

## **National Vaccine Advisory Committee (NVAC) June 9-10, 2015, Meeting Minutes**

### **Committee Members in Attendance**

#### **NVAC Members**

Walter A. Orenstein, M.D., **Chair**  
Richard H. Beigi, M.D., M.S.  
Sarah Despres, J.D.  
Phil Hosbach  
Ruth Lynfield, M.D.  
Charles Mouton, M.D., M.S.  
Saad Omer, M.B.B.S, MPH, Ph.D.  
Wayne Rawlins, M.D., MBA  
Mitchel C. Rothholz, RPh., MBA  
Nathaniel Smith, M.D., MPH  
Kimberly M. Thompson, ScD  
Vish Viswanath, Ph.D.

#### **Executive Secretary**

Bruce G. Gellin, M.D., MPH. Deputy Assistant  
Secretary for Health, Director, National Vaccine  
Program Office U.S. Department of Health and  
Human Services, Washington, D.C.

#### **NVAC Ex Officio Members**

Iris Mabry-Hernandez, M.D., MPH (AHRQ)  
Anne Schuchat, M.D. (CDC)  
Mary Beth Hance, representing Jeffrey Kelman,  
MMSc, M.D. (CMS)  
Col. Margaret Yacovone, M.D., MSPH (DoD)

Phil Krause and Valerie Marshall, representing  
Marion Gruber, Ph.D. (FDA)  
Justin Mills, M.D., MPH (HRSA/BPHC)  
A. Melissa Houston, M.D., MPH, (HRSA/VICP)  
Jeffrey McCollum, representing Michael  
Bartholomew, M.D. (IHS)  
Barbara L. Mulach, Ph.D. (NIH)  
Donna L. Malloy, D.V.M., MPH (USDA)  
Richard Martinello, M.D. (VA)

#### **NVAC Liaison Representatives**

Jonathan Temte, M.D., Ph.D. (ACIP)  
Charlene Douglas, Ph.D., MPH, R.N. (ACCV)  
Richard Doskey, representing Scott Breidbart,  
M.D., MBA (AHIP)  
Kristen R. Ehresmann, R.N., MPH (AIM)  
Kathy Talkington, representing Paul Jarris, M.D.,  
MBA (ASTHO)  
Tiffany Tate, MSH (NACCHO)  
Hanna Curtis, representing Isabella Danel, M.D.,  
M.S. (PAHO)  
Dr. John Spika, M.D. (PHAC)  
Robert S. Daum, M.D., CM (VRBPAC)

### **Day 1 – June 9, 2015**

#### **Welcome**

Dr. Gellin welcomed everyone in attendance and provided a brief update about recent activities at HHS, many of which NVAC has been instrumental in initiating. For example, the National Vaccine Program Office has recently developed a National Adult Immunization Plan as part of efforts resulting from recommendations from the NVAC to improve adult immunization coverage. In addition, an HHS interagency Immunization Safety Task Force recently developed and released a Vaccine Safety Research Agenda also based on a previous recommendation from NVAC. He also announced that the 2014

annual report on the state of the National Vaccine Plan will be available soon. He also mentioned that the NVAC website had been updated to make the NVAC website more user-friendly. Finally, Dr. Gellin announced several additions to NVPO staff: Dr. Glen Nowak, who will advise NVPO on issues related to vaccine confidence and communications, Ms. Jackie Olive, who is a summer intern from Rice University, and Dr. Michelle Blakely, who will temporarily serve as Acting Chief of Operations for NVPO.

Dr. Gellin introduced Assistant Secretary for Health, Dr. Karen DeSalvo. Dr. DeSalvo noted that NVAC is an outstanding model of a federal advisory committee. NVAC is a group of very thoughtful people from across the country and the government helping advise HHS on how to advance vaccination appropriately in this country. She is looking forward to NVAC's upcoming recommendations. Dr. DeSalvo mentioned she would discuss key vaccine-related topics at HHS related to NVAC's work.

Antibiotic resistance is a major public health problem of increasing magnitude globally and has gotten the attention of the White House, HHS, and a number of other very important stakeholders. Increasingly they are working together collaboratively to find solutions to this challenge. A recent White House Forum on antibiotic resistance discussed responsible use of antibiotics and the role of vaccines in protection from bacterial infections. It brought together representatives from 150 food companies, retailers, and human and animal stakeholders involved in antibiotic stewardship, who publicly committed to working together over the next five years to slow the emergence of antibiotic resistant bacteria and prevent the spread of resistant infections. She stated that this 5-year public commitment was one of the critical milestones to our success and is a very complex effort that will involve a multi-sectoral strategy in the U.S. and globally. This effort will include using vaccines to prevent many of the diseases we now treat with antibiotics. She emphasized that vaccines will decrease the circulation of diseases in communities, which can also impact the need for antibiotics. Dr. DeSalvo emphasized that the role of vaccines in preventing bacterial infections is a key part to our success in protecting the effectiveness of our antibiotics and she looks forward to NVAC's recommendations on the role of vaccines in strategies to combat antibiotic resistant bacteria.

Dr. DeSalvo also noted that our success in protecting our citizens depends on public acceptance of recommended vaccines, so vaccine confidence is an important issue. Because of the recent measles outbreak, there was a fair amount of media coverage on this issue. Vaccine confidence is an important part of the national conversation, and she looks forward to NVAC's final report. Dr. DeSalvo stated she is especially interested in NVAC's thoughts on the determinants of vaccine acceptance by parents as well as NVAC's recommendations on measurement of vaccine confidence to inform and evaluate future interventions. Dr. DeSalvo mentioned that she is also the National Coordinator for Health IT, so she is interested in leveraging electronic health records and state public health registries as part of advancing our opportunity for mapping, measuring, and targeting interventions to address community needs in a more effective way. She is interested in NVAC helping HHS to understand targeted community interventions to improve vaccine confidence. She described a recent vaccine hesitancy message involving the U.S. Surgeon General using the Sesame Street character Elmo, which she thought was a very clear and effective message that went out to a broad platform.

Regarding the Human Papillomavirus (HPV) vaccine, Dr. DeSalvo thanked the President's Cancer Panel as well as Dr. Schuchat and the CDC team for their efforts in increasing HPV vaccination rates. It is critical to reduce the almost 26,000 newly diagnosed HPV-associated cancers annually. However, completion rates for HPV vaccinations are well below the Health People 2020 target of 80%. Dr. DeSalvo provided

2013 data that the 57.3% vaccination rate for girls for one HPV dose, while well below the 80% target, is still much higher than the one-third of girls that complete the recommended 3-dose series. For boys, 34.6% received one HPV dose and only 14% completed the 3-dose series. HHS is looking for analyses of this situation and she looks forward to hearing NVAC's recommendations on root causes as well as NVAC's recommendations on improving HPV vaccination rates to prevent HPV-associated cancers.

Dr. DeSalvo noted there have been recent increases in adult vaccination rates, but most of them have been modest and could be improved. This could be a legacy issue for NVAC and HHS. A workable strategy for adult immunization standards and practice is an important issue. The National Adult Immunization Plan developed by NVPO will be released later this year. The release of this plan will be a very critical step in the right direction as part of an achievable roadmap of what we need to obtain optimal benefit from adult vaccinations. NVAC's recommendations on IIS to IIS data sharing that were adopted at the February meeting will be helpful in bridging the gaps on immunization rates, especially in working to exchange immunization data across jurisdictions. She stated that this opportunity to continue modernization of the public health infrastructure could be "game changing." It could improve convenience and accessibility, and there is an opportunity for the retail marketplace and consumers to work together in achieving our national vaccine goals.

Dr. DeSalvo concluded her remarks by thanking NVAC for their important work. Dr. DeSalvo reiterated that she is looking forward to NVAC's recommendations. She also thanked Dr. Orenstein and Dr. Gellin for their dedication and their time.

### **NVAC Chair's Report**

After introductions, Dr. Orenstein mentioned that the meeting was announced in the Federal Register on May 13<sup>th</sup> as a regularly scheduled NVAC meeting and the agenda was posted on the NVAC website. Dr. Orenstein explained the meeting was being broadcast as a webcast and there was a publicly available toll-free conference line to listen to this meeting. After noting that a public comment period was available both meeting days, Dr. Orenstein described the process for making public comments at the meeting or later by submitting written comments to the NVPO website. Dr. Orenstein explained that minutes were being taken and will later be published on the NVPO website. He also explained that both the meeting and conference line were being recorded.

As the first order of business, Dr. Orenstein asked if anyone had any additions or corrections to the minutes of the February 10-11, 2015 NVAC meeting. Mr. Rothholz made a motion that NVAC approve the February 10-11, 2015 minutes and Dr. Lynfield seconded the motion.

- **ACTION ITEM:** Dr. Orenstein invited approval of the minutes of the February 10-11, 2015 NVAC meeting. The Committee voted in favor of adopting the minutes of the February 10-11, 2015 NVAC meeting (12 in favor, 0 opposed, 2 absent).

Dr. Orenstein welcomed a new NVAC member, Dr. Kimberly Thompson, and noted she will be a tremendous addition to the group. Dr. Orenstein explained that she is a mathematical modeler and has used modeling to influence policy. Dr. Thompson is a Professor at the University of Central Florida, College of Medicine, and also runs the nonprofit research organization Kid Risk, Inc.

Dr. Orenstein summarized recent NVAC accomplishments. NVAC's resolution on the Immunization Registry Interstate Data Exchange will be published in the July/August 2015 issue of Public Health Reports. This NVAC meeting will be very busy, because there are three reports scheduled for a vote. The working group reports and recommendations to be voted on at this meeting are: Vaccine Confidence Working Group Report and Recommendations, HPV Working Group Report and Recommendations, and the issue of vaccines and their role in strategies to combat antibiotic resistant bacteria.

Finally, Dr. Orenstein reviewed highlights of the June meeting agenda. He reminded the Committee that the next two NVAC meetings are scheduled for September 9-10, 2015 and February 2-3, 2016.

### **2015 Measles Outbreak Response**

Dr. Orenstein introduced the session about the 2015 measles outbreak.

#### **2014-2015 California Measles Outbreak: It's a Small World After All, Dr. Kathleen Harriman, California Department of Public Health (CDPH)**

Dr. Harriman explained the U.S. has an ongoing risk of imported measles cases from foreign tourists traveling to the U.S. and from U.S. travelers returning from abroad. She provided data on confirmed measles cases in California from 2000-2014 and noted that of the 75 cases in 2014, 61 occurred in early 2014 and most were infected in the Philippines (both U.S. citizens traveling to the Philippines as well as foreign visitors). Dr. Harriman explained the Disneyland measles outbreak accounts for most of the confirmed measles cases in early 2015. The Disneyland outbreak was identified after CDPH was notified about a suspect measles case in an unvaccinated 11 year old whose only recent travel was to Disneyland. Over the next few days, additional suspected cases were reported, all with recent travel to Disneyland or the adjacent California Adventure Park. Dr. Harriman noted that CDPH considers visiting international tourist venues a plausible exposure to measles, when evaluating reports of patients with febrile rash illness.

Dr. Harriman summarized the control measures implemented in the Disneyland measles outbreak, including prompt identification and isolation of cases by quickly notifying local health departments and providers, prompt identification of contacts and assessment of immune status, post-exposure prophylaxis for high-risk suspect cases, and quarantine of suspect cases who did not receive timely post-exposure prophylaxis. She noted that most of their local health departments have voluntary quarantine. For measles testing during an outbreak, Dr. Harriman explained CDPH recommends PCR as the primary diagnostic tool because the test is rapid and specimens are easy to collect. Some local health departments also did IgM testing for immunity. Dr. Harriman described how genotyping was used during the Disneyland outbreak to identify the outbreak strain.

When reviewing data on the 131 cases in the recent California measles outbreak, Dr. Harriman emphasized that a total of 42 people were exposed to measles at Disneyland during December 17-20, 2014. Other known exposure settings included household or close contacts, healthcare settings, and a mall. Dr. Harriman summarized data on the vaccination status of measles outbreak cases, and noted that many adults over 45 years old did not know whether they were vaccinated for measles. In this outbreak, the majority of cases were adults and two adults had severe measles cases requiring long convalescence.

Dr. Harriman discussed the successes from the 2014-2015 California measles outbreak:

- Prompt identification of outbreak and notification of local health departments and providers;
- Excellent and tireless work by local health departments in case and contact investigations and lab assistance;
- Prior experience with measles, including it was especially important that measles protocols already existed and many materials were already developed for local health departments and providers;
- Statewide calls with local health departments to ensure everyone was on the same page and using the same protocols for case investigation and laboratory testing;
- Communication with providers on measles identification, infection control, and reporting;
- Regular communication with the public on the status of the outbreak, emphasizing transparency, including the relative roles of failure to vaccinate and vaccine failures (acknowledging cases who were vaccinated); and
- This outbreak was contained within two months with no more than three generations of transmission.

Dr. Harriman also discussed the many challenges encountered during this measles outbreak. For example, prioritization of large contact investigations during an outbreak is a big issue. One nurse had over 800 contacts because she worked while infectious. Where the exposure occurs makes a difference in contact investigations, because it can be hard to identify and directly contact people if exposure occurs at an airport or a mall. Many exposed healthcare workers had no record of measles immunity, although this was required by the CalOSHA Aerosol-Transmissible Diseases Standard, and assessing their immunity after exposure took time and resources.

In concluding her presentation, Dr. Harriman noted the most important question from CDPH's perspective is how to balance resources used for contact investigations with the possibility of additional measles cases in a setting with high population immunity. Their local health departments were constantly asking this question. Some types of exposures may be more likely to lead to transmission than others, such as where the host is in the most infectious period and coughing, or if the venue is an enclosed space.

#### **Measles Outbreak Response – The National Perspective, Dr. Anne Schuchat, CDC**

Dr. Schuchat provided data from the national perspective on measles in the U.S. and additional details on measles in 2014 and 2015. In 2014, 668 measles cases were reported from 28 states including 23 outbreaks. Nearly all of the 2014 cases were import-associated. In 2015, the U.S. again had a lot of measles cases (159 through April 2<sup>nd</sup>), which were mostly in adults. These 2015 measles cases occurred in 20 states, but most were in California. For the U.S. residents with 2015 measles cases of the 70% who were unvaccinated, 49% gave philosophical/religious beliefs as the reason for not receiving the measles vaccine.

In explaining CDC's role in measles outbreaks, Dr. Schuchat emphasized that state and local health departments lead the investigations and CDC supports them. CDC has recently redesigned their measles website with modules to focus on primary audiences. Public health professionals are a key audience, and CDC's new website provides examples of outreach and products to help coordinate efforts to inform providers and others about measles and vaccination as the best protection. CDC has also provided a website to gather evidence on exemptions in state vaccination requirements, to begin developing an

evidence base on the epidemiology of exemptions. Dr. Schuchat noted that CDC continues to see very few toddlers that have received no vaccines at all. CDC has analyzed 2010-2013 data on children and adolescents unvaccinated against measles to evaluate factors that explain why they were not vaccinated. Among unvaccinated children 75% were attributable to factors other than parents' negative vaccine beliefs. The new measles website, is also designed to provide outreach and educational materials for both healthcare professionals and consumers.

Dr. Schuchat noted that after the 2015 measles outbreak, there was an increase in immunization activity for measles at the state level. CDC saw an increase in public sector orders for MMR vaccine for adults in early 2015. Dr. Schuchat concluded by summarizing key points from the 2015 measles outbreak:

- Although measles was eliminated in 2000 from the U.S., it is still a plane ride away because measles is all around the world,
- Astute clinicians are needed to identify "old" diseases,
- The public health infrastructure is critical,
- Improving immunization abroad (including Europe) will reduce risk in the U.S.,
- Clinicians play a key role in parental vaccine acceptance,
- State requirements keep vaccination the default option and protect communities, and
- Improved immunization histories for adults (e.g., making sure their immunizations are captured in immunization registries) can aid understanding the changing epidemiology of vaccine-preventable diseases. For instance, in this case, 54% of the outbreak cases were in adults age  $\geq 20$  years. Among the 68 U.S. residents who had measles and were unvaccinated, 29 (43%) cited philosophical or religious objections to vaccination, 27 (40%) were ineligible because they were too young to receive vaccination (26 patients) or had a medical contraindication (one), three (4%) represented missed opportunities for vaccination, and nine (13%) had other reasons for not being vaccinated.

### Discussion

Dr. Orenstein started the measles discussion by outlining two issues: 1) would we be better off trying to reduce potential breaches in measles immunity in the U.S. by improving measles vaccination globally especially since all six World Health Organization (WHO) regions have measles elimination goals; and 2) although there was significant media attention on vaccine hesitancy, he noted Dr. Schuchat's data show only 29% of 2015 measles cases were children (1-19 years) and he wondered if adults may be the bigger problem. He suggested old vaccine hesitancy or waning immunity might be involved in the adult issue, but emphasized the recent media attention focused almost solely on vaccine hesitancy.

