there are still substantial barriers. He hoped NVAC would consider forming a working group to address them.

Immunization Priorities at the Local Level: NACCHO Immunization Workgroup—Paul Hunter, M.D., and Tiffany Tate, M.S.H., Co-Chairs

Dr. Hunter gave an overview of NACCHO and its priorities, noting that local health departments in general are the immunization champions within their communities. He said ASTHO is a sister organization to NACCHO, helping to ensure collaboration and coordination across the spectrum from local and State health departments up to Federal organizations and agencies.

Over the past year, the Immunization Workgroup has updated NACCHO policies on comprehensive immunization programs, school and child care immunization requirements, and local health department capacity for third-party billing for immunization. NACCHO's goal is to align its policies with other organizations and to share information efficiently and effectively. It aims to foster relationships by identifying key people in other organizations and to develop clear messages and passionate champions to deliver those messages.

The updated NACCHO policy statement on comprehensive immunization programs continues to support the idea that the Federal immunization program should provide sufficient funding through VFC and Section 317 for vaccination of uninsured and underinsured children, adolescents, and adults. NACCHO advocates for collaboration and coordination to bridge the gap between clinical medicine and public health to increase vaccination rates. The policy statement indicates that local health departments are key to coordinating immunization activities and lists three strategies for increasing vaccination rates:

- Adequately fund products and processes that ensure that vaccines reach residents as well as other activities to monitor vaccine uptake and need by using information systems.
- Provide timely education and training to increase the demand for immunizations among patients and parents, promote strong vaccine recommendations by clinicians, minimize missed opportunities, ensure series completion, train community vaccination champions, and reach underserved populations.

- Identify and address disparities by monitoring and responding to gaps and trends in vaccination rates (which requires interoperable IISs and EHRs), use clinical decision supports to make confusing ACIP recommendations clearer for clinicians, support local health department epidemiologists and other staff in measuring the impact of policies, and address equity of outcomes in immunization rates.

Dr. Hunter named four ways that NVAC can help achieve the ideal immunization program. First, NACCHO requests that NVAC foster bidirectional communication with local health departments, via NACCHO, to clarify how NVAC's general principles and recommendations apply to local health departments. Second, NACCHO asks that NVAC work to eliminate the deficiencies and unintended consequences of the ACA, especially for other organizations within the Federal government setting. In particular, NVAC should address the fact that the ACA includes little or no funding for immunization program infrastructure, especially for pandemic response. Also, patients are still using local health departments for vaccinations because of the high deductibles for clinic visits (and because they may have outstanding bills from when they were uninsured that they would be required to pay before they can get care).

Third, NACCHO requests that NVAC speak out about the importance of adequate funding not only to set up IISs but also to sustain them. These systems are in constant need of improvement and adjustments. Funding is needed to take the data from the registries and apply them in a meaningful way at the local level, which requires epidemiologists who can extract the data. Currently, epidemiologists doing such work are funded by emergency preparedness funds that are going away. Another option is to train nurses and other clinical staff to fully utilize the functionality of IIS. Furthermore, facilitating data exchange between IIS and medical records takes a lot of staff time.

Fourth, despite the financial and technical barriers, NACCHO asks that NVAC demand a more effective pertussis vaccine. The current situation is eroding vaccine confidence. It is not acceptable for a disease that was under control to become endemic again. In summary, Dr. Hunter said NACCHO is seeking NVAC's help in promoting, sustaining, and improving the processes that turn innovative vaccines into vaccinations that prevent disease.

Discussion

Dr. Bennett asked whether NACCHO is providing technical assistance to local health departments to enable them to reach out to health care providers in their communities around vaccination. Dr. Hunter said local health departments do play a role in bringing together providers throughout the community, and he agreed to raise the issue with the NACCHO Immunization Workgroup.

Dr. Thompson asked whether NACCHO feels that local health departments have adequate funding for communication and outreach. She also requested that NACCHO consider gathering evidence to demonstrate that insured people are still getting vaccinations at health departments because of high deductibles and outstanding financial issues. Data could reveal a meaningful indicator about access and continued barriers to care. Dr. Hunter responded that local health departments get funding from numerous sources that come and go, so it is difficult to say who has adequate funding.

Ms. Tate said NACCHO is creating a subcommittee within the Immunization Workgroup with an ACA expert that will look more closely at the anecdotal reports about access and financial barriers. She added that discussions are also underway about how to address operational

issues around immunization, such as antiquated phone and computer systems, and the difficulty of vaccinating children in a community setting in the absence of a parent.

In response to a suggestion from Mr. Rothholz, Ms. Tate said NACCHO's annual survey could be revised to ask local health departments to identify their highest-priority concerns to see where immunization issues fall. Another way to assess priorities, said Dr. Hunter, is to look at what services local health departments continue to provide as they divest from direct service provision. Immunization is often continued when other services are cut. Mr. Rothholz also suggested NACCHO document the funding cuts that local health departments are experiencing and explore how they are working with other providers in the community to fill the gaps.

Dr. Orenstein pointed out that some of the barriers may be related to grandfathered plans, which are disappearing over time. In some cases, local health departments are considered out-of-network providers, which can pose financial complications for patients. Amanda Cohn, M.D., said that understanding the access issues would be helpful, because the issues vary across urban and rural areas and are challenging to sort out at the national level. She advocated for collaboration between NACCHO and Federal partners around the topic.

Public Comments

Sallie Elkordy read a letter from Viera Scheibner, Ph.D., which states that information on the ineffectiveness of vaccines and the serious reactions to them have been documented and published in reputable medical and scientific journals. The letter noted that the only effect of vaccines is anaphylaxis sensitization, a harmful immune response resulting in increased susceptibility to the targeted diseases and also to related and unrelated bacterial and viral infections. The letter indicated there is no benefit whatsoever from vaccinations and identified the term "vaccine-preventable" as false advertising. Dr. Scheibner's letter says that the long-term deleterious vaccine effects are behind "modern diseases," such as cancer, chronic ill health, immunoreactive, autoimmune, and immune disorders, vaccines are contaminated by chemicals and biologicals which should never be injected into anything living. The letter noted that animals suffer the same deleterious effects as humans and that the deleterious effects of vaccines are characteristic but not specific to any one vaccine and instead subject to the biological concept called the nonspecific stress syndrome.

Dr. Scheibner's letter goes on to state that any further development of vaccines is futile and should be scrapped and that all mass vaccination programs should be abandoned. The only immunity is natural immunity achieved by exposure to natural infectious diseases. Natural infectious diseases are beneficial by priming and maturing the immune system, and they also represent developmental milestones. For these reasons, Ms. Elkordy asked that NVAC call for a national moratorium on vaccination.

Theresa Wrangham, executive director for the National Vaccine Information Center (NVIC), expressed concern about privacy and IRBs. It is important that as testing vaccines on pregnant women is discussed, prior samples and the conditions under which these samples were given meet privacy expectations of participating individuals. Where there is no permission to use this repository of samples outside of the original intent, privacy must be respected as the condition under which informed consent for the original procedure was given and nothing more. Ms. Wrangham also had concerns about redefining pregnant women as a scientifically complex population. Currently pregnant women are considered to be a vulnerable population, and it is difficult to imagine that there is anything more vulnerable than an unborn child or the pregnant woman.

The NVIC asks that NVAC exercise extreme caution on any recommendations that would lower the bar to allow pregnant women to participate in clinical trials in the context of the benefits for the greater good when there is admittedly little data to support that context where pregnant women are concerned. Mothers-to-be are primarily concerned with the health of their unborn child. Additionally, it is important that if pregnant women do agree to participate in vaccine trials, that the risks, both known and unknown, and any use of their information and/or samples in the future be clearly spelled out as part of the informed consent process.

