NVAC NATIONAL VACCINE ADVISORY COMMITTEE

February 7–8, 2017, Meeting Minutes

Committee Members in Attendance

Kimberly M. Thompson, Sc.D., Chair
Melody Anne Butler, B.Sc.N., RN
Timothy Cooke, Ph.D.
Sarah Despres, J.D.
David Fleming, M.D., M.P.H.
Robert H. Hopkins Jr., M.D., MACP, FAAP
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.

NVAC Ex Officio Members

Marion Gruber, Ph.D., Food and Drug Administration (FDA)
Mary Beth Hance (for Jeffrey A. Kelman, M.M.Sc., M.D.), Centers for Medicaid and Medicare Services (CMS)
Troy Knighton, M.Ed., Ed.S., LPC, Department of Veterans Affairs (VA)
Donna Malloy, D.V.M., M.P.H., Department of Agriculture (USDA)
Jeffrey McCollum, D.V.M., M.P.H., Indian Health Service (IHS)
Nancy Messonnier, M.D., CAPT, Centers for Disease Control and Prevention (CDC)
Justin A. Mills, M.D., M.P.H., Agency for Healthcare Research and Quality (AHRQ)
Barbara Mulach, Ph.D., National Institutes of Health (NIH)
Narayan Nair, M.D., CAPT, Division of Injury Compensation Programs (DICP), Health Resources and Services Administration (HRSA)
Judith Steinberg, M.D., M.P.H., Bureau of Primary Health Care (BPHC), 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 Practices (ACIP)
Rebecca Coyle, M.S.Ed., American Immunization Registry Association (AIRA, *day one*)
Kathryn M. Edwards, M.D., Vaccines and Related Biological Products Advisory Committee (VRBPAC)
Kristen R. Ehresmann, RN, M.P.H., Association of Immunization Managers (AIM)
Rhonda Kropp, B.Sc.N., M.P.H., Public Health Agency of Canada (PHAC)
Mary Beth Kurilo,M.P.H., M.S.W. AIRA (*day two*)
Kimberly Martin (for James S. Blumenstock), Association of State and Territorial Health Officials (ASTHO)
Christopher Regal (for James David Nordin, M.D., M.P.H.), America's Health Insurance Plans (AHIP)
Gillian Stoltman, Ph.D., M.P.H. (for Tiffany Tate, M.H.S.), National Association of County and City Health Officials (NACCHO)

Designated Federal Officer

Bruce G. Gellin, M.D., M.P.H., Deputy Assistant Secretary for Health (ASH)

and Director, National Vaccine Program
Office (NVPO), Department of Health
and Human Services (HHS)

Day One—February 7, 2017

Welcome and Call to Order—Bruce G. Gellin, M.D., M.P.H., Deputy ASH and Director, NVPO, HHS

Bruce G. Gellin, M.D., M.P.H., called the meeting to order at 9:20 a.m. He outlined key parts of the Federal Advisory Committee Act, its conflict-of-interest rules, and standards of ethical conduct for NVAC members. Dr. Gellin then called the roll.

Welcome—Jewell Mullen, M.D., M.P.H., M.A., Acting ASH, HHS

Dr. Mullen welcomed the participants, noting that NVAC brings together an important set of partners for HHS. Dr. Mullen thanked those who contributed to the NVPO's mid-course review (MCR) of the National Vaccine Plan (now available online) and looked forward to the recommendations of NVAC's MCR Working Group. She encouraged NVAC members to think about how to build on the insights from the two MCR processes to prioritize efforts throughout the immunization system that can optimize the prospects for success.

Regarding the transition to the new administration, Dr. Mullen said she and her colleagues at HHS continue their work as part of the political lifecycle. She emphasized that while changes in leadership occur, she and other staff continue to pursue their work. She suggested that all of those wondering how their work will be affected by the incoming administration continue their work and thanked them for being guideposts around the country and around the world.

Dr. Mullen announced that Dr. Gellin will be leaving NVPO and said HHS would miss his incredible knowledge, unwavering leadership, and dedication to strengthening the immunization enterprise. Dr. Gellin consistently takes a system-wide view in his work to improve the nation's vaccine ecosystem, said Dr. Mullen. From his first days at HHS, he has served as a physician, scientist, public servant, and strategic leader, utilizing critical partnerships to accomplish the goals of the National Vaccine Plan. He has passionately advocated a vision to improve protection against vaccine-preventable diseases across the life span, most recently with a focus on adults. His vision for improving adult immunization rates resulted in a task force, a collaborative strategic plan, and number of coordinated activities, such as the National Adult Influenza and Immunization Summit, which strengthen the adult immunization infrastructure and seek to remove barriers while improving adult vaccination rates.

With the goal of building better systems, Dr. Gellin also coordinated the expansion and integration of the nation's vaccine safety monitoring system by bringing together the Federal government's vaccine safety experts and establishing the Immunization Safety Task Force. This task force was critical to ensuring the safety of the 2009 H1N1 pandemic influenza vaccine, creating the Post-licensure Rapid Immunization Safety Monitoring System (PRISM), and formalizing the vaccine safety scientific agenda.

Dr. Gellin led the HHS team tasked with the U.S. donation of H1N1 vaccine to provide greater access to countries with limited supplies, ensuring the success of this humanitarian effort. He has also been extraordinarily active in advancing immunization by participating in a number of societies, committees, task forces, advisory committees, working groups, and boards over the years, including NVAC. As this meeting commemorates the 30th anniversary of both the NVAC

and NVPO, said Dr. Mullen, it is striking how much Dr. Gellin has influenced the work that will be acknowledged today. She presented Dr. Gellin with a plaque acknowledging his outstanding service to NVPO, NVAC, and the nation over the last 15 years.

In closing, Dr. Mullen thanked six retiring members of NVAC, acknowledging their individual contributions during their terms: Sarah Despres, J.D., Philip Hosbach, Ruth Lynfield, M.D., Yvonne Maldonado, M.D., Wayne Rawlins, M.D., M.B.A., and Mitchel C. Rothholz, R.Ph., M.B.A.

Chair's Report—Kimberly M. Thompson, Sc.D., NVAC Chair

Dr. Thompson gave an overview of the agenda and meeting proceedings. She 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). The minutes and presentations of past meetings are available online at http://www.hhs.gov/nvpo/nvac/index.html.

Dr. Thompson called for review of the September 2016 NVAC meeting minutes. NVAC members unanimously approved the minutes with no changes. The next two NVAC meetings are June 6–7 and September 26–27, 2017.

Many of the six NVAC members who are retiring from Committee had agreed to extend their service beyond their original terms so that NVAC would continue to have a quorum while it confirmed new members. Dr. Thompson thanked them for their service. She announced the four new voting members of the NVAC: Steve Black, M.D., Jay C. Butler, M.D., C.P.E., FAAP, FACP, FIDSA; Melody Anne Butler, B.Sc.N., RN; and Robert H. Hopkins, Jr., M.D., MACP, FAAP. When this meeting ends, seven new members will be sworn in and begin their NVAC terms: John Dunn, M.D., M.P.H., Leonard Friedland, M.D., Mary Anne Jackson, M.D., F.A.A.P., F.P.I.D.S., F.I.D.S.A., Melissa Martinez, M.D., F.A.A.F.P., Cody Meissner, M.D., F.A.A.P., Larry Pickering, M.D., F.A.A.P., F.I.D.S.A., and Geeta Swamy, M.D., F.A.C.O.G.

Dr. Thompson expressed appreciation for Dr. Gellin's impact in making NVAC's work visible. Since 2002, more than 25 NVAC reports have been published in the medical literature.

NVAC at 30

Remarks—Bruce G. Gellin, M.D., M.P.H., Deputy ASH and Director, NVPO, HHS

Dr. Gellin said that when he began at the NVPO in 2002, the National Vaccine Plan, published in 1994, was in need of updating. By the time the new plan was published in 2010, it was thorough and comprehensive enough to serve as the foundation for the NVPO's and NVAC's work and as a framework for the vaccine enterprise.

The 30th anniversary of NVPO and NVAC is an opportunity to reflect on the changes in the landscape since the National Vaccine Plan was published in 2010. Dr. Gellin said the vaccine enterprise is like an engine; to ensure the best function, all the gears must do their part. It is NVAC's role to look at the engine and make sure the National Vaccine Program is doing what it is intended to do.

National Vaccine Program and NVAC: Beginnings and Highlights—Alan Hinman, M.D., M.P.H., Senior Advisor, Center for Vaccine Equity, Task Force for Global Health

Dr. Hinman described the events leading up to the passage of the National Childhood Vaccine Injury Act in 1986, which created the NVPO, NVAC, the Vaccine Injury Compensation Program (VICP), and the Vaccine Adverse Events Reporting System (VAERS) and mandated a 6-month vaccine stockpile. These events included a high-profile controversy over the potential long-term harm of a vaccine (for pertussis), acknowledgement of the inherent risks of vaccines, calls for better information about risks, and the need for a no-fault injury compensation system.

Dr. Hinman described his early experience working with the NVPO. The NVPO was charged with optimizing the prevention of human infectious diseases through immunization and preventing adverse reactions to vaccines. It was given a broad list of responsibilities touching on every aspect of the vaccine enterprise. The NVPO was also required to develop a National Vaccine Plan. The NVPO reported to Congress in 1988, outlining eight priority areas that would become the framework for the first National Vaccine Plan in 1994.

