National Vaccine Advisory Committee (NVAC)
June 3-4, 2008

Meeting Minutes

Meeting Overview

The Committee heard a full series of reports from Working Groups and industry professionals over the two day session. NVAC unanimously approved the Adolescent Vaccination Recommendations for publication, with the exception of the financial recommendations, which will be voted on at the September meeting in conjunction with the Vaccine Finance Working Group recommendations. The Committee had thoughtful, engaged, animated discussions covering a host of issues throughout the two day conference, including a discussion of its statutory charge to provide a strong foundation for the transition to new federal administration in the coming months. The first day of the meeting featured the vote on the adolescent recommendations, reports from the Vaccine Financing Working Group and Vaccine Safety Working Group, as well as presentations on the Vaccines for Children's (VFC) pediatric vaccine stockpile, Immunization Information Systems, and the Healthcare Worker Influenza Immunization Initiative. In addition to reports from agency, department, and stakeholder liaisons, the second meeting day featured a progress report on Vaccine Supply as well as an industry panel on that topic. Additionally, there were presentations on global polio eradication, priorities for strategic initiatives for vaccine research, and an update on revising the National Vaccine Plan. An underlying theme of many of the discussions was the need for strategic outreach and publicity to better inform the diverse public, private, and professional immunization stakeholders about NVAC's activities, work group recommendations, and attentive due diligence regarding a full breadth of vaccine and immunization issues in accord with NVAC's statutory charge.

Committee Members in Attendance
Guthrie S. Birkhead, MD, MPH - *Chairperson*
Jon R. Almquist, MD
Richard D. Clover, MD
Cornelia Dekker, MD
Jaime Fergie, MD, FAAP
Lance K. Gordon, PhD
Calvin Johnson, MD, MPH
James Mason, MD, MPH
Marie McCormick, MD, ScD
Trish Parnell
Andrew Pavia, MD
Laura E. Riley, MD

Executive Secretary
Bruce G. Gellin, MD, MPH, Director, National Vaccine Program Office (NVPO)

NVAC Ex Officio Members
George Curlin, MD, National Institutes of Health (NIH)
COL Renata Engler, Department of Defense (DoD)
Geoffrey Evans, MD, Health Resources and Services Administration (HRSA)
Rear Admiral (USPHS) Anne Schuchat, MD, Centers for Disease Control and Prevention (CDC)
Ronald O. Valdiserri, MD, MPH, Department of Veterans Affairs (VA)

Liaison Representatives
Alan Rosenberg, MD, American Health Insurance Plans (AHIP)

Committee Members Absent
Sharon Humiston, MD, MPH
Lisa Jackson, MD, MPH
Charles Lovell, MD, FACP
Christine Nevin-Woods, DO, MPH

Day 1 – June 3, 2008

Opening Session - Dr. Gus Birkhead

NVAC chairman, Dr. Gus Birkhead welcomed Committee members and public participants. This was Dr. Birkhead's first meeting as NVAC Chair. He began the meeting with a presentation of the statutory basis for the National Vaccine Program which is contained in Title XXI of the Public Health Services Act (PHSA). The Assistant Secretary for Health is the Director of the National Vaccine Program. In particular, Dr. Birkhead discussed section 2105, which includes the charge to NVAC to: 1) recommend ways to encourage the adequate supply of safe and effective vaccines; 2) establish research priorities and other measures to enhance the safety and efficacy of vaccines; 3) assist NVPO on the implementation of PHSA Sections 2102 and 2103; and 4) identify the most important areas of government and non-government cooperation in implementing PHSA Sections 2102 and 2103 and report these findings to the NVPO on an annual basis.

Dr. Birkhead's remarks were followed by a productive discussion; then Dr Birkhead stated that he believes the Committee is prepared to step up to meet its charge. In particular, NVAC will be taking a hard look at its responsibility to ensure that the National Vaccine Program performs as directed in its statute. Dr. Birkhead then summarized the current activities of NVAC before proceeding with the day's agenda. As the first order of business, Committee members unanimously approved the February 4-5, 2008 NVAC meeting minutes.

Welcome - Dr. Bruce Gellin, Executive Secretary, NVAC

Dr. Gellin presented an historical and prospective overview of HHS's commitment and NVPO's activities to support NVAC in its mission to assure vaccine safety and availability. New staff are being hired, and a comprehensive historical and prospective evaluation of NVAC activities and recommendations has been planned.

Report from the Adolescent Working Group: Vote on Recommendations - Dr. Gary Freed

In response to the Assistant Secretary for Health's request that NVAC formulate recommendations to increase adolescent vaccination rates, the Adolescent Working Group has developed 3 papers. Two papers have already been approved by NVAC and will be published in American Journal of Preventive Medicine in August 2008. The Adolescent Working Group requested approval of the third paper, entitled *Adolescent Vaccination: Recommendations from the National Vaccine Advisory Committee*.

The draft report and recommendations have been vetted in a number of settings and presentations have been made to diverse constituents, the Finance Working Group, and the public since it was first presented to NVAC at its February 2008 meeting. The key content and policy areas that are addressed in the report are as follows:

1. Venue/Healthcare Utilization
2. Consent
3. Communication/Public Engagement
4. Financing
5. Surveillance
6. School Mandates

The Adolescent Working Group Recommendations were unanimously approved by NVAC (*final approved recommendations will be posted to the NVAC website*). A vote on the financial recommendations will follow at NVAC's September meeting in coordination with the discussion of the Vaccine Financing Working Group's recommendations.

Discussion

In the ensuing discussion, there were comments about the balance of teen consent versus parental consent and privacy issues, as well as the complexity of differing state regulations. Dr. Freed and others concurred that the 'missing link' for every NVAC approved action plan was a need for an implementation group to assure successful coordination and implementation in order to address emerging issues. It was agreed that implementation issues would be discussed at subsequent NVAC meetings.