The NVIC appreciates the suggestion that pregnant women have input into the maternal vaccination plan. Pregnant women are the most impacted by these plans, and their input, concerns, and wishes must be primary to any process put into place. They should also have the ability to exercise informed consent to opt out of any maternal vaccines.

While there are challenges with coding and reimbursement that deserve resolution, the incentivization of health care providers to administer vaccines is a conflict of interest where patient care is concerned. The provider must at all times be discharging informed consent, which means no coercion or harassment for decisions made by a patient who delays or declines one or more vaccines or another recommended treatment regardless of the reason for doing so.

The NVIC receives reports daily from consumers being kicked out of private practices and denied medical care for exercising their informed consent rights to delay or decline one or more vaccines. Vaccines are pharmaceutical products that are acknowledged as carrying the risk of injury and death, and people must have the right to exercise their informed consent rights. The health care provider's primary duty is to the patient, and incentivizing them to deliver Healthy People 2020 goals undermines patient autonomy and patient-provider trust.

Lastly, the NVIC remains concerned about the security of IISs and the ability of individuals to exercise control over their private health information. Many people do not even know that they are participating in efforts to create a Federal database for tracking vaccine status. Participation in such systems should be voluntary, and there should be more transparency with the public on the use and security of these databases so the consumers can decide what health information they wish to share with their government.

NVAC members reviewed written comments submitted in advance of the meeting.

Conclusion

Dr. Orenstein briefly recapped the highlights of the day and adjourned the meeting for the day at 4:47 p.m.

Day 2—June 8, 2016

Welcome—Walter A. Orenstein, M.D.

Dr. Orenstein called the meeting to order at 9 a.m. and began by inviting the liaison members and ex officio members to provide their updates.

NVAC Liaison and Ex Officio Updates

ACCV—Narayan Nair, M.D. (for Charlene Douglas Ph.D., M.P.H., R.N.)

Dr. Nair said the ACCV met in early June and reviewed a petition to add neurologic injuries to the Vaccine Injury Table for influenza vaccine. The group reviewed the literature and found no support for the request. The ACCV voted not to add any new language to the table.

AHIP—Scott Breidbart, M.D., M.B.A.

The AHIP participated in planning for the Third Immunization Congress: Financing Vaccines across the Lifespan. It is working with member plans on enhancing the effectiveness of vaccines across the lifespan.

AIM—Claire Hannan, M.P.H.

Ms. Hannan said AIM created a program manager shadowing program in response to members seeking training and an influx of new members. New managers will visit experienced managers in the workplace so they can see immunization programs at work. Also, AIM is planning its first regional meeting of program managers in HHS Region 5 to discuss common challenges, success, and collaboration.

AIM participated in the Third Immunization Congress on financing and the recent National Adult and Influenza Immunization Summit. At the Summit, Ms. Hannan spoke about the timing of influenza vaccine distribution in the VFC program. AIM is working with the AAP to encourage immunization programs to distribute VFC vaccines to providers as soon as possible and to communicate with medical societies and VFC providers early and often during influenza season. AIM saw some improvements this past influenza season, but there were still some shortages and delays (e.g., with FluMist) and other issues that influence timing. AIM will continue working with ASTHO and AAP on the topic.

Also, AIM participated in the national conference on IISs and presented on using data to support programmatic activities. The presentation was very popular, so it will be repeated in a webinar. One AIM priority area is to encourage program managers to use their data even if it is not as robust as they would like it to be, because the more they use it, the more robust it will become. Finally, AIM has an adult immunization resource guide coming out in July.

ACIP—Nancy M. Bennett, M.D., M.S.

At its February meeting, ACIP heard background comparing a two-dose and three-dose schedule for HPV vaccine. At the June meeting, ACIP will review further evidence and considerations around a two-dose schedule. The group also reviewed the use of meningococcal vaccine in people living with HIV and for men who have sex with men. For Japanese encephalitis vaccine, ACIP heard data on the duration of protection; it will continue to assess its recommendations for the vaccine. For influenza vaccine, ACIP approved some changes to the recommendations related to egg allergies. The manufacturer of a cholera vaccine presented data for ACIP's consideration in forming recommendations for its use in those at risk for travel-related exposure to cholera.

At its June meeting, ACIP will further review evidence around the cholera and meningococcal vaccines. It will discuss the high-risk figure in the Child/Adolescent Immunization Schedule as well as RSV vaccine for older adults, influenza vaccines, and HPV vaccine. The deadline for nominations for members of ACIP is June 30, 2016.

AIRA—Rebecca Coyle, M.S.Ed.

About 350 participants attended AIRA's annual meeting in April, including some international participants. The event included more than 50 presentations, ranging from basic information on

IISs to more advanced presentations such as what an IIS can achieve in an ideal setting. Ms. Coyle said AIRA is sensitive to concerns raised by providers about interoperability and so launched its Interoperability Testing Project in 2015 to look at how IISs were implementing HL7 interface standards. As a result, AIRA is connected to almost all of the IISs and better understands where improvements are needed. The next step will be identifying the interoperability standards to achieve. The project also created a feedback tool that programs can use to improve their interoperability.

Recently, AIRA published best practice guidance on managing inventory via electronic data exchange, which details what systems should be able to do around vaccine administration, including how to perform accounting from virtual inventory. The Joint Development and Implementation Workgroup is looking at ways to improve data quality. It hopes to determine opportunities for a nationally implemented service for address cleansing and geocoding. Ms. Coyle announced that 2 weeks ago, New Hampshire received authority to start operating an IIS, and it is the last State to develop one.

ASTHO—Kimberly Martin, M.P.H.

In 2014, ASTHO convened a meeting to discuss barriers and solutions around multistate IISs and interstate data exchange. As result, ASTHO worked with the Network for Public Health Law to develop a template memorandum of understanding (MOU) on interjurisdictional data exchange. ASTHO and AIRA are working together to get final agreement on the MOU from all six States that attended the meeting by this fall. In addition, ASTHO developed a template MOU that is intended to formalize the responsibilities between State level public health programs and pharmacies during pandemic vaccination planning and response efforts. The MOU is being piloted; it will be accompanied by a resource guide explaining the steps to implement the MOU. The guide will be ready in the fall.

Finally, ASTHO has been working to identify best practices among State health departments that provide vaccination to uninsured adults. This project will describe how States locate adults that are uninsured and identify providers that serve this population. The guide to best practices should be ready by late summer or early fall.

NACCHO—Tiffany Tate, M.S.H.

In addition to efforts by the Immunization Workgroup detailed on the previous day, Ms. Tate said NACCHO recently combined five policy statements into a comprehensive immunization program policy statement. It updated policy statements on school and child care immunization requirements and on third-party billing for immunizations for local health departments. Also, NACCHO collaborated with the CDC to survey local health departments about their use of IISs for programmatic and clinical functions.

NACCHO received funding from CDC to enhance the ability of local health departments to partner with health care providers and other community stakeholders to implement ACIP vaccination recommendations for HPV. NACCHO worked with 10 programs to develop action plans, which are now being implemented. In a second phase of funding, NACCHO is working with 10 more local health departments on action plans. In January, NACCHO updated its guide to HPV resources for local health departments. Finally, NACCHO hosts the HPV Learning Community, an online forum for local health departments to share their lessons learned, resources, experiences, and action plans developed through the CDC funding opportunity.

PHAC—Rhonda Kropp

With the new Federal government in Canada came a new budget, said Ms. Kropp, which provided $25 million over 5 years for immunization. The funding requires PHAC to 1) update national goals and targets, which it will do by the end of 2017; 2) improve Canada's ability to identify under- and unimmunized populations; and 3) develop a program to improve immunization coverage rates in Canada.

To improve coverage, PHAC is supporting continued use and development of the Immunize CA app, which is becoming incredibly popular. It puts into the hands of Canadians the evidence to make decisions about when to get immunized and what immunizations they need. It also gives personalized information on when they and their children are due for immunization. Further development of the app aims to link directly to the IIS in each jurisdiction so that Canadians can access their records and upload their information themselves.