The first NVAC meeting took place in June 1988 with Dr. Hinman serving as coordinator of the NVPO. Beginning with a 1991 report on the measles epidemic, the NVPO and NVAC published numerous influential reports covering a range of topics, which Dr. Hinman highlighted. Dr. Hinman concluded that vaccine hesitancy and opposition were important issues at the onset of NVAC and remained important throughout the years. While many financial barriers to vaccination were overcome by the Vaccines for Children (VFC) program and the Affordable Care Act (ACA), the future is uncertain. However, vaccine coverage among children has reached an all-time high, and most vaccine-preventable diseases in children are at a record low (except pertussis).

NVAC and the Future of Vaccinology—Stanley Plotkin, M.D., Emeritus Professor, University of Pennsylvania

Dr. Plotkin described several advances in vaccinology that may address current challenges.

> **Influenza**: Instead of targeting the "head" of the virus, which changes every year, a promising approach under study would use chimeric proteins to change the hemagglutinin to one never seen before by the vaccine. The vaccine would elicit immune response to the "stalk" of the virus, and the vaccine would not have to be revised every year.
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> **Pertussis**: Many efforts are underway to address the waning immunity of pertussis vaccine over time. Several companies are seeking to change from formalin inactivated pertussis toxin to a genetically inactivated pertussis toxin. Other techniques include adding virulence factors, using prime-boost regimens, and using attenuated *Bordetella pertussis* as a boost to inactivated vaccination.
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> **HIV**: Building on the moderate success of an experimental vaccine in trials in Thailand, future research must recognize the important role of non-neutralizing antibodies. The way forward for an HIV vaccine may be the induction of broadly neutralizing antibodies

through envelope trimer structures, building on prime-boost antibody-dependent, cell-mediated cytotoxicity induction with better vectors and adjuvants, or inducing effector CD8+ cells to kill first infected cells using cytomegalovirus (CMV) vectors.

Rotavirus: To address the decreased effectiveness of rotavirus vaccine in tropical countries, researchers are looking to the microbiome. A recent study found that infants with more Bacteroides than other organisms in the gut respond poorly to the vaccine.

Dengue: Half of the world needs a vaccine against dengue. One vaccine has been licensed in a number of countries. However, there is a striking difference in efficacy for different serotypes and noted that the most important issue is the titer (that is, more antibody maybe needed to prevent type 2 infection) and the need for T-cell response.

CMV: An attenuated strain of CMV can be used to prevent the disease in transplant recipients. However, evidence indicates that additional antigens must be added to CMV vaccine to increase its effectiveness.

Respiratory syncytial virus (RSV): A new line of research into RSV stresses the importance of structural biology. It has determined that epitopes in the pre-fusion form of the F glycoprotein induce a high level of neutralizing antibodies. A vaccine using the pre-fusion (rather than post-fusion) form could potentially prevent RSV.

T-cell responses: Few vaccines depend on T-cell immunity. For tuberculosis, researchers are seeking a way to induce T-cell responses that prevent the persistence of tuberculosis organisms in macrophages. For malaria, on the other hand, experimental vaccines do induce T-cell responses to some degree.

Dr. Plotkin noted that only a few vaccine manufacturing companies are investing in research and development (R&D). Future industry growth in India, China, and Brazil may boost R&D. Vaccines must be profitable, or companies will lose interest in producing them. Dr. Plotkin outlined the market forces around vaccines, including the substantial investment required and long timeline for development. Recommendations and requests from government and advisory bodies like NVAC have a strong impact on manufacturers and may appear to serve as an advanced market commitment. Such recommendations should not be made lightly.

Dr. Plotkin mentioned the recent creation of The Coalition for Epidemic Preparedness Innovations (CEPI), an international vaccine development fund that will carry vaccines from conception in academic, government, and biotechnology laboratories to development and licensure by industry. The goal of CEPI is to advance promising products through Phase II clinical trials (and possibly through Phase III studies and licensure) so they could be manufactured and stockpiled for emergency use.

To advance the future of vaccinology, Dr. Plotkin suggested that NVAC identify important targets for vaccine development in the United States, promote the need for new vaccine delivery systems, and urge U.S. Government (USG) support for CEPI in developing vaccines against

emerging diseases. Also, NVAC should support research into personalized medicine that affects vaccines. Dr. Plotkin saluted NVAC members for their work.

Discussion

Much discussion ensued about the role of CEPI, with some NVAC members pointing out the complexities and barriers to successful vaccine development and marketing. Others pointed to the importance of investing in effective delivery systems, adequate infrastructure, personnel, and training.

Further discussion revolved around the purpose of a vaccine priority target list. Much attention is paid to emerging infections and epidemics, with less attention to the most significant burden of disease. Creating a balanced list of targets without a firm advanced market commitment is challenging. Such lists cannot predict the uncertain course of emerging diseases. Also, forming and maintaining stockpiles is difficult and costly. It was suggested that regulatory harmonization would benefit new and existing vaccine technology.

Dr. Thompson pointed out that NVAC plays a critical role by taking into account all the aspects of the system. Marion Gruber, Ph.D., said FDA is working toward regulatory convergence with other countries and has had some success. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) can be a forum for more collaboration.

Dr. Hinman said the Global Vaccine Action Plan sets targets, but the only one being met addresses new vaccine development. More attention should be paid to improving coverage with existing vaccines. Dr. Plotkin said NVAC faces an uncertain future; it will take a lot of work, courage, and insight to respond in a useful way. Dr. Gellin closed the session by recognizing that the vaccine landscape has changed dramatically since NVAC was formed, but NVAC has a role in identifying where more changes are needed. He added that the National Vaccine Plan calls on non-Federal entities to play their part going forward.

Vaccine Safety Science and Personalized Vaccinology

The Case for Personalized Vaccinology in the 21st Century—Gregory Poland, M.D., Mary Lowell Leary Emeritus Professor of Medicine, Distinguished Mayo Investigator, Director, Mayo Vaccine Research Group, Mayo Clinic

Dr. Poland indicated that vaccine development has historically ignored the complexity and diversity of human immune response. Dr. Poland described the early, relatively simple vaccine development approaches as "isolate, activate or attenuate, and inject." He highlighted some relatively recent innovations in vaccine development, including reverse vaccinology, and the development of subunit vaccines and recombinant technology. Dr. Poland observed that most existing vaccines focus on preventing diseases of childhood, and recognized the opportunity to develop therapeutic vaccines for adults recognizing that the number of older and immunocompromised people continues to grow.

Dr. Poland suggested that as medicine becomes more personalized, vaccination will follow and he offered a new paradigm for vaccine development of "discover, validate, characterize, apply." Dr. Poland indicated that in the future, vaccines will focus more on adult and special population

groups' needs, and will include new vaccine delivery systems and multiple, highly-specific adjuvants. He described vaccinomics as a combination of a systems biology approach with the population-level study of immunogenetics to predict vaccine-induced immune responses and he indicated that directed vaccine development based on vaccinomics will speed up the vaccine development process. Dr. Poland described efforts underway to identify immune signatures that would indicate whether a vaccine would be effective in a given individual and indicated that in the future, the application of analytic tools will help investigators understand individual immune responses and recommend alternative vaccines, doses, or delivery methods to avoid adverse events.

Dr. Poland noted that genotyping is commonly used to determine the right drug and dose to treat resistant hypertension, depression, and some common cancers. Evidence indicates that some people may respond differently to some vaccines—for example, adult women appear to develop higher rates of arthritis from exposure to rubella virus and potentially to the live rubella virus vaccine than children or adult males. Dr. Poland presented results from his laboratory that can account for about 30 percent of the difference across individuals in responses to measles vaccine.

Dr. Poland briefly presented the results of studies conducted to understand adverse events associated with vaccines (i.e., adversomics), which included 3 studies related to the delivery of smallpox vaccine. Dr. Poland ended by hypothesizing that future vaccine demand will be driven by offering a better value proposition that allow delivery of the right vaccine to the right person in the right dose at the right time.

Metabolites as Biomarkers of Adverse Reactions Following Vaccination: A Pilot Study Using Nuclear Magnetic Resonance Metabolomics—Bruce McClenathan, M.D., Regional Medical Director, Defense Health Agency, DoD

To study adverse events following immunization (AEFIs), specifically myocarditis or pericarditis after smallpox vaccination, Dr. McClenathan and colleagues relied on metabolomics—the study of the small molecule metabolite profile of a biological organism, which provides a point-in-time functional view of the phenotype of an individual as determined by the sum total of genetic and environmental factors, such as nutrition, exercise, medications, health, disease, and other environmental factors. The goal of the study was to identify a metabolic signature that would predict whether an individual would develop an AEFI.

Dr. McClenathan outlined the study design and methodology, which involved military personnel who were mostly young, healthy, white males. Analysis found increased creatinine, creatine, creatine phosphate, and lysine metabolites following vaccination in group 1—those diagnosed with myocarditis after vaccination. After vaccination, the metabolites lactate and threonine seemed to play a significant role in group 2 subjects—who had no symptoms of myocarditis but did have elevated levels of troponine. Those in group 3—who had AEFIs not related to myocarditis—and group 4—who had no symptoms—all showed changes in metabolites following vaccination, demonstrating that vaccination alone induces changes the recipient's metabolic profile and metabotype.

Groups 1 and 2 had many common metabolites, and group 2 showed several unique metabolites. Creatinine, fructose, histidine, and serine were common across groups 1, 2, and 3. While Dr.