Report from the Vaccine Financing Working Group (VFWG) - Presentation of Draft Recommendations - Dr. Walter Orenstein

Dr. Orenstein summarized the NVPO and VFWG co-hosted stakeholders' meeting that was held on April 29-30, 2008 in Rockville, MD. The meeting was held to discuss the draft Vaccine Finance White Paper and to solicit comment regarding draft recommendations and conclusions. Forty-seven stakeholder groups were represented at the meeting. Following the stakeholders' meeting, the VFWG conducted a survey among selected participants and speakers on their views of the 32 draft conclusions and 27 draft recommendations contained in the document. In all, 20 of the 53 constituents responded, so the information is informative, but by no means conclusive.

Dr. Orenstein briefly reviewed the WG's previous work on why there is a crisis in the financing of vaccinations with the number of vaccinations increasing from 10 to 16 in the last decade, and the cost increasing 10 fold. The last time major changes were made to the public vaccine financing system was in 1993. At that time, there was a resurgence in measles' cases that garnered substantial media attention. Currently, the incidence of vaccine-preventable diseases is at or near an all-time low. The public has not yet realized the benefit of the morbidity and mortality that is preventable with the broad adoption of vaccines recommended for use since 2000. Those working in this area see a looming crisis, particularly with the newer vaccines; however, it is unclear whether this is perceived as a crisis outside of medical circles.

Discussion

A lively discussion followed as Dr. Orenstein presented each of the 27 recommendations which are contained in the separate summary report. (These recommendations will be posted on the NVAC site: http://www.hhs.gov/nvpo/nvac/reports.html). Committee members asked clarifying questions. There was some agreement on not focusing on state-by-state approaches to solve the financing problem but, instead,

to seek solutions at the national level. The Financing Working Group will be meeting with the Adolescent Vaccine Working Group to consider proposed finance recommendations regarding adolescent vaccination in the broader context of the Finance Working Group.

Dr. Laura Riley indicated that the American College of Oncologists and Gynecologists (ACOG) had recently conducted a survey on the barriers to performing vaccinations in OBGYN offices; the results of this survey may provide some interesting insights. Dr. Riley will try to get approval in order to share the results with NVAC.

In response to a discussion about the need to get insights into the political dynamics on vaccine issues from constituent, legislative, lobbying, and congressional perspectives for the September meeting, Dr. Calvin Johnson offered the assistance of the Association of State and Territorial Health Officials (ASTHO) staff. These inputs will hopefully enable NVAC to better tackle the issues and solidify recommendations during the September meeting when a vote will be taken.

This session attracted a number of comments from members of the public in the audience, largely state and non-profit healthcare organizations that were concerned about vaccine mandates and funding issues, including the fact that they are over-extended on funding gaps and policy issues.

The VFWG will continue to meet to develop a final set of vaccine finance recommendations for the Committee to consider and to vote on at the September meeting.

Immunization Information Systems - Motivating Providers to Participate - Dr. Alan Hinman

In February, 2008, NVAC and NVPO sponsored a meeting of stakeholders to address enhancing participation in Immunization Information Systems (IIS). As called for in the IIS Progress Report approved by NVAC in 2007, objectives of the meeting were to: deliberate the pros and cons of legislative and other approaches to increase provider participation in an IIS, deliberate the pros and cons of provider performance incentives based on the completeness of immunization data available in an IIS, and develop a statement noting the value of IIS and urging financial support for IIS. More than 60 persons participated in the meeting, which included individual and panel presentations as well as discussion groups addressing the three major issues – regulatory approaches, provider incentives, and financial support for IIS.

The conclusion of the diverse stakeholders was that participation in IIS was a public health imperative, and all that all people and all providers should participate. The consensus was that immunizations should be a reportable event, across a person's lifespan. Improvements are needed in the ability to share information across jurisdictions, from registry to registry as well as individual queries across jurisdictional lines. Although the Office of General Counsel (OGC) in the Department of Health and Human Services was not optimistic about the possibilities, it was recommended that a national approach be undertaken to try to alleviate the problem of having to have 50 x 50 memoranda of understanding (MOUs) between the states. OGC did not, however, specify what state laws should be passed to make immunizations reportable. In the future, immunization information systems should be interoperable with electronic health records (EHR). The ultimate goal is to have real-time, two-way exchange of information**.**

With respect to policy and regulatory approaches, it was recommended that the Family Educational Rights and Privacy Act (FERPA) should be reinterpreted to remove barriers to sharing information between schools and immunization information systems.

Physicians felt that the greatest participation incentive was to make it cost-neutral and easy to participate. Eliminating double data entry would be a really good incentive.

Other topics discussed included privacy issues; who retains/assumes ownership of the patient information, and how to safeguard the information, yet ensure compliance. How to have a national system without imposing increased costs and labor burdens on public and private organizations and physicians offices for maintaining data were also addressed as factors. The barriers are policy and procedural. Another challenge is that there are discrepancies in reported immunizations. Immunization registry coverage reports are usually provide lower estimates than what is reported in the National Immunization Survey (NIS), perhaps because the registry only counts valid, properly administered doses.

With respect to financial support, stakeholders felt that a dedicated, sustainable federal funding source is essential. Currently Vaccine for Children (VFC) funds and 317 funds are the most available. VFC operational funding is now providing more than half of state funding for immunizations. The recommendation is that VFC and 317 should be enhanced to provide more financial support.

Discussion

Dr. Riley and Dr. Almquist voiced desire for an interoperable system that would pre-populate data fields, and automatically generate immunization records and billing records, without extra work. Dr. Hinman indicated that technology is not the barrier.