PHAC is working with the provinces and territories to update the national immunization strategy, which has been in place since 2003. The process of updating the strategy will be more publicly transparent as to objectives, activities, responsibilities, and timelines. There is discussion underway about an ongoing evaluation or performance measurement strategy that would be made public.

The National Advisory Committee on Immunization is creating planning guides that provide not just technical recommendations but also cost-effectiveness recommendations so that jurisdictions can have both as they make decisions about implementation of programs.

PAHO—Cara Janusz, M.P.H., M.A.

Ms. Janusz said that, in a globally coordinated effort, 36 countries in the Americas participated in the global switch from trivalent to bivalent oral polio vaccine, and 35 of those have submitted validation reports to PAHO. The successful completion of the switch is a great milestone for global polio eradication.

Vaccination Week in the Americas took place April 23–30, targeting about 60 million people for vaccination against a wide range of diseases. In April, PAHO led a meeting of its technical advisory group on the use of dengue vaccine in routine immunization programs and the limited global supply of inactivated polio vaccine. The final report is available online. In August, a regional, international expert committee will meet to assess the feasibility of declaring the Americas free of measles. The last endemic case was reported in Brazil in July 2015.

AHRQ—Iris Mabry-Hernandez, M.D., M.P.H.

Dr. Mabry-Hernandez said AHRQ continues to spread knowledge about vaccine-related topics through funding of investigator-initiated research grants on topics such as geographic access to care and HPV vaccine uptake among at-risk girls, using health IT to improve delivery of HPV vaccine, and using a social media website for parents who are concerned about vaccines, so that they may have access to accurate information. Dr. Mabry-Hernandez announced that AHRQ appointed a new director, Andrew Bindman, M.D., in May.

ASPR/BARDA—Gerald Kovacs, Ph.D.

BARDA continues to support development of an attenuated smallpox vaccine (IMVAMUNE) to improve stockpiling efforts for this vaccine. It awarded a $100-million contract to Bavarian Nordic, the developer, to purchase a lyophilized, long-lasting product once approved. In the long-term, BARDA plans to transition to a formulation that does not have to be rotated as frequently as the liquid formulation currently stockpiled. BARDA also called on the Centers for

Innovation in Advanced Development and Manufacturing to produce a single-dose intranasal vaccine for anthrax.

A study designed to assess the usability of a long-term H5N1 influenza vaccine is underway. An independent data monitoring committee is meeting to assess the most recent results from blood sampling. The influenza division is also working collaboratively with NIAID to support the development of novel universal influenza vaccine.

BARDA continues to work closely with the CDC on the Sierra Leone Trial to Introduce the Vaccine against Ebola (STRIVE) study. Clinical samples are now at CDC awaiting shipment to a company that uses gamma radiation to ensure sterility prior to evaluation and diagnosis of the samples. Merck has presented data from trials of its Ebola vaccine to FDA for review. Another candidate being manufactured by Janssen Pharmaceutical and Bavarian Nordic is awaiting FDA validation for the adenovirus portion of the vaccine.

In response to Zika virus, BARDA activated the national medical countermeasures response infrastructure to promote rapid development and evaluation of vaccine candidates. The network is developing reagents and vaccines to support product developers. BARDA is also working closely with DoD's Walter Reed Army Institute of Research and NIAID on a whole, inactivated vaccine candidate that will be in trials in the fall of this year. BARDA continues to encourage the private sector to propose novel vaccine platforms for Zika virus.

CDC—Amanda Cohn, M.D.

Dr. Cohn announced that Nancy Messonnier was named director of the National Center for Immunization and Respiratory Diseases (NCIRD) in March. In May, NCIRD held a technical expert consultation on knowledge gaps around RSV vaccine. NCIRD will continue to make investments to prepare for the introduction of RSV vaccines. In addition, an ACIP workgroup on RSV vaccines was formed.

Monitoring for the STRIVE study of Ebola vaccine in Sierra Leone will likely be completed by the end of the summer. All the regulatory files will remain in Sierra Leone but will be reviewed by CDC, and results will be disseminated in the near future.

CDC staff continues to be engaged in a global polio eradication effort and is working to assist in laboratory containment of polio virus. As of May 24, CDC completed a survey to identify infectious or potentially infectious polio virus materials at all CDC labs. Of non-CDC laboratories, 71 percent of the first cohort targeted have completed the survey, and the rest have been contacted. The National Polio Containment Program is on track to submit its final draft on polio virus containment on July 29 to the National Certification Commission.

Influenza activity in the United States peaked in week 10 of 2016, ending March 12. Only three of the past 18 influenza seasons have peaked in March. Most of the influenza viruses circulating from October 2015 through February 2016 are antigenically similar to vaccine virus strains recommended for the 2015–2016 vaccine.

On June 5, CDC released a *Vital Signs* report that looked at Legionnaires' disease outbreaks and the sources of exposure and deficiencies in environmental controls of Legionella, highlighting the most common types of buildings associated with outbreaks and why they happened. The goal is to raise awareness and prevent future outbreaks of Legionnaires' disease.

A project to improve the usability and readability of the immunization schedule is being launched this summer. Additionally, the ACIP's Adult and Childhood Schedule Workgroups will collaborate with vaccine-specific workgroups to harmonize and simplify language in the schedule footnotes where feasible.

Finally, the National Immunization Conference will be held in Atlanta in September. Sessions will address adult immunization, IIS, programmatic issues, health and risk communications, epidemiology and surveillance, and childhood and adolescent immunizations.

CMS—Mary Beth Hance

CMS annually releases data on its core measures. This year, CMS created domain-specific appendices to accompany the report. The prevention domain includes the immunization quality measures for children as well as the influenza measures that are part of the adult report. The information is available online at Medicaid.gov.

DoD—COL Margaret Yacovone, M.D., M.S.P.H.

DoD's Accession Screening and Immunization Program is designed to ensure military recruits receive the appropriate immunizations and to gain clinical and economic advantages by delivering only those vaccines required for each individual. Cost-minimization analysis of the program has verified its importance. DoD is also projecting future cost savings by standardizing serologic testing procedures, infrastructure, and laboratory utilization, as well as the use of registry data and other resources.

The Continuous Quality Immunization Improvement Process (CQIIP) Program assesses compliance of immunization clinics with DoD's standards of military immunization. Immunization health care specialists assist immunization clinics around the world with assessment. First, the immunization clinic staff conducts a self-assessment of compliance using a CQIIP customer tool, and the Defense Health Agency (DHA) analyzes the data. Then, DHA staff visits the immunization clinic staff to review practices onsite and recommendations for improvement. Since 2013, DHA has conducted over 1,300 CQIIP assessments in agencies supporting active duty, National Guard, and Reserve components around the world.

DoD military and civilian health care personnel are required to complete 8 hours of immunization training annually. Educational offerings include an on-demand online curriculum and monthly webcast to provide consistent, accurate, and timely education. DoD also offers onsite training, Stateside and overseas, to ensure health care personnel are trained in vaccine policies, safety and effectiveness, and the standards of military immunizations. The onsite courses provide clinic leaders with an in-depth understanding of responsibilities of successful management of an immunization program. In the first 5 months of this year, DoD has conducted 40 immunization educational activities to 1,700 health care personnel.

The DHA's Immunization Healthcare Branch website is migrating to **www.health.mil/vaccines**. The new website offers new functionality and access to vaccine publications, vaccine policies, and educational material. The migration supports the Military Health System's initiative to standardize the design of web pages and consolidate public websites to the new health.mil platform.

Lastly, DoD is working with FDA on an expanded access investigational new drug application with Sanofi Pasteur for a yellow fever vaccine. DoD continues to support Bavarian Nordic with coordination of the Phase III study in the Republic of Korea.