Dr. Orenstein asked Dr. Schuchat whether she had any data on who were the disseminators of disease versus who were the recipients of the measles virus. Dr. Schuchat noted the rates of disease were highest in the youngest children for the recent measles outbreak. She also commented that adults are the majority of the U.S. population, and they saw a large number of adult cases this year. She stated CDC believes the probability of adults being unvaccinated for measles is probably high, but they cannot confirm with any data. Dr. Harriman noted the greatest number of cases were in adults for the Disneyland outbreak. She commented that for most adults in their 40s or 50s born in the U.S. you might assume they were vaccinated unless their parents were vaccine objectors, but even adults in their 20s often do not know whether they are vaccinated. This is a frustration in conducting large contact investigations for adults. They have encountered this problem even in healthcare settings, and Dr.



Harriman noted that although hospitals are usually very good, healthcare clinics often do not know the immunization status of their workers.

Dr. Lynfield asked whether Dr. Schuchat knew of any data from travel clinics or elsewhere on the proportion of patients who were offered MMR if seen before going abroad, and the proportion of them that refuse MMR when offered. Dr. Schuchat commented she will check on the answer to that question. She noted their travel health colleagues conducted a lot of outreach and messaging for international travelers and through airport signs. Dr. Schuchat explained that in the last few years CDC conducted a large effort to raise awareness that travelers should think about travel health risk not just for Africa or other less developed areas, but also for Europe. She mentioned a 2010-11 measles outbreak in France, which got a lot of attention, and current outbreaks in Germany. She commented that people might not get MMR because they usually do not go to travel clinics before going to Europe.

Dr. Thompson asked two questions. First, she wanted more information on Dr. Harriman's slides on the cost of measles outbreaks that were not discussed during her presentation. In particular, Dr. Thompson wondered how much disruption to the healthcare system can be captured in their cost analysis. Second, Dr. Thompson asked whether there was any evidence that people fully MMR-vaccinated were participating in measles transmission or whether they were just showing up as cases in the measles outbreak. Dr. Harriman replied that people fully vaccinated for measles have been involved in measles transmission. She commented that at this point, CDPH treats vaccinated people as infectious the same as all other measles cases during contact investigations.

Referring to her slide, "Cost of California Measles Outbreak," Dr. Harriman described additional information not presented earlier in this session. She explained that the total estimated public health cost in California for the 2014-2015 measles outbreak is around \$1.5 to \$4 million dollars, but does not include all costs. Examples of costs not included are costs to healthcare facilities participating in contact investigations and costs associated with lost work or school. Dr. Harriman noted that Alameda County had only six measles cases, but they had over 700 contacts and estimated personnel costs of over \$190,000 for this outbreak, which they think is a significant underestimate. Dr. Harriman mentioned that around 20-25% of measles cases are hospitalized and that those hospital costs are high. Using the around \$22,000 median cost per hospitalized measles case, total hospitalization costs for the 21 hospitalized cases are estimated at close to \$500,000 but are likely higher. Dr. Harriman added that this \$22,000 median cost is based on data from 2009-2013, when there were no intubated ICU cases. One 2008 case, which was similar to the two severe 2015 measles cases she described earlier, exceeded \$1 million in direct hospital charges. Dr. Harriman noted that it is also important to consider opportunity costs, because working on measles outbreaks takes effort away from other diseases. Dr. Orenstein commented it will be important to get this cost information published as soon as possible.

Dr. Omer commented there are misconceptions about immunization rates in other countries that are the largest sources of immigrants. He mentioned his recent work that found all but one of the top four or five of those countries had measles immunization rates higher than or similar to the U.S. His first question was for Dr. Schuchat about the source of these importations and whether any specific category of immigrants or visitors was associated with these public health implications. Dr. Omer asked a second question for Dr. Harriman regarding the contribution of adults to measles outbreaks. He noted that approximately 50% of unvaccinated individuals in the California outbreak had personal belief exemptions. He mentioned that if you look at CDC data for seven measles outbreaks with data broken

down by exemptions, 69% of cases in unvaccinated people were due to personal belief exemptions. His concern is that approximately 42% of all cases among all age groups were due to non-medical exemptions. Dr. Omer noted that people who do not get vaccinated during childhood due to vaccine hesitancy will remain susceptible to measles if they never re-visit that decision as adults.

Replying to Dr. Omer's first question, Dr. Schuchat explained that when the data are reviewed as multi-year data, CDC's data show that the majority of importations come from U.S. citizens traveling abroad not from foreign visitors or immigrants. Replying to Dr. Omer's second question, Dr. Schuchat explained that in the past several years, many of the larger measles outbreaks involving adult cases have occurred in religious communities with a tradition of not vaccinating and have included large numbers of unvaccinated adults. After most of those outbreaks, local health departments were able to work with those communities to change that practice. Dr. Schuchat stated that CDC is now working through cooperative agreements to encourage states to focus on identifying and understanding their larger pockets of unimmunized people. Those pockets are not always the same, even within a state. The states need this information because, for example, in Ohio a recent measles outbreak identified a much larger than expected unimmunized population.

Mr. Hosbach commented that we have tools, PCR, a vaccine, and funding, but he emphasized that we have a public health infrastructure problem. Specifically, he noted we seem to have smaller health departments, fewer clinics, and fewer school nurses—they get overwhelmed and overstressed in outbreak situations with insufficient resources. Mr. Hosbach commented that NVAC needs to find approaches to support public health infrastructure at the state and local level.

Dr. Temte mentioned several recent papers about modeling studies. The first study found that as measles is reduced, the average age of measles infection goes up and that causes more serious disease. The second study showed a 28-30 month window of reduced immunity following a natural measles infection. He suggested both of these recent findings could be integrated into messaging, because they show some inherent dangers of vaccine refusal.

Dr. Spika followed up on Dr. Schuchat's comments on non-vaccinating religious communities, which has been a major issue in Canada. He noted that Canada had over half of the total number cases from the Disneyland outbreak from a single person who returned to a non-vaccinating religious community. Even after this outbreak with 160 cases, they were not successful in getting this community to immunize. Last year, Canada had a measles outbreak of over 300 cases in a non-vaccinating religious community in British Columbia. The previous year, an outbreak occurred at a non-vaccinating religious community in Alberta. In both of these outbreaks, the measles importations came from Europe. Dr. Spika commented that Canada could say the U.S. has contributed to 80% of their imported measles cases so far this year.

Dr. Orenstein concluded the measles discussion by noting three issues. First, the issue of vaccine hesitancy is clearly important and this is discussed in NVAC's Vaccine Confidence Working Group report and recommendations. Second, the issue of global immunization needs more attention. Third, there are concerns about immunization gaps in adults and we need to think more about measles. Dr. Orenstein also noted it was important to think more about public health infrastructure issues, as Mr. Hosbach commented, and stated NVAC should come back to their infrastructure report. It would be useful in future meetings to get an update on implementation of NVAC's recommendations on immunization infrastructure. Finally, Dr. Orenstein stated it is important to continue to assure waning



immunity is not a problem, and suggested the U.S. will need to keep that issue in perspective if we want to keep our status of being free of indigenous measles.

### **Update from Maternal Immunization Working Group**

Dr. Orenstein introduced the session on the update from NVAC's Maternal Immunization Working Group.

#### **Maternal Immunization Working Group Phase II, Dr. Richard Beigi, NVAC**

Dr. Beigi began this update on the Maternal Immunization Working Group Phase II (MIWG II) by reading Part 2 of the NVAC charge: "Identify barriers to and opportunities for developing vaccines for pregnant women and make recommendations to overcome these barriers." Dr. Beigi and Dr. Omer serve as Co-chairs. He acknowledged the work of NVPO leads, Dr. Jennifer Gordon and Dr. Karin Bok. Dr. Beigi also pointed to a list of subject matter experts assembled for Phase II of this working group.

Dr. Beigi summarized the topics discussed at four MIWG II meetings held from January through June 2015, and mentioned two additional meetings scheduled for August and October 2015. At their June 2015 meeting, they heard from Dr. Gruber, FDA, and discussed the Pregnancy and Lactation Labeling Rule (PLLR). MIWG II members agreed that NVAC could offer feedback to FDA on implementation of the PLLR final rule. Dr. Beigi provided a brief overview of the current labeling and the new PLLR labeling, which will be effective June 30, 2014.

In describing the PLLR final rule, Dr. Beigi emphasized the following points as important to NVAC in developing recommendations on implementation. The PLLR:

- Creates a consistent format for providing information about the risks and benefits of product use during pregnancy and lactation, and by females and males of reproductive potential;
- Requires the removal of the pregnancy categories from all human prescription drug and biological product labeling and replaces the letter categories with three subsections that provide details about use of the product in "Pregnancy," "Lactation," and by "Females and Males of Reproductive Potential;" and
- Seeks to make product labeling a better communication tool in order to present the scientific information available for each drug and biological product.

After commenting that the goal of making product labeling a better communication tool for scientific information is probably the most important, Dr. Beigi described the required labeling elements under PLLR for Pregnancy (Section 8.1) and Lactation (Section 8.2). He emphasized that new information for Pregnancy and Lactation will involve risk summary, clinical considerations, and data. Dr. Beigi also provided an overview of the PLLR implementation schedule.

Dr. Beigi summarized implications of PLLR on vaccine labeling. Manufacturers are required to evaluate existing labeling to ensure it accurately reflects current knowledge about use of the product during pregnancy, and they will need to update labeling when new information becomes available. In general, data from use of vaccines in pregnancy will be derived from post-marketing studies or published maternal immunization studies. There is no requirement for the manufacturer to conduct additional studies.

Dr. Beigi emphasized the current thinking is that data should be derived from studies conducted with the specific product unless there is evidence of risk apparent from data accrued using a closely related product(s). Dr. Beigi provided observations on how PLLR would affect licensed vaccines recommended by ACIP for use in pregnancy (e.g., influenza, Tdap), and investigational vaccines specifically developed for use in pregnancy (e.g., Group B Streptococcus and Respiratory Syncytial Virus vaccines).

In reviewing next steps for PLLR, Dr. Beigi noted that it provides an opportunity to update labeling to ensure information is informative and accurate. FDA will be publishing draft guidance at the end of 2014. Implementation of PLLR provisions, as they apply to vaccine labeling, will require close collaboration between FDA's Office of Vaccines Research and Review and vaccine manufacturers in accordance with published guidance. There has already been ongoing dialogue about what data should be included. Dr. Beigi noted that MIWG II is seeking feedback and comments on NVAC recommendations for implementation of PLLR provisions.

### **Discussion**

Dr. Douglas, ACCV, noted they had done their own maternal workgroup and had talked about how the initial work on maternal immunization was very promising. She asked whether any research is being considered for following up on safety issues for the babies of mothers that we are encouraging to get immunized. Dr. Douglas commented that demonstrating no negative impact as these babies grow older would be a positive finding for increasing maternal immunization. Dr. Beigi noted this is an important consideration, and would be within the scope for MIWG II. He emphasized that long-term follow-up of those babies would require significant funding for large epidemiological studies, and he would defer that decision to the funders. Dr. Omer clarified that maternal vaccines are not new in the U.S.; for example, influenza vaccines have been used for pregnant women for several decades. He emphasized there has been an expansion of the maternal immunization platform, and it will continue to expand. He mentioned that MIWG II is looking at the safety aspects, not only for the mother but also the fetus and the infant. Dr. Omer commented that medium to long-term follow-up would be reasonable topic to consider in the MIWG II deliberations.

Dr. Orenstein asked whether MIWG II got any feedback from manufacturers and developers about whether they think the PLLR labeling change is helpful in terms of pursuing vaccines for pregnant women. Dr. Beigi noted MIWG II had just heard from Dr. Gruber, FDA, and the working group is discussing that now. The working group will be hearing from vaccine manufacturers in the summer and fall, and they have invited Dr. Gruber to return after those presentations to try to simulate more active dialogue between those two parties.

Mr. Hosbach commented that the labeling changes are missing the benefits aspect. He noted when dealing with physicians and a patient population that is risk adverse, if we want to have helpful guidance or information, it needs to include benefits as well as risks. Mr. Hosbach suggested the current information seems skewed to risks, which is appropriate for guidance, but benefits information should be included, if available. Dr. Beigi commented that over the last 40-50 years, we have seen a very risk-dominated discussion for the approach to drugs and therapeutics for pregnant women. His opinion is that pregnant women have not been served particularly well by that discussion. He agreed there needs to be more discussion about the risks and benefits, because providers need to address risks and benefits to guide the patient about whether or not they want to accept a particular intervention. Dr. Beigi read the final bullet from his slide on the implications of PLLR for vaccine labeling: "Current thinking is that

data should be derived from studies conducted with the specific product unless evidence of risk apparent from data accrued using a closely related product(s).” Dr. Beigi commented this suggests that we are not necessarily going to talk about a class effect unless there is risk identified. He suggested that if we are going to discuss a class effect, we should also discuss benefits from that class of products. He mentioned that influenza vaccines have shown no risks and significant benefits for the mother, newborns, and even the fetus in some data—this is a concrete example. If we want to make this guidance effective, we should balance risks and benefits.

Dr. Orenstein asked Dr. Krause, FDA, to comment on this issue. Dr. Krause noted that the vaccine label has the information that describes the reason for immunization, including benefits. PLLR is giving us a new way to organize information in a concise and straightforward way what the scientific data support about use of the product during pregnancy and in people of reproductive potential. It provides an opportunity for new, more informative labels because the old pregnancy categories were not very informative and often quite confusing. He noted that some vaccines given during pregnancy may have an extra benefit beyond when given outside of the pregnancy setting. Such claims (e.g., for Group B Strep) need to be evaluated scientifically and then could become part of the indication for the product. FDA hopes PLLR will provide the information people need and in a better way about use of these products.

Dr. Thompson noted the placental compartment is separate from the fetus and separate from the embryo. She wondered whether we are thinking enough about this in the context of clinical considerations. Dr. Thompson commented there might be some infection of the placenta that might lead to pregnancy loss, and asked whether MIWG II has considered that issue. Dr. Beigi commented that MIWG II has not specifically considered the issue in the way Dr. Thompson described it. Dr. Beigi commented MIWG II is considering the concept of augmenting research during pregnancy to consider the impact. He agreed that this is a relevant topic, and noted that NIH has recently launched a large new research focus on the impact on the placenta.

### **Assessing the State of Vaccine Confidence in the U.S.**

Dr. Orenstein introduced the session on assessing the state of vaccine confidence in the U.S. This session includes presentation of NVAC’s Vaccine Confidence Working Group report, adjudication of public comments, discussion of recommendations, and a vote on the recommendations and report.

#### **AAP: Countering Vaccine Hesitancy, Dr. Jesse Hackell, American Academy of Pediatrics (AAP)**

Dr. Hackell began by reading the NVAC draft report’s definition of vaccine confidence and the WHO SAGE Working Group report’s definition of vaccine hesitancy:

NVAC Vaccine Confidence definition: “The trust that parents or health care providers have in a) the immunizations recommended by the Advisory Committee on Immunization Practices (ACIP), b) the providers who administer vaccines and c) the processes that lead to vaccine licensure and the recommended vaccine schedule.”

WHO Vaccine Hesitancy definition: “Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccine services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence.”

Dr. Haskell noted that he would add the words “in the community” to the end of the first sentence of the WHO definition. He stated that over 80% of pediatricians have dealt with vaccine hesitancy, and increasing efforts at countering vaccine hesitancy will encourage vaccine confidence. Dr. Haskell commented that vaccine confidence starts with maintaining confidence in vaccine safety and efficacy, manufacturing and AAP and ACIP recommendations and if maintained at those levels in the community, confidence will filter down to the individual. Recommendations to providers must be consistent and feasible for a fast-paced pediatrician’s office. Dr. Haskell also commented that vaccine hesitancy starts with the individual and is affected by social media. Pediatricians deal with vaccine hesitancy daily on an individual basis with concerned parents and families.

Dr. Haskell stated the factors in the WHO report provide a good breakdown on countering vaccine hesitancy. He reviewed each factor: complacency, convenience, confidence, community, pediatricians and providers, and communication. Dr. Haskell read a recent statement from AAP opposing “alternative” immunization schedules. He noted that providers must have confidence in vaccines, manufacturers, clinical trials, and ACIP recommendations, which are all critical as the basis of their recommendations to families. He then explained different ways that providers face challenges in communicating the benefits of vaccines to families. In conclusion, Dr. Haskell stated that ensuring confidence in vaccines and the standard vaccine schedule is one major tool to help pediatrician’s counter vaccine hesitancy and improve vaccination rates in their daily practice.