The US is lagging behind other countries in implementing EHR and will have great difficulty achieving the president's goal that every American must have electronic medical record by 2014. The American Academy of Family Physicians has a stated goal of 50% utilization of EMR - they are currently at 37.5%. Pediatricians have even a lower rate.

The next steps, according to Dr. Hinman are for NVAC to discuss the findings, conclusions and recommendations and subsequently endorse them and recommend them to the Assistant Secretary for Health (a vote will be scheduled at the September NVAC meeting). NVPO and NCIRD/CDC would then prepare an action plan which would be implemented by NVPO and CDC.

Dr. Hinman noted that NVAC has repeatedly recommended that there should be a 5-year $50 million/year grant program to support IIS development and implementation. That recommendation has never made it past the Assistant Secretary for Health due to other priorities and budget constraints. Dr. Hinman thought that the ability of NVAC to make its recommendations public was important so that the recommendations could have significant impact even if they did not fit within a particular administration's priorities.

<u>Update on Vaccine Stockpiles - Dr. Gregory Wallace</u>

Dr. Wallace stated that the current stockpile targets would cost over $2 billion if fully funded, which is equal to what CDC purchases yearly on routine vaccines. Currently, there are over $500 million dollars of vaccines in the stockpile. The stockpile is part of the Vaccine for Children (VFC) legislation. He noted that there are now two combination vaccines that are at very low levels. Combination vaccines will be a complicating factor for stockpiles in the future.

Changing market conditions and market share will potentially lead to vaccine loss. The goal is to maximize the utility in responding to changing markets and supply issues. This makes management and insurance, avoiding wasting vaccines, and vaccine recommendations a major challenge, particularly with combination vaccines. Storage and rotation is also a major issue for maintaining viable vaccines.

Dr. Wallace introduced a preliminary model, which he presented to NVAC, to get feedback on the general appropriateness and other variables to include. An updated model with inputs will be presented at the September meeting for feedback. Subsequently, we will run the model up the chain at CDC before it is presented to Office of Management and Budget (OMB). Eventually, hopefully by the end of the year, there should be the first target recommendations for the U.S. stockpile for OMB, based on plugging in variable scenarios and including risk tolerance.

The purpose of the model is to have transparent inputs and assumptions that can be updated when new data are available or when policy decisions are made. The model should be able to accommodate policy decisions to cover the worst case scenario planning. The model should explain the costs and disease risks of any proposed policies with regard to stockpiling specific vaccines. The model will give decision-makers the ability to change assumptions, or to make tradeoffs in shortages and risk tolerance, and see the implications. This model may also help other countries who have expressed an interest in establishing stockpiles.

Discussion

Dr. Phil Hosbach from Sanofi Pastuer offered the following manufacturer's observations:

1. It may be prudent to include manufacturers among the subject matter experts.
2. Manufacturing vaccines is complex, with long lead times in scheduling and procurement. Once the production run is completed it is not always possible to schedule another production run immediately. Adding additional production capacity or adding another manufacturer are solutions to be considered when facing a potential shortage.

Dr. Hinman and RADM Schuchat commented that the model needs to accommodate qualitative factors that impact public health and vaccination policy. Dr. Wallace indicated that the model is flexible enough to accommodate such variables

Report from the Vaccine Safety Working Group - Dr. Andy Pavia and Dr. Dan Salmon

The goals of the newly formed Vaccine Safety Working Group are to undertake a scientific review of the draft 5-year Scientific Agenda of the Centers for Disease Control and Prevention Immunization Safety Office (ISO). Through this review, the Working Group will advise on the appropriateness and prioritization of research topics.

Under the leadership of Dr. Andy Pavia, NVAC member, and Dr. Dan Salmon, NVPO staff, an 18-member team has been formed. It is comprised of NVAC members, consumer representatives, and experts spanning a broad cross-section of scientific, medical, legal, international, and immunization specialties.

The Vaccine Safety Working Group's first meeting was held on April 11th. The agenda included vaccine safety research and capacity activities that are part of ISO's mission, within its ability to lead, and achievable within the next 5 years, given CDC resources and infrastructure. Dr. Pavia will present an update of the Working Group's progress at NVAC's September meeting.

The ISO Scientific Agenda includes 30 research items within four research areas:

1. Specific vaccine questions
2. Vaccines and vaccination practices
3. Special populations
4. Clinical outcomes

The Agenda also describes enhancements to ISO's capacity to carry out its mission in the following areas:

1. Infrastructure for Vaccine Safety Surveillance: Vaccine Adverse Event Reporting System (VAERS)
2. Infrastructure for Vaccine Safety Surveillance and Research: Vaccine Safety Datalink (VSD) Project
3. Epidemiologic and Statistical Methods for Vaccine Safety
4. Laboratory Methods
5. Genomics and Vaccine Safety
6. Case Definitions, Data Collection, and Data Presentation for Adverse Events Following Immunization
7. Vaccine Safety Clinical Practice Guidance

Following completion of the first charge, described here, the Working Group will undertake a formal review of the current federal vaccine safety system and develop a White Paper describing the federal infrastructure needs to fully characterize the safety profile of vaccines in a timely manner, reduce adverse events whenever possible, and maintain and improve public confidence in vaccine safety.

Discussion

NVAC members strongly supported the need and plans for public engagement. A long discussion ensued about the manner in which HHS and NVPO should be involved in spearheading this public engagement initiative. There has been success working with Keystone Center, a private group specializing in dispute mediation, to conduct interactive town hall meetings to exchange ideas and promote discussion among federal partners, interested stakeholders, and the general public. This is an HHS priority; thus, plans are underway.

COL Engler remarked about the special needs of women. She shared DoD's initiatives to advance immunization research that could also provide insight into vaccine safety for the civilian population.