McClenathan did not know the clinical significance of these metabolites, he said investigators in other fields, such as rheumatology, have seen a similar metabotype in a study of lupus, for example. Thus, there may be a common metabolic pathway of the inflammation process, whether autoimmune or triggered by vaccination.

Dr. McClenathan said the study is the first to describe the metabolic profile, pre- and post-vaccination, of patients who had AEFIs. It did not find a unique metabolic signature pre-vaccination that could predict AEFIs, but metabolomics clearly differentiates pre- and post-vaccination samples for individuals with AEFIs, and certain metabolites warrant further investigation. Dr. McClenathan concluded that individuals may have unique responses to smallpox vaccination that can be detected based on metabolic profiling and noted the need for additional metabolomic analysis for vaccines.

(Almost) All Immunity Is Local: Implications for Vaccines from Tissue Immunodynamics—Chuck Hackett, Ph.D., Deputy Director of the Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases (NIAID), NIH

Dr. Hackett explained that most information used to develop and assess vaccines comes from characterization of antibody and T-cell levels in the blood. However, blood does not provide direct information about local immunity. Dynamic changes occur in different tissues from infancy through adulthood. Immune memory is established and maintained in tissues. While studies of tissue immunity have relied on mice or human tissue removed during surgery, Dr. Hackett described new research that studied the immunological composition of tissues from deceased otherwise-healthy organ transplant donors that led to interesting insights about the rules that govern how T-cells operate in tissue. For example, investigators found that it is possible to intranasally vaccinate imprinted T-cells that then go to the intestines.

Dr. Hackett discussed the distribution of T-cells within age groups and noted that memory T-cells predominate in all tissue and accumulate with age, but aging memory cells exhibit reduced effector functions. Dr. Hackett described the dynamics of memory T-cells in different tissues from infancy to adulthood. Notably, T-cell memory establishes early in life, so early vaccines are important. Antigen specificities differ by organ and account for differences in protection at distinct sites. Responses to commensal microbiota are important for maintaining immune defenses and the regulatory responses in mucosal tissue and skin. Regulatory T-cells are strongly expressed in most infant tissues, except lungs and small intestines (which may be areas in an infant at which they are able to respond well to vaccines). Dendritic and other antigen-presenting cells provide a sentinel function in the skin and intestines.

Antigen-presenting cells that initiate responses in different tissues and age groups may be activated by adjuvants. Infants may need adjuvants to promote long-lived Th1 responses. A study of a shingles vaccine found adjuvants were especially effective in older adults. Dr. Hackett called for more analysis of adjuvants designed to boost secondary responses, so that the vaccine reaches antigen-presenting cells in subsequent immunizations. He described ongoing research capitalizing on the effectiveness of adjuvants with less inflammatory response or toxicity.

Dr. Hackett said new technology (e.g., multiplexed ion beam imaging) will allows investigators to make use of a lot more tissue from biopsies and other sources to better understand tissue

responses, tissue immunity, and interactions of cells, which will pave the way for personalized vaccines. In addition, NIH research funding is supporting sample-sparing assays for immunological assays, mucosal immunology studies, infant and elderly immunity research, new databases, and various other efforts. Dr. Hackett concluded that understanding what is happening at the protective level will help drive decision-making about vaccine and adjuvant approaches.

Discussion

Yvonne Maldonado, M.D., suggested and Dr. McClenathan agreed that studying a more ethnically diverse patient population would yield useful information. However, Dr. McClenathan noted that myocarditis following smallpox vaccination tends to occur in young, white males.

Asked to address how personalized vaccines might relate to the development of a universal influenza vaccine, Dr. Poland said vaccines could be developed that eliminate pathogen variability and antigen presentation, but the diversity of hosts would persist, which could affect immunity. Dr. Hackett emphasized the need to look at adjuvants to boost secondary responses and to better understand how T-cells can help B-cells.

Saad Omer, M.B.B.S., M.P.H., Ph.D., asked what NVAC could do to facilitate the next generation of discovery. Dr. Poland supported the notion that NVAC could weigh in on removing structural barriers to repositories that can be used for characterization of bacteria, genotypes, and phenotypes. He added that it is very difficult for researchers to accumulate enough cases of adverse events of vaccines for studies to have adequate statistical power, so coordination at the national level would be very useful. Dr. Maldonado pointed out that NIH's All of Us program (formerly the Precision Medicine Initiative) will create extensive biobanks, although the samples will only represent adults. She added that NVAC could consider how to coordinate existing biobanks to facilitate research into vaccine-associated rare adverse events.

Kathryn Edwards, M.D., asked for input on how to improve communication and data exchange in support of better understanding of individual reactions to vaccines. Dr. Poland replied that interdisciplinary team science will help, and noted the opportunity to create consortia to bring together experts from different disciplines.

Vaccine Delivery Systems

Innovative Vaccine Delivery Technologies: New Paradigms for Immunoprotective Countermeasures—Jonathan Seals, Ph.D., Director, Strategic Science and Technology, Biomedical Advanced Research and Development Authority (BARDA)

Dr. Seals explained BARDA's role in vaccine development. Developing a vaccine takes 10-15 years and costs about $2 billion. Time and costs are especially significant barriers to developing vaccines for emerging and re-emerging infectious diseases; yet addressing such diseases is now seen as a government responsibility that requires investment.

BARDA works closely with researchers, manufacturers, and biotechnology companies to understand the landscape of vaccine development. Dr. Seals described innovations in the approaches used for vaccine development and he summarized the strengths and liabilities of each of the technologies in development for immunogen production and formulation along with the estimated time for each product to go from initiation to use in humans (briefly termed "first in

humans" or FIH). With current approaches using live attenuated pathogens and inactivated pathogens, the FIH time is about 12–24 months, which is problematic for an emergency response. Newer products, some of which are already in use, include use of pathogen subunits and recombinant technology; the FIH time ranges from 9-18 months. Novel adjuvants are also in use, but they are relatively rare among licensed products leading to an uncertain FIH. With the use of virus-like particles, viral vectors, and engineered attenuated pathogens, Dr. Seals estimated the FIH may drop to 6-12 months, which the use of nucleic acids or synthetic production could bring the time down to 3–9 months. Dr. Seals described where each product currently falls in the pipeline and said BARDA will continue to monitor the field and evaluate promising technologies and noted that some technologies have advanced further in vaccine research for cancer than for infectious disease.

Some innovative products for vaccine administration have made it into the marketplace and others are in development, but BARDA saw minimal response to its efforts to encourage more innovation around administration. Dr. Seals believes that product developers do not think about routes of administration at the beginning of their work. Products are then tested using traditional routes, and it is difficult to change the route of administration once testing has started. Moreover, companies are unwilling to invest in alternative delivery approaches because of concerns that vaccine purchases will not pay the higher prices for the products requires to offset their development.

Dr. Seals emphasized the importance of working with companies to encourage work on delivery approaches early in the process. Some products are already relying on mucosal administration. There has been a lot of interest in skin patches that use microneedles or soluble microstructures. Dr. Seals concluded that after 200 years of successful vaccine development, it is time to invest in new technologies to address the threats of the future.

Discussion

Dr. Seals clarified that BARDA tries to reach a broad range of technology companies and vaccine makers. In its attempts to encourage innovation, BARDA found some technologies that might have vaccine applications, but vaccine makers were not interested in them. Dr. Maldonado pointed out that the field is so young that there are no consortia to propel research in novel technologies and the science on which technologies are based is still emerging. Dr. Seals said BARDA aims to help both small and large companies pursue work that may not have immediate commercial potential. It also seeks to broker partnerships. Dr. Seals added that BARDA is engaged with CEPI and the Gates Foundation, as all are working toward the same goals.

2010 National Vaccine Plan MCR

NVAC MCR Working Group (MCRWG) Final Report—Yvonne Maldonado, M.D., and Nathaniel Smith, M.D., M.P.H.

Dr. Maldonado described the process and timeline of the MCRWG's effort to conduct an independent mid-course review of the National Vaccine Plan and assessment of the NVPO's MCR, noting that the draft NVAC report and recommendations were presented for input at the September 2016 meeting. The current version of the NVAC report incorporates the comments of NVAC members and the public. It emphasizes the need for indicators to measure progress and identifies some key challenges to success of the National Vaccine Plan.

The MCRWG report is intended to complement the NVPO's MCR but underscores some of the nuances in priorities among the stakeholder groups and recommends activities to strengthen these priority areas and develop new indicators. While the NVPO's analysis identified nine opportunity areas on which the National Vaccine Plan should focus, the NVPO MCR focused on the top five (as ranked through stakeholder engagement exercises). The MCRWG report similarly focused on the top five opportunity areas, but also recognized the importance of the other 4 opportunity areas. The NVAC MCRWG report recommendations include:

- The ASH should charge the NVPO, in coordination with relevant departments and agencies, to adopt existing indicators (e.g., Healthy People 2020 indicators) to track progress on the National Vaccine Plan goals and to prepare an annual report to the ASH and the NVAC on progress.

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

- The ASH should continue to strongly support U.S. contributions to global immunization efforts and the integration of global immunization efforts into the opportunity areas as appropriate.

- The NVPO should continue to implement the recommendations from previous NVAC reports, such as the 2015 NVAC report, *"Assessing the State of Vaccine Confidence in the United States."* By doing so, the NVPO can highlight NVAC recommendations related to implementing the priorities outlined in the NVPO 2010 MCR. The NVPO should use the framework defined in this report to make further advancements under the existing 2010 National Vaccine Plan for both domestic and global immunization outcomes.