### **Discussion**

Dr. Orenstein thanked Dr. Haskell for representing AAP and thanked AAP for their collaboration with NVAC in developing the recommendations. He asked if there were any questions or comments on his presentation. Mr. Hosbach asked about Dr. Haskell’s statistic that 87% of pediatricians have encountered patients resisting the standard vaccination schedule or vaccines. He asked whether further research exists to determine how many pediatricians will implement an alternative vaccination schedule when they encounter patients who hesitate and those patients later agree to an alternative schedule. Dr. Haskell noted research has found most pediatricians encounter vaccine hesitancy concerns from parents. The 87% statistic includes refusal of at least one vaccine. He added that good data show over half of patients will reconsider vaccination when the pediatrician counsels them. Other data show that 40-60% of pediatricians with patients who hesitate will later agree to implement alternative vaccination schedule for them on the theory that some vaccination is better than none. He mentioned that pediatricians experience greater complexity in their work when patients are on alternative schedules and transfer doctors, which can make it very time consuming to sort out and get them on track for vaccinations. He noted an alternative schedule impacts the timeliness of vaccination. Dr. Haskell mentioned the Luman study on timeliness, which showed how significantly any delay can lead children to go for many months being susceptible to vaccine-preventable diseases when that could be avoided by the standard vaccination schedule (<http://pediatrics.aappublications.org/content/110/5/935.short>).

Dr. Orenstein noted that education of providers is included in NVAC’s draft recommendations. He asked what AAP is doing to help younger physicians understand the importance of diseases they have never treated, such as Hib meningitis. Dr. Haskell noted that AAP is reaching into residency programs and medical schools to encourage programs dealing with education about vaccine-preventable diseases and vaccination. AAP also provides learning modules about vaccine hesitancy, all of which start with information about vaccines, the vaccine schedule, and the diseases that vaccines are intended to

prevent. Dr. Haskell emphasized this education needs to start in medical school and we must count on educators and residency programs to continue focusing on those diseases.

**Vaccine Confidence Working Group Presentation: Draft Report, Public Comment, and Recommendations, Dr. Vish Viswanath, NVAC**

Dr. Viswanath reviewed the NVAC charge regarding vaccine confidence. He introduced himself and Dr. Mouton as co-chairs of the Vaccine Confidence Working Group (VCWG). He thanked all the contributors to VCWG and NVPO staff for their support. Dr. Viswanath provided an overview of VCWG activities, including summarizing the topics of VCWG meetings held from June 2013-July 2014. After hearing different perspectives at their meetings, the working group discussed recommendations, developed a draft report and recommendations, presented the draft report for NVAC review and incorporated comments, released their report for public comment, and adjudicated all public comments. Dr. Viswanath explained that hearing from parents about their concerns during focus groups was a key part of informing VCWG's report. Dr. Viswanath explained that his presentation would review the final draft report and recommendations.

First, Dr. Viswanath reviewed the parent focus groups. VCWG held three parent focus groups representing parents with children less than five years old or expecting. They selected the three focus groups to represent different attitudes and beliefs about vaccination: a "very confident" group, a "not confident" group, and a group in the middle. Dr. Viswanath reviewed the key learnings from the parent focus groups, as listed below:

- Parents fall on a continuum of attitudes/beliefs towards vaccination—no one size fits all.
- Parents felt that they—and parents in general—should be actively involved in vaccination decisions for their children. Parents trust their provider.
- Parents also want their providers to be attuned to their personal concerns and situation. The "routine" immunization schedule is not "routine" for parents in terms of how they want to be treated.
- Many believed it was important to have, and have easy access to, information on how vaccines work, their safety, how often diseases occur among children who are protected by vaccination, etc.

Dr. Viswanath also reviewed some key themes, which VCWG derived from the focus groups. One thing that kept coming up is that vaccination is the social norm. This fact should be communicated nationally, because it is clear this is often not recognized. We should work to understand specific reasons for concern at a local level and address concerns locally, paying attention to some pockets or geographic areas where vaccination as a social norm is not recognized. Messages and messaging matter, and we need to find the best way to communicate those messages. Dr. Viswanath noted that narratives or stories are effective tools to communicate messages. Most parents do vaccinate. This majority should be supported and when supported they can be powerful advocates in their communities. Methods to support providers to engage in conversations with parents about vaccination are critical, including strategies and reimbursement for time. Finally, Dr. Viswanath noted that best practices should be collected and shared.

Turning to the definition of vaccine acceptance, Dr. Viswanath re-emphasized VCWG has learned that: 1) vaccination is the norm and that most parents do intend to vaccinate even while some may have concerns or questions, and 2) parents want to be involved in the decision-making. Dr. Viswanath

explained VCWG started with this premise for defining vaccine acceptance: “the timely receipt of all childhood vaccines as recommended by Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practice (ACIP) when vaccines and vaccine services are available.” They focused on a number of system-related, situational, cognitive, and contextual factors that drive acceptance including vaccine confidence. Dr. Viswanath explained that based on their analysis of those factors, VCWG zeroed in on “vaccine confidence.”

VCWG developed the following definition of vaccine confidence: “Vaccination Confidence refers to the trust that parents or healthcare providers have in: (a) the recommended immunizations, (b) the provider(s) who administer vaccines, and (c) the process that leads to vaccine licensure and the recommended vaccination schedule.” Dr. Viswanath explained that because VCWG needs to develop indicators, these dimensions assume parents are aware of the recommended vaccinations and have knowledge of how vaccination recommendations are made. Dr. Viswanath noted all are measurable dimensions. VCWG also thinks that these concepts are inter-related, with vaccine acceptance being the desired end outcome and vaccine confidence as an important antecedent to that outcome.

Dr. Viswanath provided an overview of the public comment process for the draft report. The 30-day public comment period was from April 6, 2015 through May 6, 2015. Comments were solicited through the Federal Register, and were received from individuals and organizations. A substantial majority of the comments from individuals were from members/followers of the Alliance for Natural Health. Dr. Viswanath pointed to a list of nine organizations that submitted comments: American Academy of Family Physicians, American Academy of Pediatrics, America’s Health Insurance Plans, Association of Immunization Managers, Alliance for Natural Health, American Osteopathic Association, Biotechnology Industry Organization, Colorado Children’s Immunization Coalition, and National Association of County and City Health Officials. He noted that most of the organizational comments were supportive, but many of their comments were geared toward suggestions for implementation. VCWG took all comments into consideration and adjudicated them. Dr. Viswanath provided thematic examples of some of the public comments.

Dr. Viswanath began his presentation of VCWG recommendations by outlining the five focus areas: 1) measurement and tracking, 2) communication and community strategies, 3) healthcare provider strategies, 4) policy strategies, and 5) continued support and monitoring. For Focus Area 1: Measuring/Tracking Vaccine Confidence, VCWG recognized that the state of the science of vaccine confidence and acceptance measurement is a multi-method and multi-national work in progress. Dr. Viswanath emphasized that such work is being done in a number of countries by a number of teams. He explained that VCWG made four recommendations for *Focus Area 1: Measuring/Tracking Vaccine Confidence*.

During his presentation of Focus Area 2 recommendations, Dr. Viswanath noted that the demand for evidence-based communication came up frequently. He explained that VCWG made four recommendations for *Focus Area 2: Communication and Community Strategies*.

Dr. Viswanath explained that VCWG also made recommendations pertaining to other focus areas including *Healthcare Provider Strategies, Policy Strategies, and Continued Support and Monitoring*. [A detailed description of all of the proposed recommendations is available in the NVAC report and in the presentation slides.]



### **Discussion and Vote**

Dr. Orenstein invited discussion. Dr. Rawlins stated this is a very robust and comprehensive set of recommendations and thanked the working group. He asked two questions. First, Dr. Rawlins asked about the development of culturally appropriate communication strategies for diverse populations, which he thought was not clearly elucidated in Dr. Viswanath's discussion during this session. Second, he asked about the issue of engagement of non-provider trusted advisors to improve confidence in diverse populations. Dr. Viswanath agreed those were two good points. He noted that in their report, VCWG spent considerable effort discussing development of appropriate communications strategies. Evidence-based or evidence-informed communication strategies should be developed for different audiences. VCWG clearly acknowledged there is not one audience group and no one-size-fits-all approach given the tremendous heterogeneity, both in terms of stakeholders as well as people, culturally, racially, and ethnically. Dr. Viswanath stated that if this is not clearly coming through in the report, they will clarify it in the final report.

Dr. Doskey made three points on behalf of AHIP. AHIP supports the idea of using IIS to collect data on delays and refusals, which can help more rapidly identify areas that are underserved either through region, geography, income, etc. AHIP is not opposed to having a meeting to discuss current coding infrastructure. However, development of a provisional code for counseling where no vaccine is given increases income, but in keeping with the evidence-based idea, there does not seem to be any data supporting that such a provisional code would increase confidence or immunization rates. However, AHIP does support VCWG's recommendations for development of pay-for-performance initiatives and incentives as described in the recommendation.

Dr. Lynfield made a motion that NVAC approve the May 29, 2015 Draft Report: "Assessing the State of Vaccine Confidence in the United States: Recommendations from the National Vaccine Advisory Committee" from NVAC's Vaccine Confidence Working Group. Dr. Thompson, Dr. Omer, and Dr. Smith seconded the motion.

- ACTION ITEM: Dr. Orenstein invited formal approval of the report "Assessing the State of Vaccine Confidence in the United States: Recommendations from the National Vaccine Advisory Committee." The Committee voted in favor of adopting the report and recommendations (12 in favor, 0 opposed, 2 absent).

Dr. Orenstein concluded this session by stating the report is approved, and he looks forward to finalizing, publishing, and distributing it. He suggested that NVPO now has an important task to develop an implementation plan with the other agencies, and report back to NVAC. He thanked Dr. Viswanath, Dr. Mouton, and Ms. Mendel, and Dr. Nowak for their work on this report.

### **Progress on HPV Vaccine Uptake Among Adolescents**

Dr. Orenstein introduced the session by emphasizing the need to improve uptake of HPV vaccines in adolescents to prevent cancer. This session includes presentation of NVAC's HPV Working Group report, adjudication of public comments, discussion of recommendations, and a vote on the recommendations and report.

**Research on the HPV Vaccine: Update from the National Cancer Institute, Dr. Sarah Kobrin, National Cancer Institute (NCI)**

Dr. Kobrin briefly reviewed how NCI's mission supports the National Vaccine Plan. She noted that NCI's HPV vaccine research covers three areas: 1) intramural research at NCI, 2) international projects all over the world through the Center for Global Health, and 3) extramural funding within the U.S. for extramural science.

Dr. Kobrin began by discussing intramural research at NCI. She discussed the Costa Rica Vaccine (CVT) Trial Long-Term Follow-up, which began in 2004 in cooperation with Costa Rican scientists. Enrollment ended in 2005 and they continue to follow this group. The primary aims were to evaluate protection afforded from the bivalent HPV vaccine, by time and dose, and the clinical impact. Because the CVT Trial is collecting data on long-term protection, they can also focus on secondary aims such as 10-year vaccine efficacy. Four years after vaccination at different doses, CVT data showed that protection against persistent (six months) HPV infection with HPV 16/18 was very high at one, two, or three doses. The highest immunogenicity response occurred from three doses. Dr. Kobrin stated it was important that the endpoint was incident HPV 16/18 infections. Both the CVT Trial and the PATRICIA Trial in Costa Rica found high levels of protection. Dr. Kobrin explained there is no precedent for one dose of a protein-based sub-unit vaccine to induce stable antibody titers for several years. Currently, there are two hypotheses about the source of immunogenicity- one related to immunogenicity of the virus-like particles comprising the vaccine, and the other due to the vaccines adjuvant. Dr. Kobrin also briefly described a number of other proposed trials under consideration for intramural research at NCI.

In describing NCI's international projects, Dr. Kobrin noted they fall into two categories: technical support and advocacy. NCI is involved in technical support for the Pink Ribbon Red Ribbon program, which is using the President's Emergency Plan for AIDS Relief (PEPFAR) platforms for prevention and control of cervical cancer, including HPV vaccination. Examples of advocacy include cooperation with the Asia Pacific Economic Cooperation (APEC) on an APEC workshop with countries that have implemented HPV vaccine, and ongoing dialog with Chinese public health officials and scientists conducting Chinese HPV vaccine research since 2012.

Dr. Kobrin explained that most of their extramural funding budget goes to researchers at the 61 NCI-funded Clinical Cancer Centers, which are widely dispersed across the U.S. Dr. Kobrin noted that these centers also provide clinical care, so they are imbedded in their communities. Forty applications were received for the August 2014 competition for Center Grant Supplements. NCI made 18 awards to cancer centers to take advantage of local leadership, and to achieve the following aims: 1) gather local data on vaccine uptake, barriers, needs, and collaborators; and 2) Create—or increase—local collaborations to promote HPV vaccine uptake. To indicate the strong interest in these awards, Dr. Kobrin noted they recently had a meeting and many centers sent at least two people, including those centers not funded. Dr. Kobrin concluded her discussion on extramural funding by noting that NCI is currently developing new announcements addressing the call for research on communication about the HPV vaccine from the President's Cancer Panel. She also briefly summarized initial plans for a new HPV vaccine intervention for young gay and bisexual men, which has not begun yet.

Dr. Kobrin concluded her presentation by summarizing the goals of NCI-supported HPV vaccine research:

- Safely reducing the number of doses needed,
- Supporting vaccine programs around the world,

- Defining and promoting high quality provider recommendations, and
- Promoting local engagement and uptake across the U.S.

**Action Planning with 10 Local Health Departments to Plan for Increasing HPV Vaccination, Ms. Kate Heyer, National Association of County and City Health Officials (NACCHO)**

Ms. Heyer explained that NACCHO received funding last summer from CDC for this project to work with local health departments (LHDs). She reviewed the key components of this initial CDC-funded project:

- Direct funding and support to 10 LHD awardees;
- Technical assistance (e.g., webinars and conference calls);
- Guidance and support from the HPV Project Advisory Board;
- Development of an organizational policy statement, *Increasing HPV Vaccination Rates in Females and Males*, to make NACCHO's policy clear; and
- Release of the *Guide to HPV Resources for Local Health Departments*, which is a compilation of resources.

NACCHO solicited applications from LHDs serving a population of at least 150,000 people and from states with low HPV rates. Ms. Heyer noted that Phase I of the LHD awardee activities is ending on June 30, 2015. In Phase I, NACCHO asked the LHDs to plan and convene an action planning meeting facilitated by NACCHO staff with key community stakeholders. The LHDs were expected to use outputs from the action planning meeting to develop a draft action plan and will present their action plans at the end of June. The LHDs will also document and share lessons learned during the project period.

Ms. Heyer described the pre-work that NACCHO asked the LHDs to conduct in preparation for the action planning meetings. Each of the LHDs collected data to identify an action planning stakeholder committee, describe the community environment that might impact HPV strategic planning, and understand parent and provider attitudes about HPV vaccination. Ms. Heyer reviewed the major findings from this initial LHD data collection effort:

- Available data about HPV vaccination rates is varied in quality and quantity,
- Parent and provider attitudes about HPV vaccination are varied,
- Confusion exists about the HPV vaccine recommendations—for whom and when it is recommended,
- Social and cultural factors remain important factors in HPV vaccine uptake in many communities, and
- Access to HPV vaccine is uneven in some communities.

Ms. Heyer provided an overview of the action planning process. First, the LHDs met for a 1.5-day visioning process in their community. Local physicians were invited to an HPV overview meeting. NACCHO led the LHDs through a SWOT (strengths, weaknesses, opportunities, and threats) process. After working on strategic focus area development, the LHDs defined their commitment to action planning. Ms. Heyer explained that the core of all the LHD action plans is reinforcing the message that HPV vaccination is cancer prevention. Most LHDs plan to begin working with schools to improve education about access to the HPV vaccine. The LHDs are interested in identifying opportunities to improve data and most are interested in engaging partners as champions. Ms. Heyer stated that an important focus area of the LHD's action plans is increasing access to the HPV vaccine.

In describing the most common challenges during the action planning process, Ms. Heyer emphasized concerns and misconceptions about the safety and efficacy of the vaccine, access, and payment. She noted they found that parents heard the HPV vaccine was too expensive. In describing opportunities from this process, Ms. Heyer stated that: 1) stakeholder committees now exist in each of the 10 LHD awardee jurisdictions to guide project activities, 2) opportunities now exist for coordination with other CDC-funded HPV vaccination projects, and 3) some LHDs have been in contact with their state health departments. Moving forward, they will be establishing a NACCHO-led Learning Community for the LHD awardees.

Ms. Heyer concluded by reviewing the next steps. NACCHO will provide additional support to LHD awardees through continued technical assistance, funding to support project implementation, identifying opportunities to connect with other LHD awardees, and continued connection with the HPV Project Advisory Board.

Dr. Orenstein asked if there were any questions. Ms. Ehresmann, AIM, asked whether NACCHO was putting any effort into measurement of results and noted CDC typically does that. Ms. Heyer explained each of the LHDs has identified performance measures to guide their project going forward.

#### **National HPV Vaccination Roundtable, Dr. Noel Brewer, Chair**

Dr. Brewer reviewed the Roundtable's mission: "The National HPV Vaccination Roundtable is a national coalition of public, private, and voluntary organizations and invited individuals working together to increase U.S. HPV vaccination coverage." He pointed to a list of the many different organizations involved in the steering committee. To clarify the scope, Dr. Brewer compared what the Roundtable is trying to do versus what they will not do. He noted the Roundtable tries to provide a forum that links vaccination and cancer prevention, identify unmet needs and gaps, and stimulate collaborations to address those unmet needs. Dr. Brewer explained that the Roundtable does not duplicate member organization roles. More specifically, they are not trying to compete with member organizations, or trying to take positions on policies that are in conflict with member organizations. He described a personal anecdote from a cervical cancer survivor who spoke at a recent Roundtable meeting.