Dr. Pavia clarified that it is beyond ISO's scope to study the military population. Furthermore, RADM Schuchat indicated that CDC has collaborated with the VA and DoD on numerous occasions. Dr. Rosenberg mentioned the FDA's Sentinel Network, and how advantageous it would be to build concurrent rather than separate databases/systems. It is likely that many of these issues will be examined through the second charge of the Working Group when the federal vaccine safety system will be assessed.

Dr. John Iskander from ISO remarked on the value of the NVAC Vaccine Safety Working Group's review of the ISO Scientific Agenda for setting research priorities. "Someone should be able to look at a study and understand why that study was done, as opposed to a different study. Our focus needs to be on doing the science right. But people should be able to ask, "Are you doing the right science?' That is the role of the working group in making the recommendations. So 5 years down the road, you can ask me, 'Why was this study done instead of that study?' You should be able to get a clear answer."

<u>Healthcare Worker Influenza Vaccination Initiative - Dr. Donald Wright</u>

Dr. Donald Wright addressed facts and myths surrounding healthcare worker influenza immunization rates. Each year, between 5% and 20% of the U.S. population is infected with seasonal influenza. There is a greater amount of morbidity and ultimate mortality associated with influenza than the public realizes; in fact, annually, over 200,000 people are hospitalized with influenza, and 36,000 people die of the illness.

The most vulnerable population is nursing home patients. Once influenza enters a nursing home, the attack rate is very high, ranging from 25% to 60%, with a high mortality rate incidence (10% to 20%).

Therefore, clearly immunizing healthcare workers, which would in turn protect the patients, is a high priority.

Although they know the risks to themselves and their patients, on average, 60% of healthcare workers are not likely to get an immunization against seasonal influenza. The rate of compliance in facilities is typically in the 38% to 42% range. The reasons why the majority of health care workers are reluctant to get immunized include: 1) concerns about vaccine safety and potential side effects (e.g. "the vaccine will give me the flu"); 2) ignorance about risks of influenza or their vulnerability to getting disease; and 3) a fear of needles. Data suggest that typically between 7% and 20% of non-immunized health care workers had serologic evidence that they had contracted influenza. However, 50% had no symptoms of the disease and were unaware that they were sick, but were able to transmit infection to patients.

HHS has created a task force in order to determine what could be done to increase the rate of immunization for seasonal influenza among healthcare workers. An inter-agency work group was established to view ways of increasing vaccine coverage both within HHS as well as with external partners. Each agency within HHS was asked to develop its own strategy to increase vaccine rates. Since they serve different populations, a targeted approach was thought likely to be more effective. While progress has been made since the late 1980s when only about 10% of healthcare workers were vaccinated against influenza, there is still a long way to go to reach the Healthy People 2010 goal of 60% vaccination among healthcare workers.

Hospitals that have been most successful in increasing their immunization rates have developed multifaceted programs to encourage their healthcare workers to get regular annual influenza vaccinations. Different tools and tactics include making it convenient to get a vaccine, offering the vaccine in the employees' work area and without cost, monetary incentives, and mandatory requirements with a signed declaration or opt-out. Another important aspect to increasing the immunization rate is education. Healthcare workers need to be reminded that they are at risk of transmitting the virus to patients, thus making it is a patient safety issue.

Dr. Wright referenced a study conducted by a hospital system over a 12-year period that was able to document an increase in the vaccination rate among its healthcare workers from 4% to 67%. Healthcare workers' rate of influenza infection dropped from 42% to 9% during that period. Concurrently, nosocomial transmission of influenza decreased from 32% at the beginning of the study period down to zero. This study demonstrated the positive benefits for both the workers and the patients when there is a high rate of vaccine coverage for the staff.

In 2007 the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) modified their standards to require all hospitals to offer influenza immunizations for any healthcare worker working in hospitals. This was followed by a recommendation by the Infectious Disease Society of America that hospitals require mandatory vaccine among healthcare workers. A similar recommendation has been made by the American College of Physicians.

Discussion

Several members discussed the value of requiring a signed "informed declination" letter for those health care workers who choose not to get the influenza vaccine. Others sited examples from their institutions of steps taken to increase influenza vaccination rates among healthcare workers. Patient safety, hospital-acquired infections (nosocomial), and staff absenteeism were addressed as other factors that raised the level of importance of increasing the rate of influenza immunizations for hospital employees.

The first day of the meeting adjourned at 4:30 pm.

National Vaccine Advisory Committee (NVAC)
June 3-4, 2008

Meeting Minutes
Day Two – June 4, 2008

Dr. Birkhead opened the second day of the meeting.

Agency, Department, Advisory Committee, and Liaison Reports

NVPO - Dr. Bruce Gellin

Dr. Gellin informed the Committee that the Assistant Secretary for Health has requested that NVPO focus on vaccine safety this year through its Strategic Issues in Vaccine Research (SIVR) program. This emphasis will provide a means to forge cross-departmental and cross-governmental activities. Announcements are forthcoming that will address and identify the range of activities focusing on safety.

Dr. Gellin reported that one of the projects that NVPO will be undertaking is an evaluation to improve the effectiveness of NVAC and to improve the usefulness and uptake of the Committee's recommendations. One issue is that the Committee does excellent work and makes very strong packages of recommendations, however, it may not get the level of attention that it should within the Department. This evaluation will formally review the recommendations made by NVAC over the past number of years and review their outputs and outcomes. The goal is to try to improve the process, as well as the impact of the recommendations of the Committee. Interviews will be conducted with current and past members, and historical documents will be reviewed in order to compare NVAC to other HHS committees as part of this process.

NVPO is currently identifying potential contractors to conduct the evaluation.