- The ASH should charge the NVPO to develop the 2020 National Vaccine Plan, which should incorporate the findings in this report, and consider the impact of health care disparities on implementation and achievement of the objectives of the 2020 Plan.

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

Dr. Smith said three organizations responded to the MCRWG's request for public comments: the American Academy of Family Physicians (AAFP), PATH, and Walgreens. Their comments were generally supportive, with some suggestions for relatively limited changes or considerations. Dr.

Smith walked through each of the comments and how the working group addressed them, which the working group addressed in an adjudication report.

Discussion

Mr. Hosbach suggested and Dr. Gruber agreed that references in the report to regulatory "harmonization" should be changed to "convergence" to reflect FDA's preferred terminology. NVAC members voted unanimously in favor of the change.

Discussion ensued about the need to encourage communication and data-sharing across providers and organizations, which is addressed in the report's discussions of the medical home and provider education. The term "bidirectional" communication in the report specifically refers to immunization information system (IIS) data reporting and exchange. Dr. Hopkins pointed out that Federal law prohibits the release of information about employer-supported care to anyone outside of the employment setting, which poses a barrier to getting information about individuals vaccinated at work.

Dr. Messonier raised two suggestions, including the need to revise the wording about the 2014–2015 California measles outbreak to clarify that some of those affected were too young to be vaccinated and to fix one of the targets for the indicators in Box 3. NVAC members voted unanimously in favor of the suggested changes.

Members debated whether to revise or omit language in the report referring to the ACA. There was consensus that the report recognizes the current state of affairs and acknowledges uncertainty about the future of the ACA, so no changes are needed.

Public Comments on MCRWG Final Report

Dr. Plotkin suggested publishing a summary on the U.S. vaccine safety system. Dr. Gellin noted that NVAC published such a report in 2011, but it is concerning that even some experts in the field are not aware of it. Nancy Messonnier, M.D., CAPT, suggested CDC and NVAC consider updating materials for the lay public on vaccine safety systems, but not in the context of the MCRWG report.

> **Vote**
> NVAC members voted unanimously to accept the MCRWG report and recommendations as final, with the changes suggested at this meeting.

Updates on Mumps Outbreaks

Mumps Epidemiology and Public Health Response in Minnesota—Ruth Lynfield, M.D.

Dr. Lynfield gave an overview of mumps infection, symptoms, spread, and treatment. Surveillance is challenging because the symptoms are nonspecific. Parotitis, commonly associated with mumps, can be caused by numerous factors other than mumps infection. Mumps spreads among those in close quarters (e.g., on college campuses). In up to 30 percent of cases, infected individuals have no symptoms or nonspecific symptoms.

Polymerase chain reaction (PCR) testing is the preferred method for laboratory confirmation. Serologic testing for immunoglobulin M antibody is also used. False-positive results are

common with serology. For both methods, false-negative results may occur in vaccinated individuals.

The ACIP recommends one dose of mumps vaccine in infancy and a second in early childhood. For adults, one or two doses is recommended depending on risk. The vaccine is highly effective. Since its introduction in 1967, cases of mumps have decreased 99 percent, and complications from mumps are now very rare.

A timeline of mumps cases since the introduction of the vaccine shows occasional resurgences, and Dr. Lynfield observed the cyclical nature of mumps. In 2006, a spike caused 7,000 cases across the United States, 180 of those in Minnesota. The 2016 spike caused about 5,300 cases, with 25 of those in Minnesota. Of the 25, three had received two doses of vaccine, and one had one dose. Most of the rest reported vaccination, but their status could not be confirmed. One case was linked to exposure during international travel. Several were linked to exposure on college campuses.

The Minnesota Department of Health typically evaluates 200–300 suspected cases of mumps per year, and confirmation typically takes 1–3 days. Suspected cases are reported by laboratories, providers, or members of the public. The Department of Health gathers information from providers, coordinates laboratory testing, and communicates with key people (e.g., parents, schools, providers). If test results confirm the diagnosis, the Department of Health continues its investigation, typically for up to 5 days, to identify the source, determine possible contacts, and notify about potential exposures.

The Department of Health works with media and other public health entities to spread the word about an infection. It concluded that an individual from Washington State infected with mumps attended a national high school wrestling tournament in Minnesota in December, touching off the spread of disease in the State.

Update on Mumps Outbreaks: Arkansas—Nathaniel Smith, M.D., M.P.H.

Dr. Smith said the mumps outbreak in Arkansas began in August when an infected person from Iowa visited. At the peak of the outbreak, the State saw 50 cases per day. The outbreak appears to be slowing down, as only 5–10 cases per day are being reported. Most cases occurred in the northwestern part of the State. The neighboring State or Oklahoma experienced more than 500 spillover cases, while Missouri, Texas, and others were less affected.

As of February, Arkansas had investigated more than 2,700 cases of mumps. Unlike other State outbreaks that happened mostly on college campuses, almost two-thirds of Arkansas cases occurred in school-age children. Arkansas has a significant number of residents from the Marshall Islands who live in the north part of the State, and they typically travel back and forth between the State and the islands. Early in the outbreak, most cases occurred among the Marshallese. Now, the outbreak is mostly affecting non-Hispanic White residents. Also, although the northwest has the highest proportion of nonmedical vaccine exemptions in the State, over 90 percent of school-age children infected were fully immunized against mumps. Dr. Smith said it has been difficult to confirm the vaccine status of Marshallese residents.

Dr. Smith described the decrease in complications following clinic vaccinations. He noted that in 58 cases, or about 4 percent of positive cases, individuals continued to have positive PCR results more than 5 days after the onset of parotitis. The CDC guidelines on testing indicate that shedding after 5 days is rare. Interestingly, 69 percent of those with prolonged shedding are Marshallese, which is proportional to the number infected.

Arkansas saw 17 cases of recurrent disease, mostly in children and young adults who were female and Marshallese. Of those cases, 16 had two doses of vaccine, and one had one dose. None of these cases had a positive PCR test (in either the first or second occurrence).

In response to the outbreaks, Arkansas set up more than 50 vaccination clinics in schools, workplaces, churches, and community centers. In some highly infected neighborhoods, public health providers went to individual residences to vaccinate Marshallese residents who are reluctant to come to clinics. In some cities with ongoing transmission, third-dose booster vaccinations were provided. As of February 1, more than 7,400 vaccine doses were delivered, primarily in school and work settings.

Data from school-based clinics show a decrease in the attack rate within a few weeks of vaccination. Among students who got a third dose, no cases have been reported after 27 days following vaccination. Dr. Smith said those who received a third dose may have had a higher likelihood of exposure and so a higher attack rate (than those who did not get a third dose) in the first 26 days after vaccination. Waning immunity does not appear to be a significant problem. The number of cases since last vaccination declines steadily over time; there is no increase in infections at some point in the years after vaccination.

Arkansas took various approaches to overcome communication challenges about the outbreak. The State relied on community contacts, especially among the Marshallese, where language and cultural barriers were an issue. A contingency from the Marshall Islands, including the minister of health, traveled to Arkansas to talk with community leaders about how to disseminate information. Dr. Smith hoped the many steps that Arkansas has taken are helping, and reported that mumps cases are now decreasing.

Update on Mumps Outbreaks: CDC—Nancy Messonnier, M.D., CAPT, CDC

Dr. Messonnier said the mumps vaccine is doing its job, but there have been resurgences in mumps over the past 15 years. While Arkansas has been disproportionately affected by the recent outbreak, other States have also been affected. In most other States, the outbreaks are focused in college settings. Since the start of 2017, Washington State is experiencing the most cases of mumps.

When comparing the Arkansas cases with the college campus outbreaks in other States, it is clear that Arkansas was much harder hit. At its upcoming meeting, ACIP will discuss mumps and its recommendations for mumps vaccine now that some data are available as a result of the resurgence of disease. Dr. Messonnier said the CDC has some early data on duration of protection and efficacy of a third dose. She noted that duration of protection and efficacy may vary for different settings.

Discussion

Mr. Rothholz asked how States and CDC are thinking about the fact that most of school-aged children infected in Arkansas were fully immunized. Dr. Messonnier responded that the data suggest there are questions about the duration of coverage; Arkansas represents the first community outbreak with high attack rates despite high coverage. Dr. Smith added that a higher proportion of Marshallese children were infected despite having higher coverage rates than non-Hispanic White children. Dr. Messonnier noted that there has been no outbreak of mumps among Marshallese outside the United States. Dr. Smith said patterns of housing and other social factors may aid transmission among the Marshallese in Arkansas. The outbreak raises the question of whether the vaccine has the same efficacy in different populations.

Participants briefly discussed the role of genetics in mumps recurrence and vaccine effectiveness. Dr. Thompson said that in the case of measles vaccination, characterizing the costs of addressing measles was helpful in making the case for coverage. Dr. Smith said Arkansas will assess the costs and impact of the mumps outbreak. The fact that most of those affected were fully immunized poses a real challenge to vaccine confidence among parents. Dr. Messonnier added that indirect costs of outbreaks—such as the impact on vaccine confidence—are hard to calculate. Dr. Plotkin said he believes there is evidence of waning immunity and that genotype differences between the original and current strains may be a factor. Also, there are no good correlates of protection for mumps. Boosters are one way to address the problem, but a new vaccine may be needed. Dr. Thompson concluded that the presentations and discussion highlighted all the challenges, and attention must turn to addressing all the aspects of the issue.