Dr. Brewer explained the Roundtable is trying to focus on the best and most promising practices for accelerating HPV vaccine uptake in the U.S. They are focusing on the goals already outlined by the President's Cancer Panel for accelerating HPV vaccine uptake. The Roundtable has created some task groups, for example, provider training and survivor involvement. He emphasized that the Roundtable wants involvement of cervical cancer survivors as an important part of this process. Each of the task groups has developed a logic model for their topic, and he pointed to an example from the electronic health records task group. Pilot projects were developed that must meet certain requirements (e.g., responsive, collaborative, impactful, feasible, novel) and will be evaluated on those requirements.

#### **NVAC HPV Working Group Draft Report and Recommendations, Dr. Wayne Rawlins, NVAC**

Dr. Rawlins reviewed the HPV Working Group charge to: "review the current state of HPV immunization, understand the root cause(s) for the observed low vaccine uptake (both initiation and series completion), and identify existing best practices all with a goal of providing recommendations on how to increase use of this vaccine in young adolescents." He showed a timeline of working group activities from August 2013-June 2015. Dr. Rawlins reviewed the five topic areas for presentations to the working group: 1) current epidemiology of vaccination coverage and vaccine-preventable disease background

and proposed solution strategies, 2) provider barriers and federal opportunities, 3) systems barriers and federal opportunities, 4) parental and adolescent barriers and federal opportunities, and 5) potential changes to vaccine products and dosing.

Dr. Rawlins reviewed NVAC comments and the public comment period. The working group received one major comment after the February NVAC meeting regarding inclusion of research on alternative ages. He explained that the report and recommendations were published in the Federal Register for a 30-day public comment period from April 6, 2015 through May 6, 2015. Of the six public comments received, two were from the general public and four were from organizations. Dr. Rawlins thanked everyone who submitted public comments. All public comments were adjudicated and also grouped under four themes: 1) overall support (one comment in dissent); 2) coordinated, consistent messaging is key; 3) state-level suggestions (school requirements, such as state practice laws); and 4) coordination of care.

Dr. Rawlins reviewed votes taken at the June 2014 NVAC meeting on two recommendations regarding the President's Cancel Panel (PCP) report. Dr. Rawlins stated that because NVAC had already voted on those two recommendations, they would not be discussed during this session. He reviewed the two already endorsed recommendations, as listed below:

- Recommendation 1: The ASH should endorse the PCP report, Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer, and adopt the recommendations outlined therein.
- Recommendation 2: As the PCP recommended, NVAC should, monitor "the status of uptake and implementation of the recommendations." This should be done by hearing an annual progress report from HPV vaccination stakeholders identified in the PCP report.

Dr. Rawlins noted that Recommendation 3 addressed developing communication strategies, Recommendation 4 on strengthening the immunization system in order to maximize access to and support of adolescent vaccinations; and Recommendation 5 pertaining to reviewing the available data that could lead to a simplified HPV vaccination schedule. [For the full language of the recommendations and sub-recommendations, please refer to the written report and presentation slides].

### **Discussion and Vote**

Dr. Orenstein asked if there were any comments or questions about the proposed recommendations. Dr. Schuchat, CDC, thanked the HPV Working Group. She commented on the HPV session's presentations and that it was very exciting to see NCI, the National HPV Vaccination Roundtable, and local health departments through NACCHO coming together around this issue. Dr. Schuchat stated that clearly the way CDC and the immunization community has been trying to promote the HPV vaccine over the past decade has not been having the effects they were hoping for. She was impressed with the work described in these presentations. Dr. Schuchat also noted she was impressed by the HPV Working Group and their thoughtful recommendations.

Dr. Doskey, AHIP, stated the PCP includes a mention that healthcare payers should reimburse providers adequately for HPV vaccines to avoid missed opportunities. However, it does not provide any data to support the claim that HPV vaccine reimbursement is inadequate. Most of what AHIP has read indicates that providers who see more publicly insured patients than privately-insured patients tend to report more problems with reimbursement. Dr. Doskey asked whether that was addressed by the HPV Working Group's recommendations. Dr. Rawlins referenced Recommendation #4 and the sub-strategy

on “Develop strategies to overcome barriers regarding reimbursement . . .” Dr. Rawlins commented there is no discussion about the adequacy of reimbursement in that recommendation. He mentioned several people who had worked on the issue of providers being reimbursed based on private versus public insurance at different rates. Dr. Rawlins explained that is why this recommendation read: “Develop strategies to overcome barriers regarding reimbursement for vaccination administration and compensation of vaccine administrators and their staff.” Dr. Rawlins commented that reimbursement is an issue that needs to be addressed. Dr. Doskey agreed that reimbursement is an issue but also commented that the perception of inadequate reimbursement is a problem and that perceptions can sometimes be more difficult to overcome than reality. Mr. Rothholz stated it was not only the level of reimbursement but also who was being reimbursed to give the HPV vaccine. He commented there are some providers who are not recognized to provide the HPV vaccines, but could increase access (such as pharmacists).

Mr. Rothholz made a motion that NVAC approve the draft report and recommendations from NVAC’s HPV Working Group. Dr. Lynfield and Dr. Viswanath seconded the motion.

- ACTION ITEM: Dr. Orenstein invited formal approval of the draft report and recommendations from NVAC’s HPV Working Group. The Committee voted in favor of adopting the report and recommendations (12 in favor, 0 opposed, 2 absent).

Dr. Orenstein thanked Dr. Rawlins and Ms. Despres and the HPV Working Group for their work and noted he looks forward to getting this report published. He suggested that NVPO should begin developing an implementation plan for this report. At the request of panel members, Dr. Orenstein announced a short break.

### **Immunization Safety Task Force Vaccine Safety Scientific Agenda**

Dr. Orenstein introduced the session on the update from NVPO’s Immunization Safety Task Force.

#### **Update on Immunization Safety Task Force Vaccine Safety Scientific Agenda, Dr. Karin Bok, NVPO**

Dr. Bok began by providing an overview of the National Vaccine Safety System. She explained that NVPO coordinates and leads the Immunization Safety Task Force (ISTF). Dr. Bok stated ISTF “ensures that all federal efforts relevant to immunization safety are coordinated and integrated and that opportunities to enhance synergies across the federal government in immunization safety are identified.” She presented an updated list of ISTF members, which has grown since last year and includes all federal agencies dealing with vaccines. She discussed the Vaccine Safety Scientific Agenda webpage, which provides information for other federal agencies and also for the public. This website has links to other resources, and they hope to keep updating it. Dr. Bok emphasized that the agenda “outlines the efforts of federal agencies on vaccine safety and the ongoing and planned associated scientific activities and interagency coordination that contributes to the safety system.”

Dr. Bok noted that the ISTF recently developed the Vaccine Safety Cooperative Agreement. Under this agreement, NVPO will provide funding opportunities for vaccine safety research. The current funding announcement is \$500,000 in grants to support vaccine safety research, especially in pregnancy. They have eight applications, which are now being reviewed. Around July, NVPO expects to make two \$250,000 awards. In addition, they recently worked with the Office of the Assistant Secretary for Health



to obtain funding for evaluating the federal vaccine safety systems to test and survey the safety of vaccines administered during pregnancy.

Finally, Dr. Bok briefly described two NVPO-funded collaborations on vaccine safety research. NVPO is expecting the results soon on a large study for “Enhanced Evaluation of Risk of Narcolepsy Associated with Pandemrix and Arepanrix and MF59-adjvanted H1N1 Vaccines.” She noted that NVPO is very excited about this study. The other study is a clinical study of Tdap safety in pregnant women, which will evaluate health outcomes and growth parameters in infants born to women who received Tdap during pregnancy.

### **Discussion**

Dr. Orenstein asked if there were any comments or questions. Mr. Hosbach commented that NVAC has done a terrific job of describing the vaccine safety reporting systems in focusing on the government. He noted one component that is missing is the role that manufacturers play in vaccine development from Phase 1 through Phase 4. NVAC’s Vaccine Confidence Working Group report discussed that we need to ensure people are confident in the process that leads to vaccine licensure. Mr. Hosbach hoped that NVAC does not neglect the roles played by vaccine manufacturers, clinicians, clinical investigators, and data safety monitoring boards in the Vaccine Adverse Event Reporting System (VAERS). We should consider the complete system and it would be helpful to have an all-encompassing discussion.

Dr. Temte suggested there is a profound need for education for primary care system providers and how to get those providers to deal with the vaccine safety system and approach making reports into VAERS. Reporting to VAERS does not happen often and requires some baseline knowledge. He noted that providers think discussing vaccine hesitancy will take a lot of time and they also think that VAERS reporting will take a lot of time. Dr. Gellin agreed and noted that the NVAC’s Maternal Immunization Working Group had addressed educating obstetrician-gynecologists about the availability and use of these systems in their first recommendation. Dr. Gellin commented that most providers probably do not know VAERS or other reporting systems even exist.

Dr. Orenstein wondered if there had been any analysis of how doctors are reporting to VAERS and whether NVAC or the ISTF should address the education issue. The other issue is whether doctors are using vaccine information statements or even reading them before giving to patients. At the request of Dr. Bok, Tom Shimabukuro, from CDC’s Immunization Safety Office, came to the microphone. Mr. Shimabukuro commented there have been surveys of knowledge and attitudes about reporting adverse events and agreed that education and awareness for providers is something that CDC can work on for VAERS reporting. Dr. Orenstein suggested that vaccine safety should be included in CME credits for doctors and also in undergraduate or at least residency training programs. He suggested that ISTF could interact with some groups who develop CME curriculum, which could be a potential access point.

Dr. Thompson commented that it is fantastic we have the VAERS system, but unfortunately it is underutilized. She asked whether there was any opportunity to look at the data and say more about actual vaccine safety versus perceived vaccine safety. Dr. Thompson asked Dr. Bok if there was any opportunity for ISTF to take on the perceived vaccine safety research agenda to understand misconceptions about vaccine safety. Dr. Bok noted that ISTF could look more into perceived safety. Dr. Orenstein mentioned a recent Institute of Medicine (IOM) report and RAND Corporation study on vaccine safety, and wondered whether there were any future plans to research these issues.

Dr. Gellin asked Dr. Thompson what she meant by “perceived” in terms of data analysis. Dr. Thompson mentioned that we hear of significant concerns about the HPV vaccine, for example, yet we do not see that reported in VAERS. The fact that we do or do not see those reports in VAERS is useful information. Dr. Thompson stated that we need research about what we can or cannot say from the reporting system data to address challenges from misconceptions about vaccine safety. Dr. Gellin commented that there are two parts to this issue: what do people think and what the science shows. He mentioned that IOM had previously looked at public concerns regardless of whether they were concerns of the scientific community. It might be helpful to compare those allegations arising from what people think to what the science shows. Dr. Orenstein asked if there were any other questions or comments, and there were none.

### **NVAC Liaison Updates**

Dr. Orenstein announced that the meeting agenda would be adjusted to begin the updates from Liaison representatives early, if they were in attendance. Dr. Orenstein invited the first Liaison representative of NVAC, from the Advisory Commission on Childhood Vaccines, to report.

#### **Advisory Commission on Childhood Vaccines – Dr. Charlene Douglas**

Dr. Douglas reported that ACCV conducted its 95<sup>th</sup> quarterly meeting by teleconference on June 4, 2015. The meeting began with program updates from the Division of Injury Compensation Programs and the Department of Justice. This ACCV meeting included discussion on prevention of shoulder injury related to vaccine administration (SIRVA), and Dr. Douglas read the topics covered by Dr. Terry Dalle-Tezze’s presentation “Feasibility of SIRVA Prevention.” As part of its mandate, ACCV also reviewed revisions to CDC vaccine information statements for Meningococcal Vaccine; Serogroup B Meningococcal Vaccine; and the MMR Vaccine. ACCV provided a number of comments to CDC staff. ACCV also received program updates from CDC’s Immunization Safety Office; the National Institute of Allergy and Infectious Diseases; FDA’s Center for Biologics, Evaluation and Research; and NVPO.

#### **Advisory Committee on Immunization Practices – Dr. Jonathan Temte**

Dr. Temte explained ACIP’s February 26, 2015 meeting had a very large agenda, but was curtailed due to a snowstorm. ACIP voted to reaffirm the current core recommendations that annual influenza vaccination is recommended for all people six months of age and older. He stated ACIP revised the recommendation for the use of LAIV to read as follows: “For healthy children aged 2 through 8 years who have no contraindications or precautions, either LAIV or IIV is an appropriate option. No preference is expressed for LAIV or IIV for any person aged 2 through 49 years for whom either vaccine is appropriate.”

ACIP also voted on updated recommendations for meningococcal vaccines for certain high risk groups. Dr. Temte referred attendees to this recommendation in ACIP’s written report, as follows: “MenB vaccine is recommended for routine use in people  $\geq 10$  years of age at increased risk for meningococcal disease (GRADE category A recommendation). Certain groups who may benefit from this vaccine include people with persistent complement component deficiencies, people with functional or anatomic asplenia, microbiologists routinely exposed to isolates of *Neisseria meningitidis*, and people identified to be at increased risk because of a serogroup B meningococcal disease outbreak.”

Dr. Temte explained ACIP voted on a yellow fever vaccine recommendation to bring ACIP in line with WHO recommendations. ACIP now recommends additional doses of yellow fever vaccine for certain travelers, such as women who were pregnant when they received their initial yellow fever vaccine dose or individuals who received a hematopoietic stem cell transplant. Finally, a vote on HPV vaccines recommended 9vHPV as an option for routine vaccination.

Dr. Temte reported six votes are scheduled at ACIP's June 24-25 meeting. ACIP will consider and vote on Meningococcal, Influenza A (HSN1), Smallpox, and Pneumococcal vaccine recommendations along with recommendations for the 2015-16 influenza season and several general recommendations. Dr. Temte stated that no vote is planned for HPV vaccine recommendations regarding use of 9-valent HPV vaccination for persons who have completed an HPV vaccination series.

Dr. Temte announced that he will conclude his term as ACIP Chair on June 30, 2015. Dr. Nancy Bennett will assume the Chair of ACIP for a 3-year term, and will also serve as the ACIP Liaison representative to NVAC.

#### **America's Health Insurance Plans – Dr. Richard Doskey**

Dr. Doskey, representing Dr. Scott Breidbart, explained AHIP convened a National Adult Immunization Roundtable in February 2015 to discuss NVPO's draft National Adult Immunization Plan and identify opportunities to accelerate improvements within the adult vaccine ecosystem. Dr. Doskey summarized highlights of recommendations that AHIP submitted to NVPO on this draft plan. First, IIS have the capacity to identify health disparities and other gaps in care at the population level, in addition to tracking patient immunization history at the point-of-care. IIS can provide information on trends in disease outbreaks or adverse reactions to specific vaccines at the population health level. Use of immunization registries to increase adult immunizations, however, must involve finding solutions to the common challenges of IIS, including improving the quality of vaccination records, addressing variability in state laws, and helping providers develop the capacity to manage an immunization registry. Second, Dr. Doskey stated AHIP and its member health plans are committed to promoting the use of age-appropriate vaccines as recommended by ACIP. Dr. Doskey explained that although coverage of those immunizations is mandated as part of the Affordable Care Act (ACA), some plans are "transitional" or "grandfathered" and are not subject to the same preventive services policies. Additionally, the ACA's mandate for coverage of ACIP routinely-recommended vaccines at no cost share to the patient does not apply to Medicare, which has its own coverage rules for vaccines. Third, Dr. Doskey explained that small physician practices may find it difficult to adhere to complex vaccine storage and handling requirements, but health insurance plans along with public health and professional societies offer tools to help physician practices address challenges with vaccine management. Finally, Dr. Doskey noted that investments in research and development of new vaccines should carefully weigh the additional costs with incremental benefits. Dr. Doskey stated that AHIP would encourage transparency in research and development investments, vaccine pricing, and greater competition to support vaccine access and affordability. In addition, Dr. Doskey summarized AHIP's comments and recommendations on NVAC's draft vaccine confidence report and the NVAC HPV Working Group's proposed recommendations.

#### **Association of Immunization Managers – Ms. Kristen Ehresmann**

Ms. Ehresmann reported that AIM hosted its first leadership development conference in New Orleans in April 2015. The conference featured training and leadership skills development for immunization program managers. Prior to that meeting, AIM participated in the American Immunization Registry

Association, which was held three days before in New Orleans. AIM participated in the National Adult and Influenza Immunization Summit held in Atlanta in May 2015. The AIM Research and Development Director, Dr. Katelyn Wells, provided a presentation—"State of the States on Adult Immunization"—on sharing data and information on adult immunization policies, programmatic activities, funding, and other challenges as well as successes. Ms. Ehresmann noted that AIM is currently accepting nominations for the Natalie Smith and Bulls Eye Awards. The Natalie Smith Award is presented annually to an immunization program manager who has demonstrated visionary leadership and significant accomplishments in reaching vaccine preventable disease goals. The Bulls Eye Award is presented annually to three programs whose initiatives have "hit their mark" in achieving goals and demonstrating innovation and excellence. Ms. Ehresmann reported AIM submitted comments on the draft National Adult Immunization Plan on March 23, 2015. AIM supports this plan and its goals. AIM's comments encourage greater inclusion of the public health infrastructure and discuss the need for appropriate and stable resources to support adult immunization. She explained AIM will be launching its first virtual exhibit hall on July 22, 2015. This virtual exhibit hall will be an opportunity for program managers to learn about the latest technologies and available products from manufacturers. The Vaccine Facts and Policy website was launched in November 2014, providing information on all 64 immunization programs.