Advisory Committee on Immunization Practices (ACIP)/National Center for Immunization and Respiratory Diseases (NCIRD), CDC. - Dr. Anne Schuchat

RADM Schuchat informed the Committee that a number of ACIP vaccine statements have recently been issued. These statements include: use of Tdap and Td vaccines in pregnancy, prevention of human rabies with vaccine, and prevention of herpes zoster. These recently released statements resolve the backlog in updating recommendations.

Through May 30th of this year, 107 measles cases were reported, the highest number of cases since 1996. The May MMWR article on measles generated a significant amount of media attention. The pattern differs from previous years in that a number of imported cases come from Western Europe where they have experienced high incidence and challenging outbreaks. Nosocomial transmission has been important in some of the recent outbreaks. Most of the outbreak-associated cases affected people who were not immunized due to exemptions or personal beliefs. A few outbreaks are ongoing and a follow-up MMWR article on this topic is anticipated in the next few months. [Note: the aforementioned article appeared in August; CDC. Update: Measles-US, Jan – July 2008. MMWR 2008;57:893-6.]

CDC is observing a very unusual rotavirus season with delayed onset and decreased number of cases compared to past years. This coincides with the widespread implementation of routine rotavirus vaccination in young children, although vaccine coverage levels are not yet high. Data are going to be presented at the next ACIP meeting (June 25-26, 2008) and an MMWR article is being prepared on this topic. The cause of the decrease in cases is not clear, but it is possible that it is due to a herd effect of rotavirus vaccine at much lower levels of coverage than anticipated.

RADM Anne Schuchat's said that CDC and HHS do in fact cooperate on exchanging information; however, more needs to be done to have consistent public messaging. Although there is overlap and cooperation between ACIP and NVAC, particularly in areas such as vaccine safety activities, NVAC's role is to focus on policy areas such as vaccine financing issues, while ACIP's role is to focus on specific vaccination recommendations.

Dr Carol Baker, an ACIP member, announced that the American Academy of Pediatrics (AAP) has a major new initiative called the Immunization Alliance. The AAP would like to take a leadership role for bringing all the partners together, including PKids, Every Child By Two, various parents groups, and other partners in immunization. Dr. Baker said the Alliance will address issues of translating the scientific information into effective messaging that the public will hear and understand. Vaccination educational campaigns must address (and target) different language, ethnic, and educational barriers and biases. In addition, emotional and psychological barriers must be taken into account in order to ensure that messages resonate with parents.

HRSA/ACCV - Dr Geoffrey Evans

Dr. Geoffrey Evans updated the Committee on the Omnibus Autism Proceeding. As of June 24, over 5,400 autism claims had been filed with the National Vaccine Injury Compensation Program (VICP). Three theories of causation are being considered by the U.S. Court of Federal Claims in determining whether MMR vaccine or thimerosal-containing vaccines, or both, can cause autism or autism spectrum disorder (ASD). Evidentiary hearings in 2007 on general causation and 3 test cases considered whether MMR vaccine and thimerosal in combination (so-called "combined" theory) can cause autism or ASD. Special master's decisions in the first theory and three test cases are not expected until later this year.

In May, the Court heard evidence on general causation on 2 test cases for theory #2, the thimerosal-only theory. A third test case, and additional evidence on general causation for the thimerosal-only theory, will be presented during the third week of July 2008. Decisions in the 3 test cases and general causation are not expected until 2009. Testimony of physicians and HHS experts in toxicology and epidemiology can be downloaded from the U.S. Court of Federal Claim's website. The Court is currently working with both parties to determine when hearings will be scheduled for theory #3, which alleges that the MMR vaccine alone can cause autism or ASD.

The Hannah Poling case is still in active litigation; thus, it cannot be discussed at this time. It is true that HHS conceded entitlement, but the damages and the award amount have yet to be worked out. In terms of the remaining autism claims, it will take many years to review and adjudicate the thousands that are currently filed. We're told this will be necessary no matter how the Court decides causation. The Court has begun ordering 200 cases a month for jurisdictional review. This is being done initially by the Department of Justice; however, medical staff reviews are probably not far off. This will consume a better part of the staff resources for the next decade.

NIH-Dr. George Curlin

Dr. Curlin briefed NVAC on the vastness of NIH resources and researchers, and how much of a challenge it is to bring together experts who are working in similar arenas. Of interest to NVAC, he only recently found out that there has been a Mitochondrial Disorders Group at NIH for years.

On April 17th there was a meeting with Dr. Troy and senior leadership of the Department of Vaccine Safety at the NIH to provide an update on the science at NIH. There is interest in collaboration or information exchange between NIH and NVAC. Dr. Birkhead requested a written summary of the April proceedings. COL Engler, who also attended, indicated that all the proceedings and presentations are posted online [Note: Later discussion determined that this comment referenced another recently held meeting and not the one referenced above.]

Dr. Curlin also reminded the Committee about the availability of the Jordan Report, which recaps vaccine research and development, since it may be helpful to NVAC members.

Department of Defense - COL Engler

COL Engler reflected on the significant progress and synchronization that has been achieved using the minimum standards for quality immunization health care guidelines set forth by NVAC and the CDC. DoD has utilized these guidelines not only for vaccine delivery, but it went even further to set performance standards for a broad array of vaccines and vaccine-related issues. DoD has collaborated with the FDA on the establishment of a post smallpox vaccine myocarditis/pericarditis registry. The Vaccine Healthcare Centers Network, a DoD program supporting programs and services that enhance vaccine safety, efficacy and acceptability, is also collaborating with the Clinical Immunization Safety Assessment (CISA) Centers Network in developing competencies in causality reviews for adverse events. Joint research programs that can support enhanced phase IV post-licensure safety surveillance research required by the FDA for new vaccines like Japanese encephalitis and adenovirus are also being planned.