FDA—CDR Valerie Marshall, M.P.H.

In April, FDA approved the supplement to the biologics license application (BLA) for meningococcal group B vaccine, Trumenba®, to include a two-dose schedule, according to the regulations for accelerated approval. The approval also included a modification of the three-dose schedule. Also in April, FDA approved BLA supplements to change the product labeling for several vaccines in accordance with the FDA guidance for industry about informing users that products or product containers are not made with natural rubber latex.

There are currently no FDA-approved vaccines for Zika virus, nor is FDA is aware of vaccines in advanced development. However, FDA is prepared to work with the industry to clarify laboratory and data requirements necessary to move products forward in development as quickly as possible. Earlier in June, FDA participated in a World Health Organization (WHO) consultation on potential laboratory approval pathways for Zika vaccines during the WHO-declared public health emergency of international concern.

HRSA BPHC—Justin Mills, M.D., M.P.H.

Dr. Mills presented preliminary data for 2015 from the Uniform Data System (UDS), which collects demographic and clinical data from all the HRSA community health centers and lookalikes. The percentage of children fully immunized[1] in 2015 was 77.55 percent, a very slight increase over 2014. To modernize data collection, BPHC proposed revising clinical measures to align with CMS electronic clinical quality measures (eCQMs) specifications. As of March, the childhood immunization measure will be aligned with eCQM DMS-117. With the change, the system will include children 2 years of age instead of 3 years of age and add one hepatitis A dose, two to three rotavirus doses, and two seasonal influenza doses to the current measure description. The rationale for the changes is to align and standardize data and reduce the burden of reporting on health centers. These changes support other planned changes, including phasing out chart sampling and developing an e-portal for direct submission of electronic data into the UDS.

VICP and the Countermeasures Injury Compensation Program (CICP)—Narayan Nair, M.D.

As of early May 2016, 637 claims have been filed with the VICP, and 303 have been adjudicated, and approximately $125 million has been paid to the petitioners and $11.2 million has been paid for attorney's fees for compensated and dismissed claims during FY2016.

The VICP completed the development of proposed regulations to make changes to the Vaccine Injury Table. The notice for proposed rulemaking was posted for public comment in July of 2015 and was available for 180 days. A public hearing was held in January of 2016. Currently, VICP is reviewing the public comments to finalize the rulemaking.

[1] HRSA defined "fully-immunizaed" as the number of children fully immunized before their 3rd birthday. A child is fully immunized if s/he has been vaccinated or there is documented evidence of contraindication for the vaccine or a history of illness for ALL of the following: 4 DTP/DTaP, 3 IPV, 1 MMR, 3 Hib, 3 HepB, 1VZV (Varicella), and 4 Pneumoccocal conjugate, prior to their third birthday

As of May 2016, the CICP has compensated 27 claims, totaling $4.5 million for FY2016. VICP outreach efforts continue to focus on making the public and providers aware of both of these safety net programs.

IHS—Jeffrey McCollum, D.V.M., M.P.H.

IHS implemented a mandatory influenza vaccination policy for all nonunion health care personnel for the 2015–2016 influenza season. Influenza vaccine coverage among health care personnel working in IHS Federal facilities increased from an overall average of 77 percent during each of the influenza seasons 2008 to 2014 to 84.3 percent in the most recent influenza season (2015-2016). IHS anticipates full implementation of the policy to include all union employees and staff working in IHS health care facilities during the next influenza season.

Regarding education and outreach efforts among native communities, IHS partnered with HHS to develop a video public service announcement for adult immunizations that is tailored for American Indian/Alaska Native communities. It will debut in August as part of Immunization Awareness Month activities via Good Health TV, a subscription health education channel that targets Indian Country and reaches more than 90 IHS and Tribal clinical sites across the United States.

IHS is also relying on community health representatives (CHRs) to serve as liaisons between American Indian/Alaska Native communities and IHS or Tribally-managed clinical services. The CHRs are an important source of information for their communities. The IHS immunization program is partnering with the CHRs to develop a vaccine training module as part of the online and in-person basic training onboarding courses for new CHRs starting in June.

IHS has developed an HPV toolkit for IHS providers that includes a guide to best practices, educational presentations, and links to clinical and patient resources specific to American Indian/Alaska Native communities. It will be released to IHS providers this month. Contents of the toolkit components are evidence-based and informed by pertinent findings and results of a joint CDC-IHS quality improvement project to increase HPV vaccine coverage rates among 10 IHS and Tribal clinics.

Beginning in May, a clinical decision support tool for meningococcal group B vaccine is included in the IHS EHR. IHS is now generating automatic provider reminders about the vaccination and subsequent doses in accordance with the guidelines.

NIH—Andrew Ford, Ph.D.

NIAID continues its research on Zika virus, including development of improved diagnostics and new treatments and vaccines. NIAID is also pursuing a DNA-based vaccine that uses a strategy similar to an investigational vaccine for West Nile virus infection as well as one used to develop the dengue virus vaccine. The dengue vaccine is being evaluated in a large Phase III study in Brazil.

In May, the journal *Clinical Infectious Diseases* published a paper authored by NIAID subject matter experts on vaccines for hospital-associated infections (HAIs). Such infections not only increase morbidity and mortality but also increase health care costs and are a key driver of antibiotic use. Vaccines directed towards these pathogens could help prevent a large number of HAIs and associated antibiotic use if administered to targeted populations. The authors described the promise, challenges, and current plans for vaccines to prevent HAIs, as well as the utility of monoclonal antibodies to prevent HAIs in targeted populations.

In March, with the Bill & Melinda Gates Foundation and the WHO, NIAID cohosted the second Global Vaccine and Immunization Research Forum. The forum covered the landscape from discovery and development through delivery, including research to improve the impact of immunizations. The forum is part of the Decade of Vaccines collaboration, which was developed to discuss the research and development component of the Global Vaccine Action Plan.

USDA—Donna Malloy, D.V.M., M.P.H.

USDA continues to work internally and externally to address the strategic areas outlined by the National Action Plan for Combating Antibiotic-Resistant Bacteria. The USDA divisions involved in research include the National Institute for Food and Agriculture, the Agricultural Research Service, and the Economic Research Service. The Animal and Plant Health Inspection Service and the Food Safety Inspection Service are addressing surveillance. Cooperative extensions, the National Agricultural Statistics Service, and the National Veterinary Accreditation Program are engaged in education and outreach. One example is the recent gap analysis workshop held at the National Animal Disease Center in Iowa. The purpose of the workshop was to identify research initiatives for agricultural animals, plants, and food safety and enable the development of alternatives to antibiotics that would reduce the use of medically important antibiotics.

In January, USDA confirmed the presence of highly pathogenic H7N1 avian influenza in a commercial turkey flock in Indiana. Since that occurrence, there have been no additional highly pathogenic avian influenza outbreaks, and there are no highly pathogenic avian influenza control areas in place. USDA continues its surveillance in wild birds to provide “early warning” risk information to the States and to industries. In addition, USDA continues to promote improved on-farm biosecurity practices to prevent future avian influenza cases.

2010 National Vaccine Plan Midcourse Review

Progress Update—Jennifer L. Gordon, Ph.D., NVPO

Dr. Gordon explained that NVPO has been collecting information from a broad range of Federal and non-Federal stakeholders through a request for information, one-on-one interviews, and targeted focus groups. This information was synthesized and the findings will be published later this summer. At the same time, NVAC’s Midcourse Review Working Group has been looking at the information gathered and providing independent analysis from a non-Federal stakeholder perspective. The input from both processes will be instrumental as HHS develops the implementation plan for the 2010 National Vaccine Plan through 2020 (2016-2020).

The implementation plan is intended to assist the NVPO director in coordinating and implementing the responsibilities of the National Vaccine Plan. The implementation plan establishes priorities and describes how the various departments and agencies carry out their vaccine-related functions together. Each agency has strategies and activities that support its mission.