**Association of State and Territorial Health Officials – Ms. Kathy Talkington**

Ms. Talkington, representing Dr. Paul Jarris, discussed several current ASTHO immunization initiatives. ASTHO's IIS Meeting in August 2014 brought together relevant state stakeholders among five key states to discuss barriers and identify potential solutions for multi-state IIS interstate data sharing. As a result of the meeting, ASTHO worked in coordination with The Network for Public Health Law to develop a template IIS interstate data sharing Memorandum Of Understanding (MOU). Ms. Talkington explained that the MOU is now final. The MOU will initially be piloted with the states that attended the IIS meeting, but can be used by other interested states in the future. Ms. Talkington explained that ASTHO believes immunization infrastructure issues need more attention. To address immunization infrastructure, ASTHO conducted a survey of immunization program managers to help describe the essential staff required to implement core components of an immunization program, outline potential staffing models for immunization programs, and describe immunization program scalability in the event of an emergency situation such as pandemic influenza. Ms. Talkington discussed meetings recently held regarding pandemics and also mentioned that ASTHO recently began reaching out to faith-based organizations as potential partners in a pandemic situation.

**National Association of County and City Health Officials – Ms. Tiffany Tate**

Ms. Tate reported on two NACCHO projects: the HPV Project and General Immunizations Project. Ms. Tate explained that CDC funded NACCHO to support local health departments (LHDs) to increase their capacity to work with healthcare providers and other community stakeholders to implement ACIP's HPV vaccination recommendations. During Phase I of the HPV Project (January-June 2015), NACCHO worked with the 10 funded LHDs and their partners to develop an HPV action plan. In May 2015, NACCHO released the *Guide to HPV Resources for LHDs*, which was designed to assist LHDs with development of HPV projects and vaccination campaigns. NACCHO also hosted three technical assistance calls, focused on utilizing data, educating providers to support HPV vaccine recommendations, and conducting assessments of provider and community attitudes about HPV vaccination. Ms. Tate noted that NACCHO will be hosting representatives from the 10 LHDs and the HPV Project Advisory Board from June 24-25,

2015 to discuss action plans and prepare for implementation. During Phase II of the HPV Project (July 2015-June 2016), the sites will implement the action plans developed during Phase I.

Ms. Tate explained that, as part of the General Immunizations Project, NACCHO regularly convenes an immunization workgroup comprised of local health officials, programmatic LHD staff, and immunization coalition members. Workgroup members discuss emerging immunization issues, identify and share best practices, and review immunization initiatives. Ms. Tate announced the immunization workgroup will meet on June 25-26, 2015 to discuss priorities for next year and how NACCHO can best assist LHD immunization programs. Ms. Tate also announced that NACCHO will be hosting a workshop for LHD staff at NACCHO's Annual Conference on July 7, 2015 titled, *Moving People off the Fence: Create a local communications campaign to increase vaccine confidence*. The workshop focuses on increasing vaccine confidence within communities through targeted communication campaigns. Ms. Tate also explained NACCHO is currently working on a collaborative effort to survey health departments about methods used to collect information about patients and vaccines administered.

#### **Public Health Agency of Canada – Dr. John Spika**

Dr. Spika explained that PHAC is currently working with Canadian provincial and territorial officials on an Action Plan that will outline work necessary for vaccines that need to be available in the next six years, and in the next 6-12 years. Dr. Spika mentioned that PHAC got interesting input on the antimicrobial resistance issue from work on the Action Plan. PHAC is also conducting discussions with industry and academia on how to get research started to make progress on developing these new vaccines. Dr. Spika noted that this federally-led Action Plan on vaccine needs in Canada may be completed soon. Dr. Spika also explained that their National Advisory Committee on Immunization has not made any recommendations yet on which vaccines should be included. However, they are looking at whether the SMART Vaccine tool can be used in the consensus building process. Finally, Dr. Spika stated that PHAC is starting to look at vaccine confidence, and they hope to build upon NVAC's vaccine confidence working group report that was approved today.

#### **Pan American Health Organization/WHO – Ms. Hanna Curtis**

Ms. Curtis, representing Dr. Isabella Danel, provided selected highlights of PAHO's recent work with Member States on immunization-related activities. Ms. Curtis explained that in late April, the Americas became the first region in the world declared free of the endemic transmission of rubella and congenital rubella syndrome (CRS). This declaration was made by an international expert committee and was the culmination of a 15-year effort that involved widespread administration of the MMR vaccine throughout the Western Hemisphere. Rubella and CRS are now the third and fourth vaccine-preventable diseases eliminated from the Americas, following the regional eradication of smallpox in 1971 and the elimination of polio in 1994. Ms. Curtis stated regional efforts are now turned toward achieving the elimination of measles, hopefully in 2016. Ms. Curtis explained the announcement of rubella elimination coincided with the celebration of the 13th annual Vaccination Week in the Americas (VWA) from April 25-May 2, 2015. Country efforts included information, education and communication activities, health worker training and the integration of other preventative interventions with immunization. Finally, Ms. Curtis announced the 23rd meeting of PAHO's Technical Advisory Group on Vaccine-preventable Diseases will be held from July 1-3, 2015 in Varadero, Cuba.

#### **Vaccines and Related Biological Products Advisory Committee – Dr. Robert Daum**

Dr. Daum noted that VRBPAC has met twice. Their first meeting in March 2015 was about the choice of influenza virus vaccine components for the 2015-2016 influenza season. He commented this is not really a choice, because WHO meets before them and typically WHO recommendations are not contradicted. This year the VRBPAC meeting was postponed several weeks to ensure it came after the WHO meeting. Dr. Daum noted that first VRBPAC looked at the three components of the trivalent vaccine. For H1N1 they left it alone, because the sera that were available matched the viruses that were circulating very well. As everyone knows, this was not a great year for influenza vaccines. In particular, it was not a great year for the H3N2 strains. Previously the H3N2 strain was poorly matched to the circulating viruses. The main change from the VRBPAC meeting was to change the H3N2 component of the vaccines from H3N2 A/Texas/50/2012 (clade 3C.1) virus to H3N2 A/Switzerland/9715293/2013 (3C.3a) virus to better match circulating viruses. The Influenza B viruses, which are a fairly minor component of the annual influenza burden, underwent a change for the trivalent vaccines to B/Phuket/3073/2013. For the fourth component of the quadrivalent vaccine, Influenza B components did not change.

He learned that HHS Secretary Burwell directed Dr. Gruber from FDA and CDC to meet periodically to determine why the H3N2 component was such a bad match this year. They met once in May, and determined there were no significant changes in the circulation of any of the Influenza A components or the Influenza B components. The hope was that any new trends could be identified at these meetings before it was too late for manufacturers to adjust to the new selection. So far, they have not identified any new trends.

The other VRBPAC meeting in May 2015 was about Ebola vaccines. Dr. Daum explained that FDA was interested in VRBPAC's opinion on how to approach licensing Ebola vaccines. The Ebola trial was set up to look at disease as the endpoint, and the question was what to do now that there is no disease. VRBPAC discussed many different issues. There is more than one Ebola vaccine and they are being tested clinically in Sierra Leone and Liberia and in animals. Dr. Daum suggested, in fairness to the FDA, that he is not sure how FDA can choose without disease as the endpoint which Ebola vaccine should be licensed and when without another outbreak. They discussed licensing by the traditional method, licensing by the animal rule, and licensing by the accelerated pathway. VRBPAC did not come up with an official conclusion. If there were a disease endpoint, an Ebola vaccine could possibly be licensed on that basis. The animal rule pathway and the accelerated pathway both require discussion and interpretation by the FDA and post-licensure studies. VRBPAC made some recommendations and comments to FDA. All the Ebola vaccines are different and the markers of protection are different. Some have data that show animals are protected by the animal rule and some have no data. He noted that the FDA will face challenges interpreting the data and making a licensure decision.

In November, VRBPAC will have a meeting about maternal immunizations. He noted VRBPAC meetings are open to others and there is usually a big audience and media presence. Dr. Orenstein suggested that one or more members of NVAC's Maternal Immunization Working Group should attend, and Dr. Daum replied those NVAC members are welcome.

## **NVAC Ex Officio Updates**

### **Agency for Healthcare Research and Quality – Dr. Iris Mabry-Hernandez**



Dr. Mabry-Hernandez reported on recent AHRQ-funded grants. AHRQ funded investigator-initiated research grants on these vaccine topics: 1) Improving immunization rates in young children: a comparative effectiveness trial, 2) Understanding and addressing high rates of refusal of pneumococcal vaccination among African-Americans, and 3) Disparities in HPV vaccine awareness among U.S. parents of preadolescents and adolescents. Dr. Mabry-Hernandez explained AHRQ created the Health Care Innovations Exchange to speed implementation of new and better ways of delivering healthcare. She mentioned an example of service delivery innovation involving a hospital program modeled on their emergency preparedness plan, which features in-unit vaccinations and morning "lockdown" for increasing employee influenza immunization rates. Dr. Mabry-Hernandez encouraged people to look at their website.

#### **Centers for Disease Control and Prevention – Dr. Anne Schuchat**

Dr. Schuchat provided an update on recent work at CDC's National Center for Immunization and Respiratory Diseases. She noted that before the next NVAC meeting, CDC will be releasing the latest data for the NIS-Teen, which is expected at the end of July, and for the NIS for toddlers and the kindergarten entry exemption and immunization coverage data at the end of August.

Since the last NVAC meeting, CDC launched STRIVE—Sierra Leone Trial to Introduce a Vaccine against Ebola—on April 9, 2014. STRIVE is a combined Phase 2 and Phase 3 clinical trial that has enrolled approximately 6,000 healthcare and other frontline workers in Sierra Leone. The trial aims to assess the safety and efficacy of the rVSV-ZEBOV candidate Ebola vaccine and has an immunogenicity component to support alternative pathways to vaccine licensure in the event efficacy cannot be evaluated. The study is being conducted by Sierra Leone's College of Medicine and Allied Health Sciences, the Sierra Leone Ministry of Health and Sanitation, and CDC. In addition to accelerating development of Ebola vaccines for the 2014 and future outbreaks, the study aims to strengthen capacity in Sierra Leone for future research and public health activities.

#### **Department of Defense – COL Margaret Yacovone**

COL Margaret Yacovone reported that the Military Vaccine Agency and Vaccine Healthcare Centers transitioned to DoD's Defense Health Agency. She explained they provide all comprehensive vaccine services, education and training, clinical operations, policy and program management, and vaccine safety and evaluation for all 9.7 million beneficiaries. The DoD is also undergoing an electronic health record modernization, and the contract will be awarded this summer. This modernization will improve robustness for tracking of immunizations, and registry data exchange capabilities. COL Yacovone reported the next generation Smallpox vaccine is under Phase 3 studies, and is actively enrolling and on target. The Japanese Encephalitis awareness program is in its second year to increase awareness of this vaccine and increase vaccination rates for their beneficiaries. The Adenovirus vaccine is wrapping up its Phase 4 studies. In 2011, it was given to all recruits entering basic training. COL Yacovone stated the Adenovirus vaccine shows marked reduction in febrile respiratory illness for all serotypes, mostly serotype 4. For the influenza vaccination program, DoD is partnering with OPM and is now in the second year to increase influenza vaccination rates using the federal employee health benefits program. They provide education and even vaccine delivery for federal employees on military installations. COL Yacovone reported DoD is partnering in working on Ebola vaccine trials. DoD is also participating in the ACIP working group on the Meningococcal B vaccine.

#### **Food and Drug Administration – Dr. Phil Krause**

Dr. Krause, representing Dr. Marion Gruber reported on recent approvals at FDA. Dr. Krause stated FDA approved a new biologics license application (BLA) for Quadracel in March 2015. A single dose of Quadracel is approved for use in children 4 through 6 years of age as a fifth dose in the diphtheria, tetanus, pertussis vaccination (DTaP) series, and as a fourth or fifth dose in the inactivated poliovirus vaccination (IPV) series, in children who have received 4 doses of Pentacel and/or DAPTACEL vaccine. In April 2015, FDA approved BLA supplements for Fluzone, Fluzone High Dose, Fluzone Intradermal, and Fluzone Quadrivalent to update the package inserts to include efficacy data for children aged 6-24 months and adults aged 18-49 years. In April 2015, FDA approved a BLA supplement for HPV Quadrivalent Vaccine, Recombinant (Gardasil) to add a new subsection entitled, "Long-term follow-up studies" to the clinical studies section of the package insert.

Dr. Krause noted the Center for Biologics Evaluation and Research at FDA and the National Institute of Allergy and Infectious Diseases at NIH recently co-sponsored a Respiratory Syncytial Virus (RSV) Vaccine Workshop. The purpose of the workshop was to identify obstacles to RSV vaccine development, discuss approaches to alleviating them, and identify gaps in research that could be addressed to enable vaccine development. Dr. Krause also stated that FDA is participating in the response to the Ebola epidemic in West Africa, and continuing to work with federal partners, the medical and scientific community, industry, and international organizations and regulators to assess investigational products and provide regulatory pathways that may expedite the development and availability of products.

### **Public Comment**

Dr. Orenstein then invited public comment, noting that the comments should be limited to three minutes.

#### **Ms. Erin Fry Sosne, PATH**

Ms. Fry Sosne thanked everyone for continuing to emphasize the international elements of their work through NVAC and NVAC's different working groups. She especially expressed her appreciation for NVAC's work that has implications for low- and middle-income countries. She is looking forward to hearing more about the global immunization report developed several years ago and how those recommendations can come to fruition. She thanked everyone for their work to make the U.S. and the world a safer place.

#### **Ms. Theresa Wrangham, National Vaccine Information Center**

Ms. Wrangham introduced herself as Executive Director for the National Vaccine Information Center. She noted their earlier written comments on NVAC's draft vaccine confidence report and HPV Working Group report are part of the public record. Transparency and communication are necessary to address vaccine confidence. They were disappointed that comments by AAP today did not recognize medical informed consent and the right of patients to delay or decline vaccines or to not rely strictly on the medical home for vaccination decisions. She noted that many sources of credible information on vaccination exist outside of the medical home, and can be used to make vaccination decisions. She commented that risks associated with vaccines are not well understood. Individual susceptibilities and predispositions may increase the risk of injury and death from vaccines, so there can no one-size-fits-all schedule. Ms. Wrangham noted that informed consent refusal statements in use today are often selectively worded and do not inform patients about IOM findings or predict who will be protected and not harmed by a vaccine. Parents are not told that most children who will contract a disease will heal with no complications and enjoy even greater immunity than vaccination. Parents remain unaware of

how to recognize vaccine reaction systems or how to report them. Coercing parents and adults to sign informed consent refusal statements will not inspire trust. NVAC recommendations appear to promote a one-size-fits-all schedule, removal of non-medical vaccine exemptions, and use a very narrowly defined medical exemption. Ms. Wrangham commented, if this is the goal, that NVAC will be seen as supporting violations of basic human and informed consent rights for medical procedures and pharmaceutical products. Investments in new and improved “communication packages” designed to convince and coerce the public will not change minds. Better information is needed because a parent whose child is injured or dies from vaccine adverse effects, has a tragedy equal to a losing a child from a vaccine-targeted disease. Ms. Wrangham stated the goal of public confidence in vaccines will never be achieved until legitimate safety concerns and conflicts of interest are resolved and informed consent and human rights to delay or decline a vaccine are respected. Ms. Wrangham could not comment on NVAC’s efforts on the HPV vaccine today because of time limitations. She stated that HPV is no public emergency and that HPV infections in most children will resolve without complications.

### **NVAC Ex Officio Updates (continued)**

Dr. Orenstein announced that the meeting would continue with additional updates from Ex Officio members.

### **Health Resources and Services Administration / Bureau of Primary Health Care – Dr. Justin Mills**

Dr. Mills reported the Bureau of Primary Health Care (BPHC) is currently finalizing data on childhood immunizations for the 2014 Uniform Data System (UDS). Only preliminary data is available now. Based on the preliminary data for 2014, Dr. Mills noted they saw a slight uptick in the annual percentage of children immunized and they saw an increase of around 1 million more patients (total 7.5 million children, which is around 30%). Dr. Mills announced the finalized UDS data will be available for the September NVAC meeting. Finally, Dr. Mills reported that BPHC recently released a program assistance letter with proposed changes to the 2015 UDS, but they do not foresee any changes to the childhood immunization metric.