Public Comment

Erin Fry Sosne of PATH said her organization appreciates NVAC's recognition of the role global immunization plays in protecting Americans at home and abroad and other global citizens. Including the Global Vaccine Action Plan indicators in the MCR will be very important in ensuring that the efforts of the US government are aligned with the global community. PATH is looking forward to the implementation of NVAC's recommendations and to partnering with HHS as those implementation plans are developed.

On a related note, PATH is pleased to see the NVAC members working to ensure that U.S. efforts to combat antimicrobial resistance are also paying great attention to the role of immunization in that effort, in terms of both vaccine development and delivery. Vaccines are the safest and most cost-effective way of preventing disease, disability, and death worldwide. Robust immunization programming around the world from development through delivery is essential for the safety of Americans and the world's citizens. On behalf of PATH, Ms. Sosne thanked NVAC for its tireless efforts for 30 years to ensure that scientific evidence informs decision-making.

Theresa Wrangham, Executive Director of the National Vaccine Information Center (NVIC), commented on Dr. Hinman's presentation and noted his mischaracterized the NVIC as "anti-vaccine." The NVIC mission statement embraces the informed consent ethic. Because vaccines are pharmaceutical products that can and do cause injury and death, they are subject to informed consent, which is, in short, the human right of individuals and parents to have access to accurate risk and benefit information on disease and vaccines and the ability to voluntarily accept, delay, or decline vaccines without interference or sanction.

Ms. Wrangham said the NVIC appreciates the acknowledgement of its past service to the NVAC, and she described several other NVIC accomplishments and partnerships in support of vaccine safety. It is therefore unfortunate that recent NVAC stakeholder efforts and reports relating to, for example, vaccine hesitancy, adults and maternal vaccination, and the MCR did not include the NVIC. Ms. Wrangham hoped that future stakeholder and work group efforts led by the NVAC would be more inclusive.

Regarding the current approach to vaccine safety, the NVIC noted that the Institute of Medicine acknowledged that individual susceptibilities and genetic predispositions are likely to play a role in vaccine injury. Should scientific advances discussed today become the norm, these advances must never override the informed consent ethic and the human right to make voluntary health care choices without sanction.

In response to the statement that vaccines must be profitable for vaccine manufacturers, it does not ethically follow that the consumer should be burdened with mandates to use vaccines acknowledged as unsafe to ensure the success of corporate entities. Where there is risk there must be choice, without coercion, penalty, or demonization, particularly when the choice falls outside the majority view. Ms. Wrangham pointed out that those on the phone were not offered the opportunity to provide comment on the MCR as those attending in person were.

Adjournment

Dr. Thompson adjourned the meeting for the day at 5:01 p.m.

Day Two—February 8, 2017

Welcome—Kimberly M. Thompson, Sc.D., NVAC Chair

Dr. Thompson called the meeting to order at 9 a.m. and welcomed the participants.

Zika Vaccine Development

Zika Virus Epidemiology Update—Marc Fischer, M.D., M.P.H., National Center for Emerging and Zoonotic Infectious Diseases, CDC

Dr. Fischer described the Zika virus and its spread across the world. As of January 2017, 50 countries and territories in the Americas have reported locally-transmitted virus. In the United States, limited local outbreaks have occurred in Florida, Texas, and three U.S. territories. The outbreaks that started in 2015 demonstrated clinical manifestations not seen with previous Zika virus infection: fetal loss, microcephaly and other congenital anomalies, Guillain-Barré syndrome and other neurologic syndromes, and thrombocytopenia. This outbreak also identified new modes of transmission: intrauterine, intrapartum, sexual, laboratory exposure, and blood transfusion. Other possible mechanisms of transmission are organ or tissue transplantation, breast milk, and other bodily fluids.

The risks of adverse events following Zika virus infection in pregnancy are not fully known. The risk of fetal loss appears to be higher with earlier infection in pregnancy. The risk of congenital microcephaly ranges from one percent to 13 percent following infection in the first trimester. In

addition to microcephaly, infants exposed to Zika virus in utero demonstrate a number of conditions, including brain anomalies, neurologic sequelae, ocular anomalies, and congenital contractures. Perinatal transmission was reported in two women from French Polynesia. Several recent reports indicate sexual transmission, mostly from symptomatic men to their female or male partners. The incidence, duration, and risk factors for sexual transmission are not known. Two U.S. studies are evaluating the frequency and duration of Zika virus RNA and live virus in semen.

A few cases of transfusion-related infection have been reported in French Polynesia during 2013-2014 in, as well as in Brazil during 2016. The United States issued recommendations to prevent transmission by transfusion and instated Zika virus screening for all blood donations. One case of laboratory transmission (via needle stick) was reported in 2016. Transmission through breast milk has not been documented, although Zika virus RNA was detected in the two French Polynesian women who experienced perinatal transmission. The CDC stated that the benefits of breastfeeding outweigh the theoretical risks of transmission. Zika virus RNA has been detected in saliva and tears. One case of possible person-to-person transmission was documented in Utah, but no specific source of transmission was identified.

Interventions focus on preventing exposure to mosquitoes by vector control and use of personal protective measures. Pregnant women are advised to avoid areas with local transmission and protect themselves against possible sexual transmission. Numerous vaccine candidates are being evaluated. If approved, vaccine use would be dictated by the incidence of disease and its complications, the safety and efficacy of the vaccine, and the duration of protection.

Discussion

Dr. Fischer said it is not clear why microcephaly associated with Zika infection is seen more often in certain regions of Brazil; many hypotheses have been evaluated. Several studies plan to conduct multiyear monitoring of infants of women exposed to Zika virus during pregnancy. Dr. Fischer said the best way to identify congenital infection (e.g., molecular testing at birth, serologic testing) is not yet known, because other flaviviruses can cross-react with Zika virus, confounding test results. There are two genotypes of Zika virus, but the phenotypes are the same.

Overview: Zika Vaccines in Development—Gerald Kovacs, Ph.D., Senior Advisor, BARDA

Dr. Kovacs was unable to attend, so Dr. Gellin summarized the presentation on his behalf, focusing on the policy issues. In light of the Zika virus outbreaks, an effort was made to coordinate the vaccine development portfolio across Federal agencies. Much of the research builds on vaccines developed for other flaviviruses. Different agencies play a role in different aspects of the R&D pipeline; FDA provides guidance at all stages. The government's timeline calls for 1) identifying and assessing candidates for vaccines through 2018, 2) deploying a vaccine (possibly under emergency use conditions) to those at high risk by 2018, and 3) achieving commercial production of a vaccine for broad distribution by 2020.

Each vaccine technology has its own challenges and considerations for development. For example, commercial platforms exist for a live attenuated vaccine, but live virus vaccines are contraindicated for pregnant women. Understanding the target populations is a key concern for a Zika virus vaccine. There are candidate vaccines in the pipeline that respond to each of the

government's three goals. Candidates available for use by high-risk individuals by 2018 could go on to meet the goal of commercial production by 2020. Many candidates are supported by USG funding. Three candidates are in phase-I clinical trials, so the need to address outstanding questions, such as the following, is pressing.

- Will the incidence of the disease be large enough to support evaluation of vaccine candidates—especially given that mosquitoes and the virus are moving rapidly? Can manufacturers develop a vaccine fast enough to have an impact on the epidemic?
- Which regulatory pathway will be most feasible?
- Will human challenge studies (if ethically possible) or accelerated approval mechanisms help move the process forward?
- Will animal models provide sufficient data to support use in humans?
- Does immunity to other flaviviruses affect Zika vaccine uptake, and vice versa?
- Will previous *Flavivirus* vaccine platforms be helpful?
- Will the market sustain more than one vaccine?

Discussion

Dr. Fischer said an interagency task force is working on an executive summary that lays out the aims, objectives, and timelines of Zika virus vaccine development and includes a market analysis of potential target populations. A list of preferred product characteristics was developed and circulated among manufacturers. The ultimate market remains to be defined.

Dr. Omer called for a specific, deliberate effort to consider the needs of pregnant women in the early stages of Zika vaccine development. He observed that recent NVAC recommendations on maternal immunization were reflected in the 21st Century Cures Act. Dr. Omer suggested NVAC's Vaccine Innovation Working Group look closely at the accelerated activity around Ebola and Zika viruses.

Dr. Gruber said FDA is talking with a lot of developers about the kinds of evidence needed to demonstrate efficacy. The regulatory pathway to licensure depends on the scientific data. For example, demonstrating efficacy on the basis of immune markers would require a reliable assay for measuring the marker. Current assays cannot distinguish Zika virus from other flaviviruses.

Timothy Cooke, Ph.D., expressed concern that funding for innovative R&D may cease if products never come to fruition. He noted that the Vaccine Innovation Working Group can consider potential recommendations to ensure a stable R&D pipeline. The "push" funding is available to start the process of creating candidates, but the incentives must shift when companies reach the point of doing efficacy studies.

Dr. Maldonado noted that NIH is funding research on assays, which are vital to understanding the sero-epidemiology. Barbara Mulach, Ph.D., offered to provide an update on NIH and extramural Zika research at a future NVAC meeting.

Vaccines in the 21st Century Cures Act

Vaccine Innovation—Bruce G. Gellin, M.D., M.P.H., Deputy ASH and Director, NVPO, HHS

Dr. Gellin said the new legislation dedicates 20 pages to vaccines, thanks to work by HHS and NVAC. The legislation calls for a report from the HHS Secretary on vaccine innovations that describes the status of development, the optimal process for determining safety, obstacles to innovation, and how to overcome them. Dr. Gellin said NVAC has a role to play in developing the report, because it has broad stakeholder representation and a working group that can bring in more stakeholder insights. The draft report should go to the Secretary by October to ensure it is cleared in time to meet the due date in December 2017.