Dr. Gordon summarized the five goals of the 2010 National Vaccine Plan. Dr. Gordon said a lot of discussions around the midcourse review have focused on near-term, actionable, achievable efforts with the greatest opportunity for success by 2020. The midcourse review has served as a framework for building community consensus on priority areas. Given the timing of the review, it may also act as a roadmap for incoming political leaders.

Stakeholders have been asked to consider whether the plan is meeting its goals and objectives, whether the plan is headed in the right direction, and how implementation efforts can be better aligned with the current immunization landscape. As previous discussions revealed, the ACA did not remove all of the barriers to access. The midcourse review is also an opportunity to ensure that all the Federal partners are moving together in a coordinated fashion. Stakeholders were asked for input on measuring progress toward goals. The indicators will also inform the next National Vaccine Plan (2020-2030).

NVPO reviewed the results of stakeholder input and identified areas of greatest opportunity by looking at overlapping responses. Language was crafted to broadly address those gaps and compared with the priorities in the National Vaccine Plan. Out of nine areas of greatest opportunity, stakeholders were asked to select the top five.

1. Strengthen health information and surveillance systems to track, analyze and visualize disease, immunization coverage and safety data, both domestically and globally
2. Foster and facilitate efforts to strengthen confidence in vaccines and the immunization system to increase coverage across the lifespan
3. Eliminate financial and systems barriers for providers and consumers to facilitate access to and administration of routinely recommended vaccines
4. Strengthen the science base for the development and licensure of new vaccines, especially understanding of the host immune system and correlates of protection
5. Identify and implement solutions to overcome vaccine development barriers

Dr. Gordon pointed out that none of the opportunity areas specify global issues; rather all of these areas will include global efforts and global goals.

Once the opportunity areas were identified, Federal partners and the NVAC working group proposed indicators, coming up with 59 relevant indicators (including some global indicators) from existing immunization strategies and other documents. NVPO sought existing indicators so that it could harmonize with other strategic documents and reduce duplicative efforts. Also, creating metrics requires resources and time. Development of new metrics may be part of future efforts. Dr. Gordon described some of the indicators selected by Federal partners.

Dr. Gordon said NVPO is wrapping up the analysis of the findings identified on the Federal level. She estimated the report of results from the Federal partners would be finalized in August. The NVAC working group will continue its independent analyses and present recommendations at the September NVAC meeting. All of the analyses will inform how HHS works with Federal partners to build the implementation plan going forward.

NVAC Midcourse Review Working Group (MCRWG)—Yvonne Maldonado, M.D., and Nathaniel Smith, M.D., M.P.H., Co-Chairs

Dr. Smith said the NVAC MCRWG was charged with providing an independent assessment complementary to NVPO's work. The MCRWG identified areas of opportunity (agreeing with the Federal partners on priorities) and proposed existing metrics that could be used to measure progress. For each of the five priority areas of greatest opportunity, the MCRWG called out key elements of success and important considerations.

1. Strengthen health information and surveillance systems
   Key elements of success
   - Interoperable IISs across all U.S. States and territories

- Bidirectional, real-time exchange of data between all IISs and EHRs used by U.S. vaccine providers
- End-to-end tracking of vaccines across all sectors utilizing standardized interoperable IT solutions (e.g., practice-level use of barcoding)
- Global post-marketing surveillance

Challenges to progress
- Legal barriers to sharing IIS data across jurisdictions
- Lack of electronic record standardization to facilitate bidirectional data sharing between the EHRs and IISs
- Funding for health IT applications, such as 2D-barcoding
- Absence of the global case-based surveillance systems
- Lack of vaccine safety surveillance in many countries

Other considerations
- Potential benefits of using 2D-barcodes in managing inventory and supply chain, as well as tracking safety and effectiveness data
- Strengthening global capacity for pharmacovigilance in tracking adverse effects following immunizations

Dr. Smith said the MCRWG suggested two potential metrics in addition to those identified by the Federal partners: number of operational agreements between State and territorial immunization information systems (to assess progress toward interoperability) and percentage of providers using barcodes to populate their EHRs and IISs.

2. Foster efforts to strengthen confidence in vaccines and the immunization system
   Key elements of success
   - Improved immunization rates across all the age groups
   - Reduced number of personal belief exemptions for vaccination in all States
   - Robust vaccine communication tools available for health care providers and community advocates

   Challenges to progress
   - Lack of clear communication and understanding when changes are made in the immunization schedules
   - Undervaccination in many adults, who are not completely sold on the need for vaccinations
   - Lack of consistent reliable methods to communicate with the public

   Other considerations
   - The NVAC recommendations on vaccine confidence are a very useful tool for the implementation plan and should influence the discussion and the development of targeted metrics for vaccine confidence.

Dr. Smith said the MRWG proposed three questions for NVAC:

- Should age groups each have individual metrics for coverage?
- Are HPV vaccination rates the best metric for vaccine confidence among adolescents?

- Should the goals for HPV vaccination match Tdap and meningococcal vaccine coverage, or should there be separate targets for HPV coverage?

The MCRWG also proposed using standard school-based data collection on personal belief exemptions across States and jurisdictions as a metric. Such data would give more insight at the local level. Dr. Maldonado added that the MCRWG discussed whether the goal around personal belief exemptions should be reduction or elimination, and she asked for NVAC input.

3. Eliminate financial and systems barriers
   Key elements of success
   - Increased vaccination rates and increased offering of vaccines by providers
   - Increased number of providers that stock and administer vaccines
   - Surveillance of vaccine provider perceptions about the profitability of delivering vaccines in their practices

   Challenges to progress
   - Mismatch in the Medicare Part B and Part D payment for vaccines
   - Payment methods, bundling, and capitation issues
   - ACIP-recommended A/B ratings
   - Integrating alternate vaccinators (not in-network but part of the immunization network), addressing, for example, concerns from pediatricians regarding the medical home for children
   - Inventory costs of newer, more expensive vaccines

   Other considerations
   - Consensus that Federal programs need to align and address inconsistencies, for example, between Medicare and Medicaid
   - Need to ensure access to immunizations across the life span
   - Need to better understand the age restrictions by State for the administration of vaccines by pharmacists and other nonphysician providers

Dr. Maldonado said the MCRWG proposed two additional existing metrics: number of WHO regions achieving measles elimination by 2020 and number and proportion of countries providing a second dose of a measles-containing vaccine through routine services and coverage levels. Two other metrics would be helpful: number of providers who are not providing immunization services and number of countries that have eliminated rubella.

4. Strengthening the science base for development and licensure of vaccines
   Key elements of success
   - Clinical development of new vaccines that move more quickly through Phase III
   - Better understanding of natural immunity and correlative protection
   - Projects characterizing the human immune response and those contributing to understanding of vaccine science that are well funded, staffed, and supported

   Challenges to progress
   - The size and costs of clinical trials have grown, and efficacy studies are larger and more difficult to conduct
   - Understanding of waning immunity, and how to address it (e.g., is pertussis)
   - How to overcome poorer T-cell induction by vaccines in infants to address better persistence of antibodies following booster doses in older children and adolescence

- Improving vaccines and immune responses for the elderly

Other considerations
- Need for better correlates of protection and understanding of their roles and opportunities in clinical trials, which would relieve the need to do large efficacy trials when disease burden is not high or is unpredictable from year to year (and start by harnessing the available data and identifying data gaps)
- Need to address operational challenges around the use of large data repositories

Dr. Maldonado said the MCRWG was unable to find relevant existing metrics and seeks NVAC input. It proposed tracking funding for vaccine research and development across the stakeholder community (both Federal and non-Federal) to understand the level of funding from different stakeholders and how it changes over time. Tracking should include how Federal funds coordinate research to ensure optimal investments. The number of journal articles on vaccine science is not always a straightforward indicator.