### **Health Resources and Services Administration / Division of Vaccine Injury Compensation – Dr. Melissa Houston**

Dr. Houston reported that a total of 633 claims were filed in FY14 under the National Vaccine Injury Compensation Program (VICP), which included a record number of non-autism claims. So far in FY15, 401 claims were filed. There were 317 adjudications in FY15, of which 269 were compensable and 48 were dismissed. To date, awards to petitioners have totaled approximately \$147 million and attorney’s fees and costs have totaled approximately \$12 million. Dr. Houston noted that more data about VICP can be obtained at their website and in the attachments to their report in the meeting materials.

Dr. Houston explained they are developing regulations to make changes to the Vaccine Injury Table. A Notice for Proposed Rulemaking for changes to the Vaccine Injury Table is being reviewed within HRSA. A final rule proposing to add intussusception as an injury associated with rotavirus vaccines was also developed and is currently going through the HHS clearance process.

A Public Readiness and Emergency Preparedness (PREP) Act declaration covering certain Ebola vaccines was signed by the Secretary of HHS on December 3, 2014. Dr. Houston explained that effective February 27, 2015, FDA approved Ebola therapeutics are also covered under the PREP Act. As a result of this declaration, individuals who receive these vaccines or therapeutics and are seriously injured by the approved countermeasure may be eligible to file a claim with the Countermeasures Injury

Compensation Program (CICP). The CICP continues to work with its contractor in developing outreach partnerships. VICP outreach efforts continue to focus on making providers and the public aware of this safety net program.

**Indian Health Service – Dr. Jeffrey McCollum**

Dr. McCollum, representing Dr. Michael Bartholomew provided a quick update on seasonal influenza vaccine coverage among patient populations served by IHS and noted that overall the numbers were largely consistent with the previous five influenza seasons. Beginning in FY16, two new immunization performance measures will be introduced within IHS to track influenza vaccine coverage among children ages six months to 17 years as well as adults over 18 years of age. These two new measures will replace the existing single performance measure that looks only at influenza vaccine coverage for adults 65 years and older. Dr. McCollum stated these two new performance measures will provide better alignment with national guidelines and goals while also providing a more robust and comprehensive assessment about how IHS is performing overall on influenza vaccine coverage across all age groups.

Dr. McCollum summarized IHS efforts at increasing HPV vaccine coverage among adolescents. IHS and CDC recently completed an HPV intervention project involving 10 clinical sites within five IHS administrative areas. After interventions were implemented, all intervention sites demonstrated improved HPV vaccine coverage. Increases in vaccine initiation ranged from 6.4-35.4 % across sites and increases in HPV series completion ranged from 2.2-29.1% across all intervention sites. To put into a national context across IHS, based on data available as of March 31, 2015, 78.5% of eligible patients had received their first dose of HPV vaccine and 49.5% of targeted adolescents had completed the 3-dose series.

Dr. McCollum reviewed recent IHS efforts to limit missed opportunities for vaccination through national implementation of two new automated reminders for providers in the IHS electronic health records system. These automated reminders align with ACIP recommendations. IHS is also developing additional automated reminders for clinical decision support for patients at high risk of vaccine-preventable diseases.

**National Institutes of Health – Dr. Barbara Mulach**

Dr. Mulach reported that NIH awarded grants in April 2015 for investigators to develop tools to detect hospital-associated pathogens, specifically those that are resistant to most antimicrobials. These grants fund nine research projects supporting enhanced diagnostics to rapidly detect antimicrobial-resistant bacteria. Advancing the development of rapid and innovative diagnostic tests for identifying and characterizing resistant bacteria is a key goal of the President's recent National Action Plan for Combating Antibiotic Resistant Bacteria. Dr. Mulach also reported the West Nile Virus Vaccine Clinical Trial was launched in May 2015. With support from the National Institute of Allergy and Infectious Diseases (NIAID) at NIH, scientists at Oregon Health and Science University developed an investigational vaccine for the West Nile Virus. The vaccine was created using a novel peroxide-based platform. This is the first vaccine production system to demonstrate that hydrogen peroxide can inactivate viruses for use as vaccines while still maintaining key structures that trigger the immune system. A Phase 1 trial to evaluate the vaccine is currently underway at the NIAID-supported Vaccine and Treatment Evaluation Unit at Duke University. Dr. Mulach announced that NIH will have a Chikungunya Virus workshop at the end of June.

**U.S. Department of Agriculture – Dr. Donna Malloy**

Dr. Malloy provided a summary of the recent highly pathogenic avian influenza outbreak. Since mid-December 2014, USDA has confirmed multiple cases of highly pathogenic avian influenza (HPAI) along the Pacific, Central, and Mississippi migratory bird flyways. The disease has been found in wild birds, captive wild birds, backyard poultry, and commercial poultry operations. Dr. Malloy stated cases were reported in Arkansas, California, Iowa, Idaho, Kansas, Minnesota, Missouri, Montana, North Dakota, Nebraska, Nevada, Oregon, South Dakota, Utah, Washington, Wisconsin, and Wyoming. The HPAI strains detected recently in these flyways are H5N2, H5N8, and a novel H5N1. To date no human infections have been reported. Dr. Malloy explained HPAI is an extremely infectious and fatal form of avian Influenza that, once established, can spread rapidly from flock to flock and has also been known to affect humans.

USDA is coordinating closely with industry, state partners, and other federal agencies on avian influenza surveillance, reporting, and control efforts. Animal and Plant Health Inspection Service (APHIS) personnel have been deployed as part of emergency response teams. Many more field personnel are responding to the incidents within their affected states and/or conducting outreach and education activities throughout the country. Dr. Malloy noted that with several different viruses circulating in wild birds, it is not unexpected that a new mixed origin virus was identified. Viruses continually mutate and form new combinations with genetic material from similar viruses. This is not unexpected; it is, however, a main reason why it is necessary to continue USDA surveillance efforts for avian influenza in commercial poultry operations, the live bird marketing system, backyard flocks, and in migratory wild bird populations.

Dr. Malloy stated that vaccine strategies are under consideration, and it is a very dynamic situation. She suggested that people check the USDA website for information on outbreaks.

**Department of Veterans Affairs – Dr. Richard Martinello**

Dr. Martinello reported that the VA's National Pharmacy Benefits Management Services, Center for Medication Safety, is currently conducting two vaccine safety surveillance projects. Dr. Martinello explained the VAMedSAFE Program continues to conduct bi-weekly active surveillance on both high dose and standard dose influenza vaccines for potential adverse outcomes, such as Guillian Barre Syndrome, anaphylaxis, and idiopathic thrombocytopenia. The analysis will be concluded in July 2015 and they anticipate submitting a final report to VA later this year. Dr. Martinello reported that the VA continues the collaborative pilot surveillance with the FDA of adverse effects from the Herpes Zoster vaccine in Veteran patients. They are currently conducting validation of potential cases of adverse effects following administration of the Herpes Zoster vaccine. The safety evaluation will be completed by September 2015 and a full report will be submitted to FDA and VA by early 2016.

Dr. Martinello summarized VA's electronic health record improvements. Several immunization IT projects continue improving documentation of immunizations in our electronic medical records, including interoperability. Current efforts are focused on national VA electronic health record updates to provide VA clinicians with greater detail of a patient's immunization history.

The VA Retail Pharmacy Pilot continues, and Dr. Martinello reported that approximately 10,000 veterans received influenza vaccinations through this partnership to date. The VA is exploring expansion to other retail pharmacy outlets for 2015-16, and will continue efforts to improve bidirectional exchange of

health information and data accuracy. He will update NVAC on this pilot program at the September meeting. Finally, he thanked CDC for participating with VA in a national teleconference to their VA healthcare providers on meningococcal vaccines.

### **Adjournment**

Dr. Orenstein thanked everyone and noted it was a very productive session that finalized two very important NVAC reports: Vaccine Confidence Report and HPV Working Group Report. He hoped the two approved NVAC reports could be published as soon as possible. He encouraged NVPO to develop implementation plans for both reports. Dr. Orenstein noted both reports have implications for public sector infrastructure, and they raised issues about whether it needs enhancement. He suggested the next NVAC meeting could include an update on what these two new reports mean regarding the adequacy of public sector infrastructure and whether the resources are there or whether additional resources are needed. Dr. Orenstein noted NVAC could review systems issues related to measles outbreaks. He has asked Dr. Harriman and Dr. Schuchat to provide information about systems issues to NVAC. Dr. Orenstein suggested that international efforts and international control may be another area for discussion at the next NVAC meeting, with respect to having an update on implementation of NVAC's previous global immunization recommendations. He summarized the agenda for the next day. Dr. Orenstein declared the meeting in recess until the following morning at 9:00 a.m.

## **Day 2 – June 10, 2015**

### **Welcome**

Dr. Orenstein called the meeting to order and reviewed the revised agenda for the second day. Dr. Orenstein asked if anyone was present representing the Centers for Medicare and Medicaid Services or the U.S. Agency for International Development, which were the two agencies that did not report yesterday, and there was no response.

### **NVAC Analysis on Role of Vaccines in National Strategies to Combat Antibiotic Resistant Bacteria**

Dr. Orenstein introduced the session on NVAC Analysis on Role of Vaccines in National Strategies to Combat Antibiotic Resistant Bacteria. This session includes presentation of NVAC's Letter to the ASH and draft recommendations, as well as discussion and vote on that letter and draft recommendations.

### **Role of Vaccines in National Strategies to Combat Antibiotic Resistant Bacteria, Dr. Ruth Lynfield, NVAC**

Dr. Lynfield described the timeline of federal efforts in support of national strategies to combat antibiotic resistant bacteria, culminating in the March 27, 2015 release of the National Action Plan to Combat Antibiotic Resistant Bacteria (CARB). She reviewed the five goals of the CARB Action Plan:

- 1) Slow the emergence of resistant bacteria and prevent the spread of resistant infections;
- 2) Strengthen national One-Health Surveillance Efforts to combat resistance;
- 3) Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria;
- 4) Accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines; and



- 5) Improve international collaboration and capacities for antibiotic-resistance prevention, surveillance, control, and antibiotic research and development.

Dr. Lynfield reviewed the role of vaccines in fostering antibiotic stewardship under Goal #1. First, vaccines prevent disease, decreasing the need for antibiotic use (both appropriate and inappropriate). She emphasized that the use of antibiotics drives antibiotic resistance. Second, current vaccines against bacterial pathogens have already demonstrated benefits in reducing transmission of antibiotic resistant bacterial strains in the population. Third, vaccines also decrease unnecessary interactions with the healthcare system, which leads to fewer opportunities for colonization and infection with healthcare associated pathogens. Dr. Lynfield discussed three examples of how vaccines prevent disease, decreasing the need for antibiotic use. The *Haemophilus influenzae* Type b (Hib) conjugate vaccine could play a very important role, because this vaccine has reduced the emergence of antibiotic resistant bacterial strains. The pneumococcal conjugate vaccines (PCV7, PCV13) are important because we had started to see the emergence of antibiotic resistant bacteria strains, especially multiple resistant strains. Dr. Lynfield presented data showing how the pneumococcal conjugate vaccines (PCV7, PCV13) have reduced multidrug-nonsusceptible invasive pneumococcal disease, from 2000-2013, especially for the 0-4 year old age group. The influenza vaccine can have a significant impact, because preventing influenza can prevent antibiotic use due to inappropriate prescribing or due to secondary bacterial infections. Dr. Lynfield concluded by stating that antibiotic stewardship efforts are strengthened by advocating for increased vaccine uptake in communities.

In reviewing Goal #4, Dr. Lynfield provided two examples for how vaccines can support long-term solutions for combating antibiotic resistant bacteria. She explained that having an effective vaccine for Methicillin-resistant *Staphylococcus aureus* (MRSA) would have a significant impact in reducing severe infections and deaths. A vaccine for *Clostridium difficile* would be a cost-effective and cost-saving solution to this estimated \$1-3 billion burden on the healthcare system.

Dr. Lynfield explained that Goal #4 includes Objective 4.5: “Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates and promising vaccines that can reduce the need to treat bacterial infections.” She noted that many analyses have worked on economic incentives for antibiotics. Dr. Lynfield stated that a key question is: will the economic incentives described for antibiotics work for vaccines?

Dr. Lynfield then presented the proposed NVAC recommendations. [A detailed description of all of the proposed recommendations is available in the NVAC report and in the presentation slides.]

### **Discussion and Vote**

Dr. Lynfield noted that next she would review each of the recommendations with the NVAC members and Ex Officio members and Liaison representatives. Dr. Orenstein and Dr. Lynfield referred the panel to NVAC’s draft Letter to the ASH in their notebooks that provided the language to the draft recommendations. Dr. Lynfield asked everyone to read Recommendation #1 and noted she would then invite discussion or questions. Dr. Orenstein stated because there were no comments, they should move to the next recommendation. Dr. Lynfield asked everyone to read Recommendation #2, and there were no comments. Dr. Lynfield then asked everyone read Recommendation #3, and there were no comments. Finally, Dr. Lynfield asked everyone to read Recommendation #4, and there were no comments.

Dr. Orenstein commented that he would like to add a fifth recommendation addressing that NVPO should update NVAC on a regular basis on the status of implementation of these recommendations. Dr. Smith referenced Recommendation #4 and asked Dr. Lynfield whether that would be fundamentally different from the regulatory pathways and clinical trial designs for other vaccines. He asked how that would differ for vaccines that are useful for combating antimicrobial resistance. Dr. Lynfield explained there may be targeted populations rather than application universally for certain vaccines, for example, *Clostridium difficile*. They thought it would be important to consider whether those regulatory pathways would be different.

Dr. Smith asked Dr. Lynfield whether the regulatory pathway would be different from other vaccines, and noted many other vaccines target various populations. Dr. Lynfield commented that some vaccines may target much smaller populations and mentioned, for example, the potential for working on a vaccine for highly resistant gram negatives. She commented that they anticipated different approaches so they thought it was important to include in the recommendations. Dr. Smith asked how it would differ from something like a rabies vaccine. LCDR Valerie Marshall, FDA, commented that the sponsor would need to come to FDA and discuss the regulatory pathway and it would follow the same standards of efficacy and safety as any other vaccine. Dr. Orenstein commented that it is like rabies or more complicated. He mentioned there are economic issues associated with the types of clinical trials expected, compared to other pathogens. Dr. Orenstein suggested that Recommendation #4 is not saying these vaccines are totally unique, but they are encouraging early discussions with FDA for incentivizing development of these vaccines. If clinical trials are needed with efficacy for some of these pathogens, it may be economically a major disincentive to vaccine development. Dr. Smith commented that he thought Recommendation #4 is a little fuzzy in terms of what NVAC is asking for and wondered whether FDA will consider it.

Mr. Hosbach commented that large manufacturers follow the standard procedure for the vaccine R&D process, and he is not sure what NVAC is approving for Recommendation #4. Dr. Lynfield thought Recommendation #4 was an effort to recognize that there may be unique considerations. It may be necessary to determine the endpoints or protective markers. She noted it will be important to recognize that investments in R&D will be challenging for many companies when there will be a limited population for a vaccine. She added that it will also be challenging to develop a clinical trial design for some of these vaccines. Dr. Lynfield emphasized Recommendation #4 was just a recognition that there will be different considerations, although certainly it will be important to develop appropriate safety and effectiveness data for licensing, and also a recognition that there may be complexities with these vaccines.

Ms. Despres commented that she hears smaller companies do not know how to navigate the process, because generally they may not have routine conversations with FDA or be newer to the business. Ms. Despres noted that the process may be challenging for smaller companies, for example, when the requirements for designing clinical trials may be different. Ms. Despres added that smaller vaccine companies often do not find the concept of going in and talking to FDA intuitive, compared to large companies that routinely talk with FDA. She emphasized that NVAC is not suggesting FDA is not responsive to industry. Ms. Despres thought everyone should be having these discussions with FDA because, for example, there may be different kinds of endpoints for these vaccines. She noted this may

be new territory for some of the smaller companies. Dr. Lynfield emphasized that they are highlighting early discussion with FDA.

Dr. Beigi commented that what he thought NVAC is trying to say is to have early discussions with FDA to look at the appropriateness of current regulatory pathways and consider alternative regulatory pathways that could help foster development of these vaccines. Dr. Lynfield replied that Dr. Beigi's summarization was not exactly what NVAC is trying to say. Dr. Lynfield commented that instead they are trying to recognize that different types of clinical trials and considerations might be required. She stated NVAC is encouraging vaccine manufacturers to have that discussion with FDA early, and understand what FDA will be requiring from them. Dr. Lynfield emphasized that NVAC is not suggesting an alternative pathway, because the current regulatory pathways can be used, but instead suggesting early discussions with FDA. Dr. Orenstein commented that NVAC is not saying these vaccines are unique, but just trying to highlight this as an important issue to avoid some companies stopping work on vaccines given what they think might be needed to get a licensure application.