Impact on the VICP—Narayan Nair, M.D., CAPT, DICP, HRSA

Dr. Nair explained that a few provisions of the act affect the VICP—some on covered vaccines that are administered to pregnant women and some on new vaccines recommended only for pregnant women. It requires revising the Vaccine Injury Table to include vaccines recommended by CDC for routine use in pregnant women. Such inclusion means that manufacturers and those who administer vaccines to pregnant women would not be liable for injuries (that is, injury claims would go to the VICP).

The act also clarifies that when a vaccine is administered to a pregnant women, the recipients are both the woman and her fetus. Until now, neither statute nor court decisions resolved the question of who received the vaccine and was thus eligible for compensation. Previously, compensation was limited to one injury claim per individual; this new legislation treats the pregnant woman and her fetus as two individuals, allowing for separate injury claims for the mother and her child.

Impact on CDC—Nancy Messonnier, M.D., CAPT, CDC

Dr. Messonnier said the legislation calls for predictable review of vaccines by ACIP. She said ACIP tries to review new vaccine licenses and indications in a timely manner, but a transparent review process requires some time. The legislation also calls for a review of ACIP processes and tools for making recommendations, with the goal of ensuring consistency across ACIP working groups. Input from stakeholders will be used to improve processes.

The act requires CDC to encourage vaccine innovation by meeting with stakeholders and aiming to coordinate efforts across the field. Dr. Messonnier said CDC works closely with stakeholders and communicates about epidemiology, prevention, and control. She appreciated the need to coordinate requests so that all stakeholders have equal access to data and know how to get the data they need for vaccine development and administration. Staff from CDC are requesting input from vaccine developers about their experience with the ACIP process; the input will be used to ensure that ACIP working groups deal with all companies openly and in the same manner. Other CDC divisions play a role, so the goal is to ensure that stakeholders have a similar experience no matter what division they contact.

Additional Comments from NIH—Barbara Mulach, Ph.D., NIH

Dr. Mulach pointed out that the legislation does not address vaccine innovation at NIH, but it does talk about NIH's role in innovation generally, including the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, All of Us (formerly the Precision Medicine Initiative), the Cancer Moonshot, and the Regenerative Medicine Program. Current NIH Director Francis Collins, M.D., Ph.D. has been asked to stay on as NIH Director for now.

Additional Comments from FDA—Marion Gruber, Ph.D., FDA

Dr. Gruber said the act dictates many changes to FDA regulations; she focused on four areas related to trial design and evidence development. Under the new legislation, FDA is required to hold public meetings and issue guidance on novel clinical trial designs that can meet FDA evidence criteria. Also, FDA must establish a program to evaluate the potential use of real-world evidence to support new indications for an approved drug. Such evidence could include data from safety surveillance mechanisms, observational studies, registries, claims, and patient outcomes. Within 5 years, FDA must issue draft guidance on use of real-world evidence.

The act requires HHS and FDA to update and harmonize regulations on human subjects protections, modernizing them and reducing duplication. It directs HHS and FDA to allow joint or shared institutional review board (IRB) evaluation. The act allows clinical trials to be exempt from informed consent requirements when the study poses no more than minimal risk and has appropriate safeguards in place to protect the rights, safety, and welfare of subjects. Dr. Gruber noted ongoing discussion of whether the informed consent waiver applies to vaccines; FDA has always maintained that vaccines pose more than minimal risk to recipients.

Discussion

Dr. Thompson noted that the 21st Century Cures Act requires HHS to establish a task force on research for pregnant and lactating women that will inform the HHS Secretary on relevant research. She said NVAC should receive briefings from the NVPO Director about the new task force and work to ensure that NVAC's recommendations for maternal immunization are addressed. Dr. Thompson also mentioned that issuance of the final rule of the Common Rule, which removed pregnant women from the classification of "vulnerable" populations. Dr. Thompson suggested NVAC monitor how that provision plays out.

Dr. Gellin discussed the prioritization of vaccine development efforts. He reminded the NVAC about the SMART Vaccines project that the Institute of Medicine initiated and NVPO sponsored and mentioned that the World Health Organization (WHO) is piloting the tool in the context of WHO's R&D blueprint to determine if it can be used to assist with decision-making more broadly.

NVAC Liaison and Ex Officio Updates

Dr. Thompson invited some of the liaisons and ex officios to give highlights on some initiatives undertaken by their organizations.

VA Retail Immunization Program—Troy Knighton, M.Ed., Ed.S., LPC, VA

Mr. Knighton explained that VA first piloted a retail immunization program to increase veterans' access to influenza vaccine in 2014 with Walgreens in Florida, which it subsequently expanded nationally with Walgreens as a partner. As of December 2016, 66,000 veterans received influenza vaccines from Walgreens this influenza season. Currently, the pharmacy notifies VA about the vaccination, and VA pays for the vaccine if the veteran meets the criteria for coverage. The individual's medical record is updated to reflect the immunization. Eventually, the program will support automated bidirectional data exchange, which would allow the pharmacy to see the medical record and offer other vaccinations on the basis of the veteran's vaccine history.

Walgreens has been the only retail partner since the program started, but the VA hopes other pharmacies will join the program. The program requires investment not only in technology to support information exchange but also marketing and training for pharmacists and VA staff. It is hoped that the program will be cost-effective for both retailers and the VA. Challenges remain around information systems and bidirectional data exchange.

DISCUSSION

Discussion centered around reporting retail-based vaccinations to State IISs. Mr. Knighton acknowledged the difficulty of getting data out of the VA system to share with other agencies. Mr. Rothholz noted that providers at community pharmacies report to State IISs, but it would help to distinguish the veterans from other groups. He added that a quality measure in development will incentivize more reporting to IIS and use of that data. Dr. Thompson suggested NVAC address questions around IISs again in the near future, and she welcomed input from NVAC members.

PHAC Immunization Partnership Fund—Rhonda Kropp, B.Sc.N., M.P.H., PHAC

Ms. Kropp noted that PHAC received $25 million to develop immunization coverage targets to reduce vaccine-preventable diseases, identify under-immunized populations, and create a program to support improved immunization coverage in Canada. To meet the latter goal, PHAC established the Immunization Partner Fund, a grant program for scaling up best practices. The fund will provide as much as $3 million annually to help providers to vaccinate clients, increase demand for immunization, and enhance access to immunization services.

As part of these efforts, PHAC launched the CANimmunize mobile application, a free service Canadians can use to store immunization records on their mobile devices. Ms. Kropp noted its growing popularity and that the application gives information on recommended vaccinations depending on the immunization schedule in the individual's province and territory, plus personalized reminders and notifications of outbreaks. Work is underway to allow users to submit and retrieve vaccination information between the application and the province's or territory's record system, which would be very helpful for Canadians when they move to other provinces and territories.

In addition, PHAC funded an external review of the influence of current immunization policies and practices in each jurisdiction. The agency also called for proposals for the grants to improve and support health care providers in immunizing clients. Ms. Kropp said the response was very positive, and PHAC is in the process of making awards. The proposals included projects such as active recall reminder systems, efforts to address vaccine-hesitant clients, and creation of a national repository of evidence-informed tools and strategies. The Immunization Partner Fund's goal is to serve as a one-stop-shop where providers can learn about best practices that may be applicable to their local populations. All the information gathered from funded projects will be shared across all the provinces and territories. Awards focused on increasing demand for and access to immunizations will be given in 2018.

DISCUSSION

In response to Dr. Thompson, Ms. Kropp said the uptake of the mobile application has been strong. Currently, it is mostly used by families to keep track of needed and past vaccinations. Schools and other organizations do not have access to individuals' vaccine records, but that could be considered for future versions.

Asked to discuss the differences among the provinces and territories in terms of vaccine schedules and requirements, Ms. Kropp said the grant program deliberately focused on broad topics so that funded projects would be applicable to other jurisdictions. She noted that representatives from the provinces and territories are regularly at the table with Federal partners, which provides another platform for sharing experiences.

Vaccine Supplies and Stockpiles—Nancy Messonnier, M.D., CAPT, CDC

Dr. Messonnier clarified that the VFC program maintains a stockpile of pediatric vaccines; it is distinct from the Strategic National Stockpile (SNS). The pediatric stockpile is available for outbreaks and to mitigate unintended shortages. To ensure the stockpile is constantly replenished, CDC uses a modeling process to ensure a supply that would serve the VFC program for about 6 months (equivalent to about a 3-month supply for combined public and private use). The amount stockpiled depends on the disease; for example, there is a large supply of measles vaccine because of the high potential for infection.

Vaccines from the stockpile can be provided to State health departments for their VFC programs to prevent shortages. With CDC's permission, vaccine manufacturers can borrow from the stockpile to sell vaccine to the private sector and then replenish the stockpile. The stockpile also holds some seasonal influenza vaccine as strategic reserve for late-season use in the event of a shortage or unexpected demand. The influenza vaccine reserve has been funded since 2004, in response to the shortages experienced in the 2003–04 influenza season. The vaccine remains in the stockpile until it is used or expires.

In other CDC news, Dr. Messonnier reported, as part of the national survey of poliovirus in laboratories, CDC completed the survey of its laboratories, identifying a large amount of infectious or potentially infectious material and ensuring that all type-2 poliovirus is contained. The next phase of the national effort is an audit to ensure that laboratories that want to keep poliovirus meet the containment requirements. Dr. Messonnier said CDC is establishing an auditing unit and a Federal advisory committee to oversee the audit.