DoD has created a "one-stop-shopping" website for vaccine research and clinical data. It is located at http://www.vaccines.mil and www.VHCinfo.org. One of the military's key interests is the vaccine adverse events registry process and complex vaccine mixtures. DoD is vaccinating in ways no one else is mixing vaccines, particularly with biodefense vaccines like anthrax and smallpox vaccines. DoD is focused on epidemiological population indicators of causality but is evolving increased capabilities for more active post licensure safety surveillance, including enhanced adverse events causality investigations. The CDC, NVAC, and NVPO may be able to gather valuable insights by seeing the effects of vaccines in real life situations before formulating policy for public distribution of biodefense vaccines in the future.

According to COL Engler, once you have standards on which you can agree, you can perform individual causality assessments to systematically work toward developing case definitions based on well characterized similar cases. Lessons learned from the Vaccine Healthcare Centers Network adverse events clinical causality assessment registry can support guidelines development and a platform for future more focused research that supports quality improvements in immunization healthcare.

COL Engler proposes one of the areas within quality improvement of immunization healthcare is the serious need for educating people about what it takes to truly refine the precision of causality assessments for monitoring, assessing, and treating diseases potentially related to vaccine reactions. Enhanced clinical outcomes data about adverse events will enable clinicians and patients to have a better understanding of prognosis and overall risk.

Another DoD initiative is to reduce the number of vaccines given to new recruits, thereby reducing side effects as well as potentially more serious adverse events while also conserving vaccine supply. By improving the specificity of immunization practices to actual need for a given vaccine, both acceptability and vaccine supply management can be facilitated. Further research is needed on subpopulation differences, such as evidence that gender differences may enable reduced vaccine dosing for women in the future, which could enhance public health delivery of a limited vaccine supply, such as in the case of influenza pandemics.

Vaccine Supply Progress Report - CDR Angela Shen

CDR Shen's presentation began with a recap of previous NVAC recommendations on vaccine supply presented at the February NVAC. The five issues identified by stakeholders as a means to strengthen vaccine supply in the U.S. are as follows:

1. Provide incentives to maintain current vaccine manufactures and encourage new players into the market;
2. Streamline regulatory authority to ensure reliable production of safe and effective vaccines;
3. Strengthen liability protections for consumers, manufacturers, and providers;
4. Implement more comprehensive program vaccine stockpiles; and
5. Develop education programs to provide information to parents and consumers about usage and value of vaccines.

CDR Shen provided a progress report on these past NVAC recommendations.
Regarding Stakeholder Issue #1: The Government provides direct incentives to manufacturers for vaccine development. Liability protection is now included in new legislation, such as bio-defense, in addition to current liability protections in place. In addition to increased reimbursements, there has been increased growth in the vaccine sector compared to the pharmaceutical portion of the industry.

Regarding Stakeholder Issue #2: In an effort to streamline regulatory authority to ensure reliable production of safe and effective vaccines, there is increased utilization of regulatory pathways, such as accelerated approval and fast track designation, to speed the process.

The FDA Critical Path Initiative for Medical Product Development will provide guidance on aseptic processing and quality systems approaches that would help companies with Current Good Manufacturing Practice (CGMP) compliance. These guidelines will help streamline regulatory authority to ensure reliable production of safe and effective vaccines. In addition, the FDA issued two Direct Final Rules in May 2004 and March 2008 that modified existing regulations to provide more flexibility to manufacturers and encourage innovation.

With new technology, there is more flexibility to manufacture multiple products and different manufacturing capabilities today than there was before. The goal is to capitalize on innovative technology and to ensure that regulations written years ago can adjust to the technological advances of today.

Regarding Stakeholder Issue #3: Supply concerns led to the creation of Vaccine Injury Compensation Program (VICP) in 1986. There is no evidence that recent supply issues are related to liability. Ensuring liability protection keeps the industry strong; moreover, there is potential for future problems if VICP is not maintained. There have been 4 new vaccines added to the national, routine childhood recommendations since 2004 (HAV, influenza, meningococcal, HPV).

Regarding Stakeholder Issue #4: As far as vaccine stockpiles, the goal is to implement more comprehensive program vaccine stockpiles. The SEC's (Securities and Exchange Commission) Ruling on Revenue Recognition issue has been resolved.

Regarding Stakeholder Issue #5: CDR Shen cited a diverse array of educational and outreach programs and components across HHS agencies that reach different constituents and address worldwide health issues. These programs and components illustrate possibilities for future comparable NVAC public outreach initiatives.

Discussion

The group discussed that, due to the complex and constantly changing vaccine environment, the lessons of past vaccine shortages may not always apply now. The current situation must constantly be reevaluated to assure that shortages don't occur.

CDR Shen agreed to re-circulate materials from the February meeting, including the JAMA articles on vaccine supply, and to have these posted to the NVAC website. NVPO plans to work on improved searching and indexing capabilities of its website though the date for this revision is unclear.

Industry Panel: Ensuring and Sustaining Vaccine Supply-Industry Panel

The panelists included representatives from the following agencies/companies:

Merck – Dr. Gregg Sylvester
Novartis – Marguerite Baxter
Sanofi Pasteur – Dr. Phil Hosbach
Wyeth – Dr. Peter Paradiso
CDC – Dr. Greg Wallace

The manufacturer representatives echoed many of CDR. Shen's findings from a manufacturer's perspective, and they were fairly consistent in their remarks. The consensus was that it takes a lot of time, money, and overcoming hurdles to develop new vaccines – typically $500 million dollars or more, and over 11 to 18 years of research and development to take a new vaccine to licensure.