Dr. Doskey, AHIP, commented that the cost effectiveness of these vaccines seemed to be an important consideration based on Dr. Lynfield's presentation. AHIP would like to encourage transparency in R&D efforts, and AHIP would like to foster value pricing and greater competition to improve access and affordability. Dr. Lynfield asked whether Dr. Doskey had any specific language to add. Dr. Doskey stated he did not. He commented that transparency to foster competition is important because one of the problems they have is that competition in many arenas does not really exist, and it would be good to have more competition. Dr. Lynfield wondered whether this transparency issue might instead go under Recommendation #3 under analysis of economic incentives. Ms. Despres noted that challenges to the business model were discussed when developing Recommendation #3, for example, with respect to developing *Clostridium difficile* or MRSA vaccines. Ms. Despres commented that these challenges relate to the broader issue of economic incentives and disincentives to this market.

Dr. Temte suggested looking at the profound effect of measles on non-measles infections. As a pediatrician, he observed that any virus that causes febrile respiratory illness in children is a gateway to inappropriate use of antibiotics. Dr. Temte commented that developing vaccines for these "gateway" infections is also important, and suggested the current prototype is RSV. He explained that most children who get RSV very early in life will receive an antibiotic, which trains parents to expect an antibiotic for a respiratory infection. Dr. Lynfield commented that they agree, and have included RSV in the Letter to the ASH and discuss the indirect effects. She absolutely agreed these issues are critical and this is a major reason that under stewardship they thought vaccines are incredibly important.

Dr. Lynfield stated that she would like to come to a conclusion to take a vote. Dr. Lynfield asked everyone to read Recommendation #3 on analysis of economic incentives and to comment on whether they had any specific language for it. Dr. Doskey, AHIP, suggested that where it says "a more robust and comprehensive pipeline that includes vaccines" consider adding "We encourage the ASH to promote transparency in R&D investments." Mr. Hosbach questioned the intent of Dr. Doskey's addition, and asked whether it was transparency by the government or private industry. Dr. Doskey replied that there is a limited amount of transparency that will come from private industry so he intended it to start with government. Ms. Despres stated that whatever the solution is, such as transparency or delinkage, first it is necessary to determine the problems. She suggested developing a full list of the economic incentives issues, diagnose the problems first, and then look at solutions. Dr. Doskey commented that the current

language on economic incentives appeared to discuss the same idea. Dr. Orenstein asked whether the existing language on incentives in Recommendation #3 is acceptable and stated that evaluation of potential burden will play a major role in economic incentives. Dr. Doskey stated that the current language should cover the issues. Dr. Lynfield asked whether there were any other comments, and there were none.

Dr. Lynfield commented they will review Dr. Orenstein's suggestion for a fifth recommendation. Dr. Gordon, NVPO, typed the new Recommendation #5 proposed by Dr. Orenstein on the screen for everyone to review: "Recommendation #5: The NVAC requests that NVPO provide an annual update on the progress made in supporting the role of vaccines in strategies to combat antibiotic resistant bacteria." Mr. Hosbach asked whether this should be imbedded in Recommendation #2 instead. Dr. Orenstein recommended it be kept separate, to highlight it.

Mr. Rothholz made a motion that NVAC approve the Letter to the ASH and draft recommendations on combating antibiotic resistant bacteria. Dr. Smith and Dr. Viswanath seconded the motion.

- ACTION ITEM: Dr. Orenstein invited formal approval of the Letter to the ASH and draft recommendations on combating antibiotic resistant bacteria. The Committee voted in favor of adopting the Letter to the ASH and draft recommendations (12 in favor, 0 opposed, 2 absent).

After the vote, Dr. Gellin added that NVAC had a long session about antibiotic resistant bacteria at their February meeting, and that the White House was involved. He mentioned their NVAC February meeting was influential for the antibiotic stewardship forum held at the White House several weeks ago. He commented that for febrile respiratory illnesses, there is a heavy emphasis on diagnostics, but that does not discount the need for some emphasis on vaccines.

### **Summary of the National Adult and Influenza Immunization Summit and Implementation of the Adult Standards**

Dr. Orenstein introduced the session on the National Adult and Influenza Immunization Summit.

#### **Summary of the National Adult and Influenza Immunization Summit, Dr. Carolyn Bridges, CDC**

Dr. Bridges provided background on how the National Influenza Vaccine Summit began in 2000 in response to U.S. influenza vaccine supply shortfall, as a partnership between the American Medical Association (AMA) and CDC's National Immunization Program. The goal was to bring together a wide range of stakeholders to solve issues regarding ordering, distribution, communications, and other issues. The summit evolved after AMA ended its co-sponsorship in 2011. In 2012, the Immunization Action Coalition (IAC), CDC, and NVPO, as lead organizations, developed an MOU for the National Adult and Influenza Immunization Summit (NAIIS). The MOU established a formal NAIIS Organizing Committee, which included IAC, CDC, NVPO, and other organizations. Work is conducted throughout the year by working groups, and NAIIS holds in-person meetings periodically. Dr. Bridges explained the goals of NAIIS are:

- Convene adult and influenza immunization stakeholders,
- Facilitate identification of specific actions to be taken by NAIIS members that will lead to improvements in uptake of ACIP-recommended vaccines, and
- Develop and sustain working groups within the NAIIS that meet throughout the year whose goals are implementation of specific actions identified by NAIIS that will lead to improvements

in awareness and uptake of ACIP-recommended vaccines for adults and influenza vaccine for persons of all ages.

Dr. Bridges reviewed the five NAIIS working groups: Patient Education, Provider Education, Access and Collaboration, Quality Measures, and Information for Decision Makers. She noted that all but the Information for Decision Makers working group have federal participants. Dr. Bridges provided a brief overview of the NAIIS May 12-14, 2015 meeting, and noted the overall theme was improving implementation.

In reviewing NAIIS accomplishments, Dr. Bridges described the overall accomplishments as: 1) active engagement in problem identification and mitigation activities by a wide range of partners, and 2) identification and inclusion of best practices on the NAIIS website and highlighting best practices at their annual summit awards. Recent accomplishments of the Patient Education Working Group were: 1) developed key messages and a social media primer in support of NAIIS members and conducted a workshop at the May meetings—will support National Immunization Awareness Month and other observances, and 2) a resource library on IAC's website.

Recent accomplishments of the Access and Collaboration Working Group were: 1) developed and worked with NVAC to publish updated Standards for Adult Immunization Practice in 2014, 2) worked with NVAC to plan actions for 2014-2015 by multiple NAIIS organizations to encourage and implement the Standards, and 3) developed three sets of slides to provide information about adult vaccines and the Standards for providers, the public, and public health professionals. Dr. Bridges also explained that two surveys were conducted of state IIS. The second internet-based survey in 2015 was developed by the NAIIS Access and Collaboration Working Group and led by the American Immunization Registry Association (AIRA).

Dr. Bridges reviewed recent accomplishments of the Provider Education Working Group: 1) serves as a forum for educating, discussing, and exchanging information on key adult immunization issues affecting healthcare providers, 2) reviewed business tools for adult vaccine and identified gaps in knowledge, 3) advocated for a study to determine the true cost of administering adult vaccination in a clinical practice setting, and 4) developed fact sheets and resource lists. Dr. Bridges emphasized this working group found the main gap in knowledge is identifying the actual cost of administering adult vaccines. She provided examples of fact sheets, Medscape pieces, and web page resources to encourage physicians and residents to consider quality improvement projects targeting immunization.

The Quality Measures Working Group also had recent accomplishments. Dr. Bridges focused on their work last year on an IHS and VA project to test the feasibility of implementing an adult immunization composite measure. IHS is developing a maternal immunization performance indicator, which would measure the proportion of pregnant women who received influenza, Tdap, and influenza+Tdap vaccines. Although implementation is planned for FY2016, Dr. Bridges noted some remaining challenges are identifying pregnant women, identifying administration of vaccine(s) during pregnancy, and identifying trimester.

Dr. Bridges presented some recent data that suggest improvements in adult immunization. She also reviewed challenges to progress. The most important for providers are challenges with implementation of immunization programs overall and reported payment issues for providers. Challenges also exist with

communications among providers regarding vaccinations and adult provider access to and reporting to IIS. For the Summit, NAIS resources are limited because they rely on voluntary efforts of participating organizations. Dr. Bridges briefly mentioned several examples of partner activities to implement the Standards for Adult Immunization Practice. She reviewed several slides taken from a recent presentation by Dr. Brian Mittman on implementation of the Standards. Finally, Dr. Bridges briefly reviewed NAIS priority activities for 2015-2016.

### **Discussion**

Dr. Bridges and Dr. Orenstein asked if there were any questions. Dr. Viswanath noted that most of the NAIS discussion appears to focus on providers, but from a health disparities perspective, some patients seldom visit clinics or see a provider. He wondered if that is potentially where the gaps are, and whether any discussions are exploring these issues outside of the clinical systems and providers. Dr. Bridges commented many organizations that have been at the Summit go out into the community, and are taking vaccines to where people are, and have shown that is where you make big improvements. She mentioned an Emory University program that has funded faith-based organizations and had a big impact. Dr. Bridges explained they have focused on providers, because multiple studies have shown a provider recommendation makes the biggest difference in vaccination decisions. If they can get people in to see a provider, that provider recommendation can make a big impact. Dr. Bridges agreed those other community efforts are important in making progress.

Mr. Rothholz added that the NAIS Immunization Excellence Awards program highlights some of those best practices in the community that are getting results. A new partner organization within the Summit, The National Quality Minority Forum, has a database with zip code-level data to look at disparities and vaccination rates and chronic diseases. Dr. Bridges added that many of the large pharmacy chains have worked with nursing schools, pharmacy schools, and medical schools to help provide outreach in the community.

Dr. Gellin asked Dr. Viswanath what strategies he would consider if he wanted to make adult immunization more of a social norm. Dr. Viswanath commented that the focus has mostly been on the influenza vaccine, but we need to look at other adult vaccines. We also need to develop an understanding of all platforms in the community, such as large pharmacy chains. Dr. Viswanath noted that some groups of people who disproportionately suffer from disease do not really get any information about vaccines from any sources, and trying to identify access points for them is a challenge. Community partners appear to be the closest access points for them. Dr. Viswanath stated his three strategy issues are: 1) knowledge, 2) platforms, and 3) access points.

Dr. Orenstein pointed to Dr. Bridges' slide showing preliminary data that only 5% of recent visits to pharmacies included vaccine assessment. He mentioned that he receives his annual flu vaccine at his local pharmacy, and asked if NAIS has any efforts with them. Dr. Bridges explained that representatives from Walgreens and Safeway were at the recent Summit, and were asked about providing vaccine assessments at pharmacies. Both are currently working on ways they can routinize conducting vaccine assessments at their pharmacies. Dr. Bridges noted that the Pharmacy Quality Alliance is also working on some quality improvement initiatives that may help with assessment, and Mr. Rothholz is the co-chair of that group. Mr. Rothholz explained that the Pharmacy Quality Alliance standards require that pharmacists provide vaccine assessments at every encounter, but they have been getting many questions about whether this means every refill or certain other pharmacist interventions with patients.



He noted the annual comprehensive medication review might be a good point for the vaccine assessment. They are now trying to develop some models for pharmacists on how to implement the standard, considering feasibility and potential IT tools. Through the Pharmacy Quality Alliance, they are working on the development of a metric for vaccine assessments at the plan level and the practice level.

Dr. Orenstein commented it is not clear what proportion of adult immunization registries will allow access by pharmacists. Dr. Bridges explained most states that have adult registries allow pharmacists to submit data. Mr. Rothholz commented the bigger problem is that pharmacies were not included under the incentive payments for meaningful use, so it was a slow process to get pharmacies to sign up. One challenge is that the onboarding of pharmacies into IIS has not been supported by sufficient resources. Ms. Ehresmann, AIM, explained that resources are limited in Minnesota so they have had to prioritize adding other providers into their IIS instead of pharmacies. She added this is a very real issue for states and for pharmacists who want to submit data.

Dr. Orenstein asked about performance standards established for IHS and VA, and he wondered about the rewards for good performance or potential consequences for poor performance. Dr. Martinello, VA, stated that in the past the VA has had standards and goals established for certain vaccinations that are measured at the facility level and this may continue in the future. Some individual VA facilities may use provider-level feedback within their own facility, but VA does not do that nationally. Dr. Orenstein asked whether there was any public recognition for VA facilities doing the best job. Dr. Martinello replied that VA providers have been recognized for influenza vaccination in the past, but not for all patient vaccination. Dr. McCollum, IHS, mentioned that IHS reports these data in aggregate nationally. The IHS data is available by site, but IHS does not share site-level data publically. That data is used for quality improvement and performance improvement at the local sites. Dr. Bridges commented that what IHS is doing is effective, because vaccination rates are often three times higher than the U.S. average. Dr. Rawlins added that the VA system works well to get adults immunized and lessons learned should be considered to improve community efforts.

### **NVAC Ex Officio Updates (continued)**

Dr. Orenstein invited the Centers for Medicare and Medicaid Services to report.

#### **Centers for Medicare and Medicaid Services – Ms. Mary Beth Hance**

Ms. Hance, representing Dr. Jeffrey Kelman, noted that CMS had just a brief update. CMS had a call in March 2015 with all of the Medicaid Directors to remind them of the importance of immunizations and the importance of ensuring that CMS maintains a high level of coverage in the Medicaid program. CMS is working closely with their Immunization Service Director colleagues at CDC on this effort. CMS is continuing to work directly with states to encourage prevention activities in general. They are encouraging states to undertake prevention activities related to the managed care programs as well as in the general Medicaid program. CMS is working with state Medicaid programs to better understand their activities and will share any new information later.

#### **U.S. Agency for International Development – Dr. Angela Shen**

Dr. Orenstein noted that no one was present from USAID. There is a written report from USAID in the meeting materials.

### **Congressional Initiatives on Vaccine Innovation**

Dr. Orenstein introduced the session on Congressional initiatives. He introduced Ms. Pfaff and Ms. Fristedt, who are staff on the U.S. Senate Health, Education, Labor, and Pensions (HELP) Committee.

#### **Congressional Initiatives on Vaccine Innovation, Ms. Melissa Pfaff and Ms. Andi Fristedt**

Ms. Pfaff explained that she works with Senator Lamar Alexander (R-Tennessee) and Ms. Fristedt works with Senator Patty Murray (D-Washington). Ms. Pfaff noted they attended primarily to listen to NVAC's thoughts on how to promote innovation in the vaccine space. They will start by providing an overview of their process and what they are working on now in the HELP Committee. In early February 2015, Senator Alexander and Senator Murray, together as the HELP Committee's top Republican and top Democrat, announced a bipartisan initiative to examine the process of bringing medical products from the discovery phase all the way through FDA approval or licensure. This includes the role of NIH and FDA in that process. Ms. Pfaff noted they have all been hearing from constituents, researchers, companies, and others about the importance of maintaining our country's global leadership in biomedical research and medical innovation, and the time was right.

Senators Lamar and Murray announced a series of hearings to examine the discovery and development process and how to better align public policies to support medical innovation while maintaining high standards for patient safety. Ms. Pfaff explained the HELP Committee has held four hearings thus far:

- Continuing America's Leadership in Medical Innovation for Patients (March 10, 2015), with Dr. Collins and Dr. Hamburg to hear from them as leaders of NIH and FDA, respectively, about what they believe are the most pressing issues facing the biomedical industry;
- Continuing America's Leadership: Advancing Research and Development for Patients (March 24, 2015), to hear from outside experts, researchers, venture capital, a CEO, and a think tank, about the issues that they and their colleagues face;
- Continuing America's Leadership: The Future of Medical Innovation for Patients (April 28, 2015), to hear from FDA Center Directors and an NIH Center Director and Institute Director, who provided their perspectives on the challenges and opportunities for biomedical innovation within their respective fields; and
- Continuing America's Leadership: Realizing the Promise of Precision Medicine for Patients (May 5, 2015), to learn more about the President's Precision Medicine Initiative.

Ms. Fristedt explained that in February 2015 Senators Alexander and Murray also announced a bipartisan staff-level working group to look at issues around medical innovation. Initially they brought in a broad range of stakeholders to look at the discovery and approval process and start the path toward working on legislation. For many weeks, they brought in experts from industry, advocacy groups, patient groups, and agencies to educate themselves and their colleagues about work happening across the spectrum of medical innovation. Subsequently, they broke into a number of subgroups to work on specific issues and begin drafting legislation. Ms. Fristedt stated that while the focus of this initiative is largely on NIH and FDA, they are interested in discussing issues across the spectrum of medical innovation and issues related to other agencies the HELP Committee has jurisdiction over.

Ms. Fristedt noted that the House Energy and Commerce Committee approved a bill, H.R. 6 or the "21<sup>st</sup> Century Cures Act." She explained the Senate process is complementary to that, but they are working on a parallel track drafting their own Senate bill on their own timeline. Although they welcome thoughts on elements in the House bill, she emphasized they are not starting with the House bill but

drafting their own Senate bill. Later, the Senate will come together with the House of Representatives to discuss further.

Ms. Fristedt noted the HELP Committee wants to hear NVAC's thoughts about the vaccine space, especially anything that their legislation may be able to address to make progress. She mentioned the HELP Committee held a hearing earlier this year focusing specifically on vaccines and vaccine-preventable diseases. This is an issue the HELP Committee is engaged on outside of this initiative. She mentioned that Dr. Gordon will share their contact information with NVAC members so NVAC can continue sharing their thoughts.