Dr. Messonnier described a specific operational problem of great importance: some manufacturers assign lot numbers to their vials and syringes but use a different lot number for the unit of sale (e.g., a carton). This practice has contributed to confusion in monitoring inventory in relation to vaccine coverage. Manufacturers are working closely with FDA, CDC, and AIRA to sort out the issue.

DISCUSSION

Mary Beth Kurlio said AIRA hopes to convince manufacturers to use a single lot number for both the unit of use and unit of sale. Mr. Hosbach noted that the products comply with Federal regulations, but manufacturers want to lessen the chance for error and confusion that arises at the provider level.

Dr. Messonnier observed that the pediatric vaccine stockpile has run relatively smoothly and cooperation with manufacturers is good. Dr. Gellin pointed out that the pediatric stockpile includes routinely used vaccines, and the SNS includes vaccines for emergencies. Some things fall through the cracks, such as rabies vaccine, and NVAC may want to look more closely at those, Dr. Gellin suggested. He added that pandemic influenza vaccine is unique; the SNS has bulk antigens stockpiled that would be used to produce such a vaccine rapidly if needed. Dr. Gellin noted that BARDA and FDA are working together to ensure that stockpiled antigens are effective and usable.

Dr. Maldonado hoped NVAC would address concerns about maintaining adequate supplies of vaccines for adults that are not included in the SNS. A representative of Sanofi Pasteur acknowledged the ongoing shortage of yellow fever vaccine. In response, the company has applied to FDA to use in the United States the yellow fever vaccine it supplies to other countries.

AHIP—Christopher Regal

Mr. Regal said AHIP named a new liaison to NVAC, James David Nordin, M.D., M.P.H., from HealthPartners in Minnesota. He will be at the next NVAC meeting.

AIM—Kristen R. Ehresmann, RN, M.P.H.

Ms. Ehresmann reported that AIM is holding its business and leadership meeting in Charleston, SC. She said the Prevention and Public Health Fund (PPHF) created in 2010 as part of the ACA is very important to State immunization programs, which received roughly 47 percent of their funding from the fund. Losing that money would have a significant impact at the State level on program activities, vaccine coverage, and outbreak response.

AIRA—Mary Beth Kurilo, M.P.H., M.S.W.

Ms. Kurilo echoed concerns about the impact of PPHF dollars on immunization programs and IISs specifically. She said AIRA released guidance recently on confidentiality protocols and privacy for IISs; a companion document on security is in development. AIRA is continuing its measurement improvement efforts under the umbrella of assessment and certification. It published baseline measures for transport (i.e., sending messages from one system to another) and is currently measuring bidirectional exchange and submission and query, which will be reported next month.

Recently, AIRA completed a pilot project for a data quality initiative, providing access to a shared service for address cleansing. Four States participated in that pilot. It will roll out community-wide in 2017. The Joint Public Health Informatics Taskforce has been discussing interjurisdictional information exchange. The Network for Public Health Law and AIRA are drafting an issue brief that will explore a model law to support exchange. Ms. Kurilo concluded that AIRA's national meeting will be in Chicago April 11–13, 2017, and registration is open.

ASTHO—Kimberly Martin

Ms. Martin said ASTHO has been working to find best practices to help public health and pharmacies plan for and respond to a pandemic. To that end, ASTHO developed a memorandum

of understanding (MOU) that clearly outlines the rules and responsibilities of each entity during a pandemic. A few States have implemented the MOU. Based on experiences in those States, ASTHO developed a toolkit, available on its website, to help other States considering a similar MOU.

The Network for Public Health Law and ASTHO developed an IIS inter-State data-sharing MOU, and ASTHO continues to work with AIRA to create a community of practice around the issue. Five out of the six States involved in the community of practice have signed the MOU. Now, ASTHO is helping those States think about how to implement the MOU.

Shortly, ASTHO will release a report detailing best practices among State public health programs that have adult vaccine programs for the uninsured. It is based on interviews with State programs that vaccinate uninsured adults and their partner organizations, such as community health centers. The report will address how States identify uninsured adults in the community and how they get services to them, as well as unique vaccine programs for this population.

NACCHO—Gillian Stoltman, Ph.D., M.P.H.

Dr. Stoltman said NACCHO recently published three new policy statements that particularly affect local health departments. The first addresses the need for continued improvement in both information and the safety of vaccines. Local health departments are intimately involved in vaccination at the local level, although less often as vaccine providers but certainly as the local coordinator in terms of education about vaccination and responses to questions and concerns about vaccination and vaccine shortages. Safety is a big issue for all local health departments.

The second policy statement encourages requiring influenza vaccine for all employees of local health departments, not just those who have direct client contact. The third policy statement addresses access to school health data for public health surveillance. Lack of access is often a problem when dealing with disease outbreaks. Federal law prohibits local health departments' access to a lot of school-based information.

Dr. Stoltman echoed concerns about the future of the PPHF and its funding for vaccination programs. NACCHO is surveying local health departments about their concerns and upcoming challenges to implementing their immunization programs. Recently, NACCHO put out a position statement, "Protecting the Public's Health: The Power of Vaccination," which is available on the NACCHO website. Also, NACCHO is working with a number of health departments across the country to see how they can work with private and other partners to implement new ACIP HPV vaccination recommendations and increase vaccine coverage, particularly for adolescents.

PHAC—Rhonda Kropp, B.Sc.N., M.P.H.

Ms. Kropp said PHAC is setting new immunization coverage goals and targets for reducing vaccine-preventable disease. Canada's last set goals and targets in 2005; they will serve as a benchmark for measuring progress. The aim is to have the goals and targets approved through the public health governance structure in Canada, including provinces, territories, and the Federal government, by December of this year.

VRBPAC—Kathryn M. Edwards, M.D.

Dr. Edwards said the 144th VRBPAC meeting was held by teleconference on October 13, 2016. Members discussed the selection of strains to be included in vaccines for the 2017 Southern Hemisphere, which has not been done previously, in preparation for the possibility of American companies providing Southern Hemisphere vaccine for both U.S. citizens and visitors. Presenters gave an excellent overview, using global surveillance data to help members understand each of the variants and their relevance. The committee voted unanimously in favor of proposed changes to the Southern Hemisphere formulations of trivalent and quadrivalent influenza vaccines that included one change in the H1N1 strain, but the other strains will remain the same.

AHRQ—Justin Mills, M.D., M.P.H.

Dr. Mills said AHRQ funds investigator-initiated research grants and conferences on vaccine topics such as looking at the impact of infant vaccination with a 13-valent pneumococcal conjugate vaccine, improving immunization rates in young children, and examining higher refusal rates in pneumococcal vaccination among African Americans. Also, AHRQ supports knowledge generation through conducting evidence reviews.

CMS—Mary Beth Hance

Ms. Hance said an updated Healthcare Effectiveness Data and Information Set (HEDIS) measure has been adopted for adolescent vaccines. She said CMS has a core set of pediatric measures for the Medicaid program for which reporting is voluntary; CMS has updated the core set and now uses the combined adolescent measure, which includes HPV vaccination. The separate HPV vaccination measure has been retired.

DoD—Margaret Yacovone, M.D., M.S.P.H.

Dr. Yacovone reported that DoD met its goal of vaccinating 90 percent of the force by mid-December, thanks to industry, which worked closely with DoD to fill gaps so that DoD could provide injectable vaccine for all age groups. In addition, DoD developed some educational programs and tools for providers about minimizing pain associated with injections.

Also, DoD requires health care workers to complete an educational program before delivering influenza immunizations. The program includes five modules with quizzes for influenza plus a cold-chain management educational tool. So far, 23,000 health care providers have completed the educational programs, and 11,000 more have completed the cold-chain management training.

Dr. Yacovone said DoD included information about the importance of immunizations and available services into education that is part of the deployment cycle. In addition, DoD embraces the One Health concept that seeks to solve critical global health challenges through integration of human medicine, veterinary medicine, and environmental sciences. It invited leaders to come to DoD to talk about the One Health approach to increase awareness about this interdisciplinary approach to reducing overall burden of disease throughout the world.

Lastly, like others, DoD is also struggling with concerns about data sharing and quality improvement and indicated that DoD would like to have an IIS connection to all 50 States, because DoD delivers care in every State. Dr. Yacovone asked that NVAC address the barriers to information exchange.

FDA—Marion Gruber, Ph.D.

Dr. Gruber reported that in November, FDA approved a supplement for the license application for FluLaval and FluLaval quadrivalent influenza vaccine so that the products can now be used in children 6 to 35 months of age. FluLaval is now the second seasonal influenza vaccine for that age range. This vaccine was previously approved for individuals 3 years of age and older.

Also last fall, FDA approved a supplement for Gardasil 9, the HPV 9-valent vaccine to include a two-dose regimen for individuals between the ages of 9 through 14 years. For Daptacel (diphtheria, tetanus toxoids, and Acellular pertussis vaccines), FDA also approved coadministration of Meningococcal vaccine (Menactra) with a fifth dose of Daptacel in children 4 to 6 years of age.

Lastly, FDA approved an extension of the age range for influenza A virus monovalent vaccine, which addresses the pandemic H5N1 virus. The age range now includes those 6 months through 17 years of age who are at increased risk of exposure to the influenza A virus H5N1 subtype, which was previously approved for use in persons 18 years of age and older.

HRSA BPHC—Judith Steinberg, M.D., M.P.H.