Dr Gregg Sylvester, Senior Medical director from Merck, stressed the importance of collaboration and communication to their success. He reiterated CDR Shen's comments that vaccine manufacturing is a very complex process and that vaccine shortages involve a number of factors.

Marquerite Baxter from Novartis stated that her company focuses on three overarching areas: public health environment, strengthening of public-private partnerships, and stockpiling of life saving vaccines. Ms. Baxter discussed issues related to ensuring vaccine safety, reliability, cost-effectiveness, and supply chain integrity. Citing influenza vaccine as an example related to supply chain, Ms. Baxter addressed two factors that are necessary to sustain the current production level. The first is demand, including the factors that drive demand. The second is the federal contract for purchase of influenza vaccine. Manufacturers engage in contracts with the government to ensure supply. However, since there is no safety net for manufacturers: if there is unused vaccine at the end of the season, they are left with the unused inventory which may decrease their willingness to produce more vaccine the following year.

Dr. Phil Hosbach from Sanofi Pasteur encapsulated the key challenges faced by manufacturers, as well as government oversight and policy groups, namely:

1. Policymakers need better understanding of the inherent complexities of biologics production;
2. Manufacturer expertise should be used to help formulate sound immunization policy;
3. Government and policy advisory bodies need to act with greater predictability;
4. Vaccine stockpiling needs to be an integral part of planning; and
5. We need to strengthen the message to all audiences that prevention is the most desirable intervention.

The manufacturers are committed to delivering a good, safe product. However, in many instances, they haven't been making significant profits on vaccines until recently, when reimbursements have grown from $2 per dose to $10 [for influenza vaccine purchase]. Add to that the FDA rules, regulations, and hoops in drug approvals and facilities inspections, and the result is that there are many delays, often made worse by the inadequate FDA budgets and staffing. Manufacturers are also concerned about stockpiles, wasted products, rotations, and insufficient supply. Once they complete the production run to meet their annual commitment, it is not easy to gear up and produce more; in addition, there are ROI (return on investment) considerations.

Dr. Peter Paradiso of Wyeth discussed the importance of building redundancy into production, which would make the process less susceptible to issues and complications. However, building redundancy and capacity is a risk because it is expensive and inefficient. The important issue is how to manage supply problems.

Manufacturers commended the FDA and the CDC for their efforts to work as partners to ensure safety and efficacy in the supply of vaccines. They recognized the importance of the National Vaccine Injury Compensation Program, which spreads the risks of the small percentage of people who may have adverse reactions to vaccines. Moreover, they applauded efforts to augment FDA staffing.

Managing stockpiles is understandably a complex process. Shortfalls are often due to unforeseen situations or manufacturers dropping out, without sufficient back-up capacity available with remaining manufacturers. This creates a challenge for the manufacturer that is not having supply problems. There needs to be sufficient annual volume in order to run vaccine production cost effectively, especially if new entrants are competing for volume and market share. This is one of the reasons why manufacturers choose to leave the market, which is equally disruptive to the vaccine supply. The issues and contributing factors to supply disruptions are dynamic; therefore, it is difficult to draw conclusions about causality based on what happened 5 or 10 years ago.

Discussion

The CDC and NVAC members said that the manufacturers were operating out of concern for public safety, and that they should be recognized for their diligence.

NVAC members were also concerned about FDA staffing issues, how NVAC should consider them as part of its mission. CDR Shen volunteered to follow up with the FDA and provide an update to the NVAC on the current staffing initiatives at FDA. Ms. Baxter said that writing Congress can often be an effective way to advocate for issues.

COL Engler said the challenge remains how to have sufficient vaccine supplies, as well as how to develop alternative strategies to effectively stretch supplies in the wake of a vaccine shortage.

Global Polio Eradication-RADM Anne Schuchat and Dr. Steve Cochi

There has been significant progress in reducing polio cases from 2000 to 1310 annually, with promising signs of eradication except in the 4 challenging countries of Nigeria, Pakistan, Afghanistan, and India. Monovalent poliovirus vaccines have been very successful in reducing polio cases, and early intervention with supplementary immunization activities has contained the spread of polio from importation into previously polio-free countries. Type 1 virus is targeted for eradication by the end of 2008; in 2009 the focus will be on eradicating type 3 virus. There is concern about mutant strains of vaccine-derived poliovirus, particularly in rural areas of Nigeria. The G8 Summit this July will determine whether G8 countries will continue to meet their commitments to adequately fund immunization programs in the remaining polio endemic countries in the wake of other priorities. PAHO (Pan American Health Organization) has asked for an update of the 2004 survey and inventory of all U.S. laboratories storing live polio virus and potential infectious materials. Only six labs have been added to the 2004 survey count of 122.

Dr. Steve Cochi reported that a tremendous amount of progress has been achieved toward controlling polio. From 1988 to 2004, we dropped from 125 polio endemic countries down to 4 endemic countries: Nigeria, Pakistan, India and Afghanistan. Beginning with the 2003-2004 cessation of use of polio vaccines in several states in Nigeria, poliovirus spread from Nigeria to 20 different previously polio-free countries, including as distantly as Indonesia. This combined with its spread from the reservoirs in India to additional 7 polio-free countries, lead ultimately to 27 previously polio-free countries becoming re-infected between 2003 and 2007. So that has been quite an ongoing challenge for the program.

Another challenge that the program has faced is the recognition and documentation of currently 10 different vaccine-derived poliovirus outbreaks since 2000. The largest such outbreak is still ongoing in northern Nigeria, with now more than 100 cases in northern Nigeria. The main risk factor for occurrence of these outbreaks is low immunization rates which leads to pockets of susceptible children who become infected with a vaccine-derived poliovirus that has mutated to a more virulent and transmissible form.