5. Identify and implement solutions to overcome vaccine development barriers
   Key elements of success
   - For priority targets, there are enough vaccine candidates in the pipeline to lead to at least one licensed vaccine, taking into account the expected attrition rate
   - New products addressing incremental improvements for priority targets are accepted and supported and encourage further incremental development
   - Emerging pathogen threats can be addressed by vaccination before the outbreak ends
   - Year-to-year funding is tracked and increased for vaccine R&D
   - An increasing number of regulatory authorities harmonize and upgrade their standards for vaccine licensure and distribution (e.g., to support multilateral agreements)

   Challenges to progress
   - Building and maintaining a pipeline of vaccine candidates robust enough likely to lead to at least one licensed vaccine against a priority target
   - Preparing in advance for developing vaccines against emerging pathogen threats so that responses to outbreaks can be more proactive
   - Harmonizing global regulatory requirements for the development and distribution of vaccines

   Other considerations
   - Drivers of innovation should take into account incentives for smaller biotech firms
   - Reward manufacturers for incremental improvements in vaccines
   - Efforts to harmonize regulatory reviews globally

Dr. Maldonado said the MCRWG did not feel that the only existing metric (around licensure and launch) adequately addressed all of the concerns. It noted that the WHO has developed a pipeline tracker that is currently limited to clinical-stage vaccines (e.g., malaria, HIV, tuberculosis, and RSV). The MCRWG suggested developing an expanded pipeline tracker.

Proposed metrics in this area are 1) tracking the clinical stage vaccine development pipeline, including a specific number of target, priority pathogens (prevalent, emerging, and improved) so that the number of candidates and length of time spent in each phase can be tracked over time

and 2) agreements signed and acted upon by key regulatory agencies to perform joint reviews (in an effort to harmonize regulatory reviews globally).

Dr. Maldonado concluded that the MCRWG will be gathering some additional data but will likely focus on discussion of feedback from Federal stakeholders and from NVAC. The MCRWG plans to present a draft report for input from NVAC members over the summer so that it can be presented at the September NVAC meeting.

Discussion

Dr. Orenstein said that once there is a list of priority candidates (i.e., vaccines needed), metrics can be created to measure the number of candidates in trials. Dr. Maldonado pointed out that the concept of a list has been discussed many times, and some believe that NVPO should take responsibility for generating the list. Dr. Smith pointed out that deciding what to track is difficult. He noted that the WHO published a list of 25 pathogens for which vaccines are coming along. Dr. Smith suggested CDC and NVPO comment on the WHO list as a starting point for discussing which vaccine candidates to track. He noted the tension between the need to fund candidates identified as priorities and the potential for funders dismissing worthy candidates because they are not on the list. Mr. Hosbach requested that some entity list all vaccine candidates in trials now, both public and private.

Dr. Fleming appreciated the integration of global and domestic issues throughout and suggested the MCRWG state clearly in its report that the two are intentionally integrated. He said the suggestions highlight the need for implementation science and called for the MCRWG to make the case for investing in research on the best strategies to address the challenges and needs.

Dr. Lynfield asked which entities are best qualified to anticipate emerging pathogens and identify outbreaks early. Dr. Kovacs said BARDA identifies potential pathogens that could have an impact globally or domestically, but it is difficult to prioritize them. Ebola and Zika viruses would not have risen to the top of the list, he noted. BARDA is putting in place resources and facilities for rapid development of vaccines and other biopharmaceuticals using interchangeable platform technology, so that as soon as a pathogen and potential antigens are identified, clinical trials can begin.

Dr. Gellin proposed looking at the process the WHO used to generate its list of 25 vaccines in development. Dr. Orenstein pointed out that the NVPO/NAM's SMART tool for vaccines attempted to put forth priorities, but they were not well accepted. Dr. Gellin suggested reviving the conversation around those efforts. He added that any such list must begin with a transparent declaration of the criteria, which may be the best way to start the conversation.

Ms. Kropp said Canada released a list of short-, medium-, and long-term priorities around vaccines in 2015 but it is still struggling with how broadly to define the criteria. The new Federal government of Canada is focused on results and transparency, so it is seeking indicators that make sense. There must be a balance between indicators that reflect the ultimate outcome and those that describe immediate and intermediate outcomes. It is challenging to find indicators that are meaningful to the public. Canada is grappling with whether indicators should be limited to those things under Federal control. Another question is whether indicators should be achievable or aspirational. Finally, there is a struggle between choosing indicators that can be measured with the current infrastructure versus indicators that are needed but cannot be measured now.

Dr. Gordon said NVPO is also weighing outcomes against process indicators and tends to lean toward outcomes. The National Vaccine Plan focuses on Federal activities and aims to drive Federal efforts, so indicators must be attainable metrics that apply to Federal entities. Because of the short time to achieve the goals of the current National Vaccine Plan, the implementation plan is limited to using existing metrics, but the proposed metrics are critical to future planning. Dr. Maldonado added that she believes all the vaccine coverage goals are achievable but would require a lot of effort.

Dr. Smith pointed out that in some cases, there are no adequate existing metrics. Dr. Omer said HPV vaccination in itself may not be an adequate measure of vaccine confidence; however, a concrete measure of provider confidence would be the number of providers who give Tdap and meningococcal vaccines at the same time but not HPV vaccine. Dr. Orenstein felt that receipt of the first dose in the HPV vaccine series may be a reasonable indicator, and Dr. Maldonado said HPV vaccination as a surrogate for confidence may be reasonable for now.

It was noted that the opportunity area on strengthening health information and surveillance systems seems to focus on IISs and interoperability. Dr. Gordon said there was consensus around the need to incorporate disease and safety surveillance in this opportunity area. Dr. Orenstein said he feels there are major deficiencies globally around disease surveillance that limit understanding of transmission. He suggested measuring how well resources around polio surveillance are converted into surveillance resources for other diseases.

On the use of evaluating the number of scientific publications to track scientific progress, Dr. Omer said the h-index goes beyond the number of publications to assess the impact of publications in the field. He also suggested looking at not just the amount of money invested in research but the amount invested by the degree of innovation. Regarding vaccine candidate lists, Dr. Omer expressed support for the WHO list of diseases likely to cause major epidemics, which is likely to be updated annually, because it draws on resources globally and provides a lot of useful context.

Dr. Bennett pointed out that while there is an RSV vaccine in development for adults, there are no surveillance mechanisms for RSV. It is important to anticipate surveillance needs. Dr. Orenstein added that important details that would inform understanding of transmission are not always included in surveillance. Dr. Smith said some useful detailed data are collected by States but not forwarded to national surveillance systems.

Dr. Orenstein also suggested surveillance distinguish preventable cases of disease (in someone who should have been vaccinated but was not) from nonpreventable cases (which involved either a vaccine failure or someone without an indication for vaccination). Such data would provide better information on the proportion of cases involving vaccinated or unvaccinated people and would reveal both vaccination failures and failures to vaccinate.

Action Item
The draft MCRWG report will be sent to NVAC members for additional comments.

Annual Update on Efforts to Increase HPV Vaccination Among Adolescents

Update on Activities to Improve HPV Vaccination Coverage—Achal Bhatt, Ph.D., CDC

Despite encouraging increases in HPV vaccination rates in recent years, said Dr. Bhatt, more progress is needed to reach national goals. In 2013 and 2014, CDC awarded funding to 22 sites

to increase HPV vaccination coverage among adolescents. While HPV vaccination rates increased modestly from 2013 to 2014 across the country, there were significant increases in uptake around the funded communities, including substantial increases in the number of young women who completed the full series.

The funded jurisdictions credited their success to various combinations of interventions. For example, the Arizona State health department collaborated with the Arizona Cancer Coalition and the Arizona Partnership for Immunization to recruit additional stakeholders. Chicago leveraged social media as part of a public outreach campaign; a survey found the children of parents and caregivers who saw the campaign were more likely to get the HPV vaccine.