Dr. Steinberg said data from community health centers for 2015 indicate 77.6 percent of children served are fully immunized by the age of 3 years. The goal is to reach the Healthy People 2020 target of 80 percent. Data for 2016 will be available later this year.

Dr. Steinberg said BPHC has invested in initiatives to improve the quality of care delivered, including the provision of immunizations. Support is provided to help health centers become patient-centered medical homes, an advanced primary care delivery model that uses a multidisciplinary team and health information technology (HIT) to improve quality. So far, 67 percent of health centers are recognized as patient-centered medical homes.

In addition, BPHC supports optimal use of HIT and development of control networks that work together with health centers to optimize HIT and its use. To date, 70 percent of health centers are enrolled in a health center control network. Lastly, BPHC is expanding health centers. In December, it approved 75 new access points, which improves access to affordable quality care, including immunizations, to underserved areas.

HRSA DICP—Narayan Nair, M.D., CAPT

Dr. Nair said the DICP continues to see an increase in the number of claims received. Historically, and particularly in the early part of this decade, a typical year would bring 400 to 500 claims. In 2014, the DICP received 633. In fiscal year (FY) 2016, 1,120 claims were filed—the highest number received since the program began. In FY 2016, 856 claims were adjudicated, and 677 (more than 70 percent) were compensated, while 179 were dismissed.

In FY 2016, the DICP spent $250 million on compensation for vaccine injuries and attorneys' fees. The DICP is unique among compensation programs in that it pays attorneys' fees regardless of whether injuries are compensated. Also, the DICP published a final rule in January that updates the Vaccine Injury Table, adding a few injuries to the table.

Dr. Edwards asked for more details about the claims filed. Dr. Nair said that although claims are increasing, in the context of the number of doses of vaccines distributed, the number of claims is relatively small. The increases are primarily coming from claims related to seasonal influenza among adults. Historically the program was focused on alleged injuries in children. Now, almost 80 percent of claims are for adults, and most of those are related to seasonal influenza vaccine. Many claims involve Guillain-Barre syndrome and other demyelinating conditions as well as shoulder injuries related to vaccine administration.

IHS—Jeffrey McCollum, D.V.M., M.P.H.

Dr. McCollum said that IHS established a mandatory influenza vaccine for all of its health care workers in 2015 and has been working through labor relations processes since then to implement the mandate. The current influenza season reflects the first year in which approximately 97 percent of IHS clinical staff are impacted by the rule.

Also, IHS collects influenza coverage data on staff twice during the influenza season. For many years, coverage percentages hovered in the mid-70s. Preliminary data for this year show IHS close to 90-percent coverage among personnel, and IHS is very proud of that. An analysis of more comprehensive data will be conducted at the end of the influenza season.

NIH—Barbara Mulach, Ph.D.

Dr. Mulach highlighted a September article in the *New England Journal of Medicine*, co-written by NIH, HHS, and FDA, which talked about considerations for developing a Zika vaccine, such as who would receive the vaccine and which vaccines might be used in which cases. Also, NIAID announced its new director of the Division of Microbiology and Infectious Disease, Emily Erbelding, M.D., M.P.H. She comes from the Division of AIDS at NIAID and prior to that spent 14 years at Johns Hopkins University.

USDA—Donna Malloy, D.V.M., M.P.H.

Dr. Malloy said the United States experienced its worst highly pathogenic avian influenza (HPAI) outbreak in history between December 2014 and June 2015, with an isolated outbreak in 2016. Preparedness and response planning for foreign animal diseases is crucial to protect animal health, public health, the food supply, and the environment. Based on these experiences and the lessons learned last fall, USDA's Animal and Plant Health Inspection Service revised its Foreign Animal Disease Framework Response Plan.

The revised plan includes lessons learned from the HPAI outbreak; incident coordination, authorities, funding, relationships, and roles among Federal departments; incident management; and communication strategies during a foreign animal disease outbreak. Vaccine and disease prevention, including emergency vaccination, are among the control points in any animal disease response plan. The National Veterinary Stockpile also has sufficient amounts of animal vaccines, antivirals, and therapeutic products for responders to use appropriately as needed.

VA—Troy Knighton, M.Ed., Ed.S., LPC

As of January 21, the VA vaccinated over 1.56 million veterans in outpatient settings, and 16.6 thousand of those received the high-dose influenza vaccine. Last year, the VA initiated a policy

requiring health care providers to be vaccinated for influenza. The VA has approximately 315,000 employees. The policy has reached the upper echelons of the Veterans Health Administration for approval and will go to labor relations next. Mr. Knighton said the VA hopes to implement the policy in fall of 2017.

NVPO—Bruce G. Gellin, M.D., M.P.H.

Dr. Gellin said NVPO is announcing an awards program on behalf of all the agency partners to support non-Federal entities, which aligns with the goals of the National Vaccine Plan. The award seeks to identify people who are demonstrating leadership, promoting collaboration, encouraging innovation, advancing research, or improving practice. Also, NVPO recently released its guide to implementation of the National Adult Immunization Plan. As with the National Vaccine Plan, the effort calls for national, not just Federal, work. Dr. Gellin hoped NVAC would continue to focus on what non-Federal partners can do to advance the field.

Other Liaison Reports

The ACIP, the Advisory Commission on Childhood Vaccines, and the Pan American Health Organization submitted written reports.

Childhood Immunizations: Taking the Pulse of the Public

Public Views about the Measles-Mumps-Rubella (MMR) Vaccine and Trust in Medical Scientists and Their Research on Childhood Vaccines—Cary Funk, Ph.D., Associate Director, Research on Science and Society, Pew Research Center

Dr. Funk presented some key findings from a recently published Pew Research Center that found that most Americans (82 percent) agree that healthy children should be required to have the MMR vaccine to attend public school because of the potential health risk of infection to others. A minority believe parents should decide whether to have their children vaccinated, even if it creates health risks for others. Parents with young children perceive the risks of MMR vaccine as higher and the benefits lower than other Americans, and they are less likely to believe the benefits outweigh the risks.

Dr. Funk said all of Pew's studies on vaccines expose generational differences about the benefits of vaccines. African Americans express more concern about risks compared with Whites; Dr. Funk noted that it is not uncommon to see differences between African Americans' and Whites' Pew found mixed results around public trust in medical scientists related to MMR vaccine. For example, asked how well they thought medical scientists understand the health risks and benefits of MMR vaccine, 47 percent said "very well," 43 percent said "fairly well," and 10 percent said "not at all well." Dr. Funk said it is concerning that respondents did not express more confidence in medical scientists. Ratings of trust show more confidence in medical scientists than in pharmaceutical industry leaders, alternative health advocates, media, and elected officials, but trust overall (in government, media, industry) is low right now.

The survey revealed some skepticism that medical scientists' research findings on the health risks and benefits of childhood vaccines are influenced by the best evidence and conducted out of concern for the best interests of children's health (55 percent responded "most of the time", 35 percent "some of the time" and 9 percent "not to often/never"). Again, age influences perceptions—younger people, including parents with young children age 0 to 4 years, express more skepticism than older people about the abilities and motivations of medical scientists [46

percent responded "most of the time" to the same question]. Those with more knowledge about science have more confidence in medical scientists, and those with less science knowledge tend to be more skeptical.

Dr. Funk said that facts are not going to be enough to convince the public of the safety of the MMR vaccine. The patterns demonstrated in the research suggest that people with more science knowledge tend to be more educated and may harbor more general support for science—that is, the willingness to give scientists the benefit of the doubt—than for industry, media, or the government. However, a large share of the public (those with low to medium science knowledge) is not strongly convinced that there is strong consensus among medical scientists around MMR vaccines. Most of the respondents believe medical scientists should be involved in policy decisions about childhood vaccines. Finally, the Pew study found that medical scientists ranked second, after the military, in terms of public confidence that they would act in the best interests of the public. Medical scientists are often seen in a more positive light than other occupational groups, including other scientists. However, the survey indicates there is room for improvement.

Discussion

Dr. Omer expressed disappointment with the way the study results were presented, highlighting the concerns of parents with young children, who made up only 8 percent of the sample. He acknowledged that the findings were interesting but other studies with more parents indicate that childhood vaccination remains a social norm. Dr. Omer emphasized that the perceptions of 122 parents should not be overstated as representing the general public on this topic, which has real consequences for policy-making. Dr. Funk defended the methods, interpretation, and presentation of the data.

Wayne Rawlins, M.D., M.B.A., noted that people may perceive "medical scientists" differently than "doctors." He hoped researchers would delve more deeply into respondent characteristics to provide more nuanced interpretations of the results (e.g., opinions of African Americans with high science knowledge). Dr. Funk said the terminology was tested; Pew sought to gather perceptions that distinguished medical scientists from other scientists and from one's own doctor. Dr. Thompson hoped that in future iterations of the study, NVAC would have the opportunity to give input on questions that might elicit more information about public perceptions that could inform NVAC deliberations.

Public Comment

No public comments were offered.

Closing Remarks and Adjournment—Bruce G. Gellin, M.D., M.P.H., Deputy ASH and Director, NVPO, HHS, and Kimberly M. Thompson, Sc.D., NVAC Chair

Dr. Thompson thanked all the meeting participants. She said all should feel free to give input about the meetings, especially reactions to changes in the meeting format and agenda. Dr. Gellin thanked Lauren Chambers and her team at NVPO for their work. Dr. Thompson thanked Dr. Gellin for his many years of hard work and adjourned the meeting at 12:48 p.m.