Because of all of these events and circumstances, the polio eradication initiative is now considerably past the original target date of global polio eradication by 2000. There has been some push-back by the G8 countries regarding funding and investment in the program. However, recent progress has restored confidence that polio eradication can be achieved.

With all of these developments, the Director General of the WHO, Margaret Chan, called an urgent stakeholder consultation last February 2007. The meeting, with the major partner organizations and political leaders of the 4 endemic countries demonstrated her resolve to eradicate polio. A 2-year timeframe was established that will end in the spring of 2009 to demonstrate progress in polio eradication and reassess the situation at that time.

A major issue in ensuring progress is the scale of new tools and tactics. One of these tools, monovalent oral polio vaccines, has been used successfully since 2005. The vaccine's per dose effectiveness is 2-3 times greater per dose than the trivalent oral polio vaccine. The Advisory Committee on Polio Eradication (ACPE) concluded that monovalent oral polio vaccine (mOPV) significantly enhanced the potential for success of the eradication effort and offers a powerful new tool to interrupt transmission of the Wild Polio Virus (WPV).

In 2007, there were 1310 polio cases, down substantially from the approximately 2000 cases per year during 2005-2006. The May 2008 MMWR (provided as reference to NVAC members) is a summary of the last year's global situation.

Special techniques, tools, and strategies have also been tailored to each particular country. For reasons not fully understood, ,the type 1 poliovirus has a greater propensity to spread and to cause paralysis than a type 3 virus, so it has been specially targeted for eradication using multiple rounds of mOPV1 immunization.

Africa has had some resurgence in type 1 cases, almost entirely in Nigeria, where there are more than 100 cases; exportation of both type 1 and type 3 virus to neighboring countries, like Chad, and across sub-Saharan Africa has led to a few new polio cases along the border of South Sudan and Ethiopia. The situation with the seven countries re-infected with type 1 WPV still remains challenging, even though the number of cases is quite low.

NVAC advised and provided input on a comprehensive 2004 survey of more than 32,000 institutions/laboratories in the U.S., comprising a total of more than 105,000 individual laboratories. The survey had a nearly 100% response rate. It revealed that only 122 institutions comprising 180 labs retain polioviruses and/or potentially infectious poliovirus materials. Six new labs retaining wild poliovirus have been added to the list since 2004, and these labs will be reported to Global Polio Eradication Initiative (GPEI) and PAHO in July 2008.

Discussion

Several NVAC members asked what the role of oral polio vaccine would be in containing a polio outbreak in the U.S. Dr Cochi stated that since there is no longer any licensed OPV in the U.S., Inactivated Polio Vaccine (IPV) would be the vaccine of choice. Another issue discussed was the need for an OPV stockpile after the last case of wild polio has occurred worldwide.

Adult Immunization Working Group - Dr. Richard Clover

The first teleconference for the newly established Adult Immunization Working Group was held on May 28th, 2008. The mission of the Working Group is:

1. To identify gaps, and make recommends to address them,, particularly in the national adult immunization effort.
2. To ensure coordination, evaluation and collaboration across Federal agencies to improve vaccinations for adults

Additional working group members were identified based on their interest and expertise in the proposed mission of the Working Group. New membership included both NVAC members as well as outside consultants. The Working Group agreed that they want to ask HHS agencies to review their adult immunization programs and discuss potential gaps. The Adult Vaccine Working Group is accepting new members to round out its specialty knowledge experts.

The second meeting for this Working Group is scheduled for July 2008. The Working Group will identify finance issues related to their mission statement; afterward, they will then share with the Vaccine Finance Working Group in order to develop recommendations.

Update on Development of National Vaccine Plan - Dr. Bruce Gellin

The National Vaccine Plan (NVP) was originally written in 1994. An update is now in development. NVPO is working with the Institute of Medicine (IOM) on this rewrite. Ray Strikas is taking the lead on this effort for NVPO. The original plan had four goals; however, a fifth goal, Global Health, has been added for the revised plan. The goals in the 1994 plan are:

1. To develop new and improved vaccines;
2. To ensure optimal safety and effectiveness of vaccines;
3. To better educate the public and members of the health professions on the benefit and risks of immunizations; and
4. To achieve better use of existing vaccines to prevent disease, disability and death.

Dr Gellin reminded the group that NVPO's charter addresses infectious disease vaccines only so that, while there is promising research on the use of vaccines to control other diseases, the updated NVP is limited to vaccines for infectious diseases.

IOM has been asked by HHS to review the draft NVP. They reviewed the 1994 plan when it was drafted as well. IOM is currently reviewing the 1994 plan and they will provide a letter report to NVPO shortly. Dr Gellin reviewed the timeline for the review process. The next step is the July 24-25 meeting in Chicago. During this meeting, the IOM will focus on childhood, adolescent and adult programs as well as vaccine surveillance for diseases and vaccine coverage. A series of subsequent meetings has been scheduled by the IOM to occur over the next six months to review other priorities with stakeholders. A draft NVP will be available for review by IOM and NVAC later this fall. NVAC is encouraged to review the draft and provide input as well. The final IOM report with recommendations is expected in late 2009. In the meantime, NVPO will conduct town hall style meetings to obtain public input on the plan.

Discussion

There was some confusion as to the exact role of IOM in this process. Dr. Gellin summarized IOM's tasks as follows: first, to review the 1994 plan and provide guidance on the development of the update of the plan (letter report pending) and, secondly, to review the thirteen priorities in the update to the NVP (late 2009). He further stated that the NVP revision is a cross-agency process within HHS as well as with other Federal partners (VA and DoD). NVAC will also have access to the draft plan and is invited to provide input.

Closing Remarks

Dr. Birkhead made some closing remarks and officially closed the meeting.

There were no public comments. The meeting adjourned at 1:05 pm.