### **Discussion**

Dr. Orenstein asked whether anything impressive regarding vaccines emerged from the hearings. Ms. Fristedt noted that their hearing on vaccines was focused on the measles outbreak at Disneyland. She added it was a bipartisan hearing and every Senator on the HELP Committee at that hearing talked about the importance of vaccines and the importance of reducing vaccine-preventable diseases. Ms. Fristedt stated that vaccines have not been a focus of their hearings about biomedical innovation. There have been a lot of conversations about medical innovation, but not specifically about needs in the vaccine space. Ms. Pfaff commented they heard about problems with clinical trial design and enrollment as well as the product approval process in the hearings, but did not hear specifically about vaccines.

Ms. Despres commented that both Ms. Fristedt and Ms. Pfaff have public health expertise. The challenges of vaccine innovation can be vaccine-specific. Ms. Despres commented that it may be good to discuss the issue of maternal immunization during this session. NVAC's workgroup has identified some of the challenges with maternal immunization. NVAC has discussed challenges in development of vaccines and antibiotic resistance, which may also be good to discuss during this session. Ms. Despres commented that she would welcome any legislative or oversight roles to help make progress.

Dr. Omer commented that NVAC's Maternal Immunization Working Group has looked at how to facilitate development of maternal vaccines. NVAC has found that the legislative efforts that went into facilitating childhood research on vaccines are a good template for some of the issues that need to be overcome to expand and strengthen the maternal immunization platform. Dr. Omer noted that most child mortality happens before the vaccination schedule starts at two months old.

Dr. Omer suggested another topic regarding federal grants as a mechanism to facilitate innovation. While peer review has been useful to ensure the best science is funded, over the years high-risk science has faced hurdles. The structure of the federal grant process is part of those hurdles. Dr. Omer wondered whether there has been any thinking in Congress about facilitating innovation through making the federal grant process more efficient. Ms. Pfaff replied that Congress has looked at efficiency in the federal grant process in terms of how to reduce the administrative burden to have more time to conduct research. They have also discussed high-risk, high-reward science that might have a greater impact, but does not necessarily get funded through the peer review process.

Dr. Beigi noted that NVAC has looked at the issue of what was successful in moving the study of all therapeutic products, not just vaccines but also medications, into the underserved and understudied population of children. He noted that legislative acts were especially helpful in encouraging more

research on children. Dr. Beigi asked whether any legislative efforts were being considered for research on pregnant women. He commented that even more than children, pregnant women have been almost completely excluded from research for all drugs and therapeutics. He emphasized that exposures will occur in pregnant women often inadvertently during pregnancy. Dr. Beigi commented that for many products there is a more thoughtful way to study pregnant women systematically before a drug is approved. Ms. Fristedt replied that Senator Murray would like specific thoughts on issues regarding pregnant women. Dr. Beigi stated that NVAC would provide information.

Dr. Orenstein commented that it is important to conduct a comprehensive review to identify the barriers for vaccine development to foster future legislation to overcome those barriers. There are a range of barriers, from scientific issues that are holding up development of certain vaccines, to vaccines being developed but perhaps not used and discouraging the pharmaceutical industry. He wondered whether it would be helpful to develop a list of vaccines that are needed. Dr. Orenstein noted that NVPO supported the IOM to develop SMART vaccines as a potential strategic ranking tool. He suggested there should be an overall, national list of vaccines needed to stimulate investment in them. He noted that the Bill & Melinda Gates Foundation developed target product profiles to try stimulating investment in certain vaccines. Dr. Orenstein suggested that IOM or other groups could participate in the process of conducting this comprehensive review. Ms. Fristedt commented that was a helpful suggestion.

Mr. Hosbach stated that his industry is pleased that Congress is looking at stimulating innovation and access for vaccines. He commented that placing fixed timelines on ACIP vaccines and inserting manufacturers into the request for making ACIP recommendations, as outlined in the 21<sup>st</sup> Century Cures Act, are not appropriate. Mr. Hosbach emphasized that legislating a timeline for vaccinations is alarming, from his perspective.

Dr. Spika, PHAC, commented they are trying to do something similar in Canada for vaccine innovation, but it is complex. There are a lot of complex and interrelated technologies associated with vaccine innovation. Some vaccines are simpler to develop and others are more complex. Dr. Spika stated that he recently heard at a WHO meeting that Ebola vaccine development has become a priority for two manufacturers, which halted development of all other vaccines in Phase 2 and Phase 3 trials. He wondered if those companies would have made the same corporate business decision on vaccine development priorities if an overall vaccine list existed to identify vaccines needed based on prioritization from a public health perspective. Dr. Orenstein commented that the SMART vaccines tool could play a role in helping to generate those public health priorities.

Dr. Temte, ACIP, stated that the House bill forcing our hand on timelines for ACIP-recommended vaccines is a huge problem. He hoped the Senate bill would take this into consideration. The House bill's section on evaluation asking for consistency among ACIP working groups is also problematic. He commented that ACIP's working group process was already designed to foster the transparency and consistency that is important in evaluating evidence.

Dr. Daum, VRBPAC/FDA, commented that Congress has undertaken a huge issue and concerns exist about which vaccines are being developed and which are not. NVAC thinks there must be some consideration of what vaccines should be developed ahead of others. Dr. Daum suggested that some kind of body needs to be formed to look at what vaccines we need that we do not have, and who will develop them. He noted there are a lot of players and a lot of moving parts to the vaccine industry, and

if any part collapses then we could have a shortage. Congress should act to prevent possible problems of vaccine shortages. Dr. Daum suggested we need a comprehensive list of which vaccines need to be developed and what the barriers are for each vaccine. Consideration of the scientific issues is also very important. Dr. Daum suggested we need to outline the steps for all the players and he emphasized they must all cooperate to develop those vaccines or we need a new system.

Dr. Orenstein commented that another issue in terms of incentivizing vaccine development is the delivery side, including market share, and getting high vaccine uptake to get the benefits of a vaccine. Problems have occurred with some vaccines recommended for adults not getting use or uptake. Mr. Hosbach noted that one great example is what happened after the influenza summit. The vaccine manufacturers' capacity to develop influenza vaccine doses increased significantly after 2000. There was stimulation of the market and good policy involved and appropriate valuation of the products' return on investment to begin innovation.

Dr. Orenstein asked if Congress was putting any focus on global health with regard to the need for vaccines. He provided the examples of vaccines that do not require temperature stability or delivery through a needle and syringe. Ms. Fristedt noted they were limited somewhat by the jurisdiction of the HELP Committee, which focuses on HHS agencies, but there is some interest in global issues. Ms. Pfaff commented that their primary focus is domestic, but she added that the examples of innovative vaccine delivery devices provided by Dr. Orenstein could have U.S. applications.

Dr. Smith commented that policy should be driven by data, but currently there are problems with immunization data. He provided three examples to illustrate the problem. As the first example, Arkansas has data showing the lowest childhood immunization rates, but the way Arkansas is collecting data through phone surveys may lead to unreliable data. As another example, the questions we are asking adults during contact investigations after measles outbreaks are not a reliable way to obtain information on their childhood immunizations. As a final example, if asked, he could not readily remember the exact dates for some of his own child's immunizations. Some states have an IIS, but they vary in quality and have little interoperability among states. Dr. Smith suggested that a national IIS or developing IIS with interoperability to allow states to exchange data might be helpful to obtain reliable real-time data about immunization status for patients and populations. He noted that NVAC has already discussed both technological and legal barriers that exist. Dr. Smith emphasized this problem cannot be solved at the state level, but suggested it could be addressed at the federal level. Ms. Fristedt noted that the HELP Committee chairs are thinking about Health IT.

Dr. Orenstein stated that one of the questions is whether resources are adequate to facilitate vaccine discovery or vaccine development and delivery. He suggested it may be possible to create a targeted vaccine development fund that HHS could use as dedicated resources for this purpose. For a revenue mechanism, he suggested increasing the existing tax on every vaccine dose administered.

Ms. Amy Pisani, Executive Director of Every Child by Two and a former NVAC member, came to the microphone and noted she had met with Ms. Fristedt and Ms. Pfaff earlier and had brought up several of NVAC's recent reports and recommendations. She suggested providing NVAC recommendations from their recent reports to the HELP Committee. Dr. Orenstein asked Dr. Gellin if NVPO could send the NVAC recommendations to the HELP Committee. Ms. Despres emphasized it would be more helpful to specifically identify those recommendations where there is a role for Congress. This could be an

oversight role and/or a legislative role. Ms. Despres suggested that first NVAC should distill the actionable items for Congress from the NVAC reports. Dr. Orenstein asked the NVAC Working Group chairs and co-chairs to identify those NVAC recommendations that might have implications for Congressional action. Ms. Pfaff mentioned that Dr. Gordon had offered to gather ideas or thoughts from NVAC members and send them to Ms. Pfaff and Ms. Fristedt. Dr. Orenstein encouraged individual NVAC members to write to Dr. Gordon at NVPO with their ideas on potential ways that Congress could help in incentivizing vaccine innovation.

Ms. Pfaff and Ms. Fristedt stated they would like to hear about ideas related to NVAC recommendations. However, because these Congressional activities are an ongoing process, Ms. Fristedt recommended that ideas or thoughts be sent sooner rather than later. Dr. Gellin thanked Ms. Pfaff and Ms. Fristedt for attending and asked how NVAC could be most helpful in providing information. Ms. Pfaff noted that their areas of interest focus on examining the process of bringing products from the discovery phase through FDA approval or licensure. They are also interested in whether we need to align federal policies to make this process more efficient or effective. Ms. Fristedt noted that sometimes it is not obvious what relates to innovation, so the HELP Committee has an open mind about what issues to think about regarding innovation. Dr. Orenstein asked whether there were any other comments, and there were none. Dr. Orenstein thanked Ms. Pfaff and Ms. Fristedt for attending the NVAC meeting. He again encouraged NVAC members to write directly to Dr. Gordon with their thoughts and ideas, and encouraged NVAC chairs and co-chairs to look through their approved NVAC reports for their recommendations that might benefit from Congressional action to seek better implementation.

### **Update on the National Adult Immunization Plan**

Dr. Orenstein introduced the session on the National Adult Immunization Plan.

#### **Update on the National Adult Immunization Plan, Lt. Maggie Zettle, NVPO**

Lt. Zettle explained the Draft National Adult Immunization Plan (NAIP) is intended to facilitate coordinated action by federal agencies. It established four key goals, which are:

- Strengthen the Adult Immunization Infrastructure,
- Improve Access to Adult Vaccines,
- Increase Community Demand for Adult Immunizations, and
- Foster Innovation in Adult Vaccine Development and Vaccination Related Technologies.

She briefly described several activities involved in development of the Draft NAIP, including an environment scan of the literature, a survey to generate feedback on possible plan priorities, eight focus groups, and one-on-one meetings with thought leaders.

Lt. Zettle noted the Draft NAIP was made available for public comment from February 7, 2015 to March 23, 2015. They received 5,496 comments from the public and 18 comments from professional organizations. Over 4,000 comments were directly related to mandatory vaccinations. However, there is no language in the Draft NAIP on mandatory vaccines. Another theme of the public comments was to further prioritize objectives, strategies, and the populations. Lt. Zettle noted the Draft NAIP contains a list of strategies and many are interdependent. She stated that they will review information on alternative financing mechanisms from the public comments on resources and funding.



Lt. Zettle quickly presented the Draft NAIP's goals and objectives. She emphasized that to increase community demand for adult immunizations, they want to educate and encourage both individuals and healthcare professionals. With respect to innovation, they want to focus on developing new vaccines and improving the effectiveness of existing vaccines. Technological advancement is also important.

Lt. Zettle explained that inclusion of indicators is a key element that distinguishes the Draft NAIP from previous efforts. Each goal has measureable indicators and they will be reported annually. Goal #1 has six indicators to strengthen the adult immunization infrastructure, and she read the first three of them. The first three indicators for Goal #1 are: adult vaccination coverage levels for HP2020 measures, racial/ethnic disparities in adult vaccination coverage for HP2020 measures, and percentage of surveyed primary care physicians who record information on adult immunizations in a state or regional IIS. Goal #2 has three indicators to improve access to adult immunizations. Goal #3 has five indicators to increase community demand for adult immunizations. Goal #4 has two indicators on vaccine development.

Lt. Zettle summarized the next steps. They hope to publish the next draft of NAIP by the end of this year. The Adult Immunization Task Force will be charged with implementation of the final plan, and they will be building this task force soon.

### **Discussion**

Dr. Orenstein asked Lt. Zettle if she needed input on any specific issues from NVAC members, and she replied that she had heard from most of them already and thanked everyone. Dr. Orenstein asked if there were any comments. Dr. Viswanath questioned why indicators for Goal #1 focused only on racial and ethnic disparities in adult vaccine coverage, and why inequality related to socioeconomic status was not included. He wondered why the indicator was so narrowly defined, but then noted there were multiple indicators of inequality or disparity. Dr. Smith commented that geography is important too. Dr. Gellin explained that although several hundred indicators were suggested initially, NVPO must be able to measure indicators and have ongoing data systems to use as a baseline and continue to monitor over time.

Dr. Mouton asked whether the Draft NAIP addressed immunization of older adults in long-term care and similar facilities. Lt. Zettle explained that older adults are not in their indicators but are part of their sub-objectives, which she did not include on her slides. Dr. Mouton emphasized it is important for NAIP to include indicators related to older adults in long-term care and assisted living facilities. Lt. Zettle will provide him information about that specific sub-objective later. Dr. Mouton commented it may be helpful to start paying attention to the low uptake for some vaccines for older adults as part of this plan. Dr. Gellin mentioned that the NAIP will not be completed in five years, but will continue beyond and it is being phased along with other NVPO activities over the next decade.

### **Public Comment**

Dr. Orenstein then invited public comment, noting that the comments should be limited to three minutes. No commenters were present at the meeting or on the telephone.

### **Adjournment**

Dr. Orenstein noted the NVAC members accomplished getting three reports approved at the June 2015 NVAC meeting. He outlined four action items that will move these accomplishments forward:

- 1) NVAC's Vaccine Confidence Working Group and to some extent the HPV Working Group should address concerns about the adequacy of resources and infrastructure for implementation, and NVAC should get an update at the next meeting on implementation of the recommendations in NVAC's infrastructure report;
- 2) NVAC should review concerns about global immunization, specifically how much and whether or not NVAC's recommendations on global immunization are being implemented;
- 3) Presenters during the 2015 Measles Outbreak Session should bring up any systems issues where NVAC might contribute to preventing future measles outbreaks; and
- 4) Given the extensive discussion of Congressional initiatives on vaccine innovation, he asked NVAC members to send their thoughts and ideas on how to overcome barriers to vaccine innovation to Dr. Gordon, and he will also ask Dr. Gordon to send recent NVAC reports to working group co-chairs to review those reports for recommendations to identify which might benefit from Congressional action and identify any potential specific actions.

Dr. Gellin noted that the Vaccine Confidence Working Group focused on children, and asked Dr. Viswanath whether any other sectors of the population are relevant. Dr. Viswanath explained other issues kept coming up in their working group, but the consensus was to focus their first phase on childhood vaccines. Dr. Viswanath commented that if the working group continues and shifts focus to other areas, then NVAC should add new members. He also mentioned if the Vaccine Confidence Working Group continues, they should work together with other working groups with similar charges. Dr. Mouton agreed and emphasized that the issue of older adults and immunization is important, especially the issue of decision-making using surrogates. Dr. Orenstein noted another assignment is that the Vaccine Confidence Working Group should look at the steps necessary to address adult immunization.

Dr. Orenstein mentioned that Dr. Temte will be completing his service as ACIP Chair soon, and will be missed at NVAC. He mentioned that Dr. Martinello is leaving the VA and thanked him for being helpful to NVAC on a variety of VA-related issues. Dr. Orenstein commended the staff at NVPO for their efforts on the meeting and the NVAC reports. Dr. Orenstein adjourned the meeting.

#### **List of Ex Officio Member and Liaison Representative Abbreviations**

ACCV	Advisory Commission on Childhood Vaccines
ACIP	Advisory Committee on Immunization Practices
AHIP	America's Health Insurance Plans
AHRQ	Agency for Healthcare Research and Quality
AIM	Association of Immunization Managers
ASTHO	Association of State and Territorial Health Officials
BPHC	Bureau of Primary Health Care (under HRSA)
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
DoD	Department of Defense
FDA	Food and Drug Administration
HRSA	Health Resources and Services Administration
IHS	Indian Health Service

NACCHO	National Association of County and City Health Officials
NIH	National Institutes of Health
PAHO	Pan American Health Organization
PHAC	Public Health Agency of Canada
USAID	U.S. Agency for International Development
USDA	U.S. Department of Agriculture
VA	Department of Veterans Affairs
VICP	National Vaccine Injury Compensation Program (under HRSA)
VRBPAC	Vaccines and Related Biological Products Advisory Committee