Almost all of the most successful jurisdictions engaged in assessment and feedback using site visits consistent with Federal AFIX (assessment, feedback, incentives, exchange) guidance, ensuring decision-makers participated in those visits, and including a clinician-to-clinician education component.

In 2014, CDC announced a 5-year funding opportunity for national HPV partnerships around outreach and education with organizations that represent providers. Funded partners included NACCHO, AAP, Academic Pediatric Association, the National AHEC (Area Health Education Centers) Organization, and the American Cancer Society. NACCHO in turn funded local health departments to identify stakeholders, determine strategies to address local HPV vaccination rates, and develop community-specific action plans reinforcing key themes (e.g. HPV vaccination is cancer prevention). The Academic Pediatric Association is drawing on its academic constituency to implement quality improvement projects in 15 residency training clinics and to strengthen the immunization content of three residency curricula used for primary care training. So far, these efforts have reached 2,000 clinicians and 7,000 residents and increased vaccination rates in 15 pediatric residency training clinics and in 50 practices.

The AAP's initiatives include training for pediatric offices, interventions for quality improvement, mobilization of State AAP chapters, and working with IIS' to evaluate immunization rate increases. The AAP also created an HPV champion toolkit to support practice changes. The National AHEC Organization created a national training center that will develop and provide HPV-related training sessions to clinicians nationally, as well as provide toolkits, State data, webinars, and continuing education. Nearly 10,000 people have participated in some form of training so far.

The American Cancer Society (ACS) is targeting safety-net clinics. Its activities include demonstration projects at 29 Federally-qualified health centers (FQHCs). It is also piloting 10 capacity-building projects for 1 year. The ACS initiatives involve clinician training and tools, capacity assessment, baseline setting, and EHR modifications. Dr. Bhatt highlighted the ACS contact map, where users can select a State and see the names and contact information of partners working within that State.

Dr. Bhatt said CDC gave additional funding to the IIS sentinel sites, a group of high-performing IIS awardees with vigorous data quality standards, for targeted provider outreach and to increase HPV provider participation in IISs. The effort represents a collaboration between CDC's IIS branch, the sentinel sites, State cancer registries, and the CDC's surveillance branch. Dr. Bhatt described some of the strategies sites will use. Other CDC projects around HPV include analysis of National Immunization Survey-Teen data from 20 CDC awardees to identify promising practices and conducting more AFIX site visits aimed at increasing HPV coverage.

Updates from the HPV Roundtable—Jennifer Sienko, ACS

Ms. Sienko said the National HPV Roundtable is the second CDC/ACS cooperative agreement. Its mission is to bring together cancer prevention and immunization organizations to prevent HPV-associated cancers and pre-cancers by increasing and sustaining U.S. HPV vaccination rates. Ms. Sienko summarized the work of each of the Roundtable's task groups.

The Best Practices Task Group is hosting a conference this summer to convene researchers, clinicians, and other stakeholders to identify promising and best practices to increasing HPV vaccine coverage. An EHR and IIS/Registry Task Group seeks to understand how practices are currently using EHRs and IISs to schedule and document HPV vaccination and barriers, both technological and behavioral, that prevent effective use. The National Campaign Task Group is augmenting CDC's national communication campaign and working to promote and disseminate the products of the Roundtable. This task group is developing a letter for insurers and providers emphasizing that what they say and how they recommend the vaccine matters. It is also providing case studies that demonstrate successful integration of State-based data to inform local immunization efforts.

The Roundtable is developing a universal HPV vaccination symbol or slogan that member organizations can use to visually unify efforts around cancer prevention and immunization, as well as promote the work of the Roundtable.

The Pharmacy-Located HPV Task Group is piloting referral networks in which community pharmacies administer and document administration of the second and third HPV vaccine dose. One pilot site includes rural and urban communities, and another includes Appalachia and Pacific Northwest Indian Tribes across three States. The Provider Training Task Group has developed a publically available clearinghouse of HPV education and training resources as well as educational videos on head and neck cancer and AFIX and office site visits.

The School-Based Parent Education Task Group is creating an electronic toolbox for school nurses to use with students who are transitioning into middle school. The Survivor Involvement Task Group put together an HPV-related cancer survivor speaker database to amplify the role of survivors, specifically in the context of provider trainings or conferences. This group is also developing a series of short HPV cancer survivor videos.

The products of the Roundtable and results of pilot projects will be presented at a national meeting in August. If further funding is granted, the Roundtable members will determine how to follow up on pilot projects and how to plan for future HPV vaccination activities.

Society for Adolescent Health and Medicine (SAHM) Efforts to Improve HPV Vaccination Among Adolescents—Annie-Laurie McRee, Dr.P.H.

Dr. McRee described her organization, which includes not only clinicians but also, for example, professionals from public health, social work, education, and law. Understanding how to increase uptake of HPV vaccine requires a multidisciplinary approach, from epidemiology and health psychology and health behavior to clinical disciplines and advocacy and policy efforts.

Ongoing HPV efforts of SAHM include dissemination of research through the *Journal of Adolescent Health*, annual meetings, online guidelines and resources, and a Vaccination Committee with liaisons to many vaccine-related organizations that makes recommendations to SAHM. Several SAHM position papers address vaccines recommendations and policy. Dr.

McRee said SAHM has started using press releases more frequently as a way to respond rapidly to emerging issues of interest.

In 2011, SAHM received funding from Merck to implement and evaluate innovative public health demonstration projects to improve immunizations among adolescents. In 2012, SAHM awarded grants for 10 projects over 2 years, all of which included HPV vaccinations. The projects used diverse strategies to mitigate barriers and reduce disparities. A number of key themes came out of the projects:

- No single strategy will universally improve HPV vaccination rates among adolescents or young adults.
- There is a clear need to increase awareness and knowledge of specific vaccines not just among parents and adolescents but also among health care professionals.
- Technology can be used to increase vaccinations through automated tracking systems, reminder-recall systems, and education kiosks, for example.
- Advocates and providers must foster trust in targeted communities and develop culturally and linguistically competent methods and materials.
- Increasing access is key to reaching adolescent patients without a defined medical home or other traditional primary care venue.

Data from most of the projects were presented in a supplement to the *Journal of Adolescent Health* published in 2015.

Also in 2015, SAHM launched a free mobile app called Teen Health Resources Information and Vaccine Education (THRIVE) as part of a collaboration with Pfizer and the Unity Consortium. It provides interactive resources directed to teens and young adults and aims to foster health-oriented discussions between parents and their children. It has an extensive library of teen health and wellness topics, such as risk-oriented behavior, consent, confidentiality, health insurance, heath examinations, and preventive health information. The app also gives parents "conversation starters" around sensitive topics, such as alcohol use, social media, and preventive health care.

Notably, the app allows parents to create a profile for each of their children to keep track of their health records and view a tailored checklist of developmentally appropriate health care information, medical visits, and conversation starters. Parents can map their progress as interventions are provided, and they can upload vaccination and other medical records, so they have all the information with them for health visits.

Dr. McRee outlined some opportunities for promoting HPV vaccination and coordinating with NVAC.

- Increase the evidence base, translating the strong epidemiological and observational data into interventions. The upcoming HPV Roundtable meeting can help identify relevant demonstration projects and evidenced-based communication strategies.
- Maximize vaccination at every opportunity, such as integrating vaccination with other adolescent preventive services (e.g., sick visits and sports physicals). Strategies include the use of standing orders and vaccination reminder systems. Obtaining parental consent can be a significant barrier to vaccination for young people. To maximize opportunities to vaccinate minors when parents are not present, a deeper understanding is needed of State and national laws around consent. Increasing minors' ability to

consent to receive vaccines (e.g., during visits for confidential care such as sexual health care) or to allow vaccination based on previously obtained parental consent should be evaluated.
- Promote convenient access to adolescents in qualified alternative settings, such as schools and pharmacies. SAHM encourages efforts to connect young people with adolescent and other qualified providers who can provide a full range of services, including health education and guidance. These providers should be able to coordinate care.
- Strengthen the vaccination infrastructure and financing, e.g., by eliminating financial barriers for adolescents and young adults. The ACA has helped reduce financial barriers for young adults, but there is still no guarantee that vaccines will be universally recommended or covered. In addition, SAHM supports providers participating in VFC and would like to see that program extended. Nontraditional providers should be encouraged to participate in VFC so that young people can be vaccinated at pharmacies or other locations. It is also necessary to increase use of IISs among all providers who deliver vaccines to adolescents and young adults to coordinate care, reduce resource duplication, and decrease missed opportunities for vaccinations.

DISCUSSION

Ms. Despres applauded the comprehensive efforts around increasing HPV vaccine uptake. Dr. Omer suggested evaluating the evidence base around communication. Specifically, he proposed that increasing the focus on disease (i.e., cancer) rather than vaccination may affect uptake. Also, there seems to be some confusion in the field about the relationship between the HPV vaccine and cancer. Dr. Omer recommended that messaging explain more directly that the vaccine prevents HPV-related cancers.

Announcement

Dr. Maldonado announced that the International Society for Vaccines will meet in October in Boston. The organization promotes research, and the meeting is open to all those interested.

Public Comment

Bob Benjamin, MD, MPH, a public health physician from California and member of NACCHO's immunization workgroup, raised the issue of vaccine confidence. Dr. Orenstein's point about distinguishing vaccine failure from failure to vaccinate gets to the heart of the issue. The field is seeing an incredible erosion in vaccine confidence that began with the Wakefield Report, and it has impacted all perceptions of vaccine efficacy, said Dr. Benjamin. But it was based on a lie. There is increasing evidence that the pertussis vaccine is failing. Dr. Benjamin believes the erosion of vaccine confidence combined with a vaccine failure leads to continuous loss of confidence.

In California in 2015, the State Department of Health found the rate of Tdap uptake in pregnant women was only 46 percent. Was this a failure of the physicians to adequately educate their populations? Was it a failure of the physicians to believe in the vaccine? Was it a failure of the target population to say this is worth doing? Dr. Benjamin said we should not accept a return to endemicity of pertussis. He said NVAC is in a position to call for an improved vaccine and to call for Federal incentivization for the industry to manufacture it.

John Merrill-Steskal, M.D., a family physician from Washington State, said he is very passionate about vaccines and has a special interest in the role of technology and social media for promoting vaccines. He was excited to hear about the app from Canada as well as the teen

and adolescent apps to promote health in vaccination. He was also very excited about all the interest in a national vaccine registry so that immunization data on individual patients can be readily accessible to primary care providers across the country.

Dr. Merrill-Steskal said an element of success with social media in terms of public acceptance and participation may well involve an app that has the ability for patients to track their own immunizations as well as the ability to exchange information (bidirectionally) between a national registry and a personal database on a phone. CDC has a great preventive services app. Dr. Merrill-Steskal was very confident such an app can be created, and he thought it should go hand-in-hand with the creation of a national registry for vaccinations.

Amy Gardner said she is from Rhode Island, and it is extremely discouraging that there is not more focus on addressing other concerns that have come out. The ACP put out a caution that there needs to be further study of the relationship to ovarian failure with the [HPV] vaccine. Ms. Gardner expressed concern that the studies did not use a true saline placebo.

Ms. Gardner stressed the public's right to know. She said NVAC should put a better focus on doing more third-party and independent studies. If NVAC's focus is truly that vaccines are a good thing, NVAC should prove it, not simply by advertising and marketing them.

Ms. Gardner said the Rhode Island Department of Health is one of the only departments of health in the nation that has the full authority to mandate vaccines. In 2014, it mandated the HPV vaccine. Mandating a vaccine and then boasting about high vaccination rates is not something to be proud of, said Ms. Gardner. She continued, "We're people. We're patients. And we need informed consent. We need to be properly informed of both risks and benefits." The HPV vaccine has not been proven to prevent cancer, she noted. A physician who helped with Phase II and Phase III trials to create the vaccine has said on record that we do not know yet whether the HPV vaccine prevents cancer because enough time has not passed. It is possible, but is more probable that it only delays cancer.

Ms. Gardner said she supports vaccines being available as an option, but marketing them without giving the public all of the real information from all sides makes everyone much more skeptical. More and more people do not trust NVAC and CDC because there is more and more proof coming to light that pieces of information are not being publically disseminated so that individuals can make proper informed consent decisions. That is not acceptable, said Ms. Gardner. There are thousands of reports to the Vaccine Adverse Event Reporting System, and it must be noted that there are four times more reported reactions to the HPV vaccine than there is for all other vaccines combined. Ms. Gardner asked that NVAC look seriously at what is out there for the public. The public is concerned because the data show us we should be concerned, Ms. Gardner concluded.

Ms. Wrangham, executive director for the NVIC, expressed concerns around the use of immunization systems as a way of tracking individuals. There must be transparency in these systems. There must be the opportunity for people to opt out, and there must be transparency that they may already be in these systems. Particularly with the discussion on HPV vaccines today, using these systems for reminder-recall is considered harassment by some because they are not aware that they are in the system. The NVIC advocates for a higher level of transparency and the ability of individuals to have control over this sensitive health information and how much of that information they want to share with public health officials in their government.

With regard to minor consent to HPV vaccine, it seems striking that at age 18 in some States, a person cannot even drink, but the HPV discussion included allowing individuals to make medical decisions who are not 18 years of age. It has been shown through some data that one must be into the 20s before an individual actually understands the ramifications around risk. Vaccines are not risk-free, and the ability of a minor to consent to this medical procedure of vaccination without parental consent is striking. Ms. Wrangham doubted that a young child really understands the risks involved. It is also important for parents to be aware of any medical procedures and medical products that their child is receiving so that when there is an adverse event they are aware and can get proper medical attention. Parents understand risks far better than their children do, and they have historically held that role for their children, looking out for the well-being of their children.

Ms. Wrangham noted that there is not an epidemic of cervical cancer. It is highly treatable. One only needs to look at the CDC's report to Congress in 2005 to understand this and to also understand that for many, HPV is not a threat. Most people resolve this risk on their own systematically with no complications. So, the marketing of this product as a cancer vaccine is somewhat misleading considering that most everyone within 2 years will resolve the virus on their own. It is a very expensive vaccine. Ms. Wrangham suggested NVAC discuss whether the money could be used in different ways to fill gaps where there are questions or perhaps where there is no screening for those at risk.

This world is bigger than vaccines and vaccines are not the only preventive health option available to consumers, said Ms. Wrangham. Vaccines are pharmaceutical products that carry the risk for injury and death. Choice and informed consent must be a part of the equation. From the NVIC's perspective, NVAC discussions about vaccine confidence consistently leave out this piece.

The vaccine confidence issue is not solely about Dr. Wakefield. It is not solely about vaccine failure. There are many pathways by which individuals will judge whether or not a vaccine is appropriate for them or their children, one of them being the perception of risk that the disease presents, the incidence of the disease in the population. Many childhood illnesses will resolve without complications. Parents may see better options than vaccines. It is their right to do so. Ms. Wrangham called for more perspective-taking in discussions about vaccine confidence or hesitancy and asked NVAC to take a broader look at that landscape.

Closing Remarks and Adjournment—Walter A. Orenstein, M.D.

Dr. Orenstein summarized the issues of the day. He thanked the NVPO staff, NVAC members, liaisons, ex officio members, and all those who help make NVAC meetings successful. He adjourned the meeting at 1:10 p.m.