SUMMARY REPORT
of the
NATIONAL BIODEFENSE SCIENCE BOARD
PUBLIC TELECONFERENCE
May 22, 2009

NBSB VOTING MEMBERS PRESENT

Patricia Quinlisk, M.D., M.P.H., Chair
Stephen V. Cantrill, M.D.
Albert J. Di Rienzo
Kenneth L. Dretchen, Ph.D.
John D. Grabenstein, R.Ph., Ph.D.
James J. James, Brigadier General (Retired), M.D., Dr.P.H., M.H.A.
John S. Parker, Major General (Retired), M.D.
Andrew T. Pavia, M.D.
Eric A. Rose, M.D.
Patrick J. Scannon, M.D., Ph.D.

NBSB VOTING MEMBERS NOT PRESENT

Ruth Berkelman, M.D.
Roberta Carlin, M.S., J.D.
Thomas J. MacVittie, Ph.D.

EX OFFICIO MEMBERS PRESENT

Diane Berry, Ph.D., Chief Scientist, Director, Threat Characterization and Countermeasures, Office of Health Affairs, U.S. Department of Homeland Security
Bruce Gellin, M.D., M.P.H., National Vaccine Program Office, Office of the Secretary, Office of Public Health and Science, U.S. Department of Health and Human Services
Rosemary Hart, Special Counsel Office of Legal Counsel, U.S. Department of Justice
Carol D. Linden, Ph.D., Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services
Boris D. Lushniak, M.D., M.P.H., Rear Admiral, Assistant Surgeon General, U.S. Public Health Service, Assistant Commissioner, Office of Counterterrorism and Emerging Threats, Office of the Commissioner, Food and Drug Administration, U.S. Department of Health and Human Services
Daniel M. Sosin, M.D., M.P.H., F.A.C.P., CAPT, U.S. Public Health Service, Acting Director, Coordinating Office for Terror Preparedness and Emergency Response, U.S. Department of Health and Human Services *(designated by Richard E. Besser, M.D.)*

STAFF OF THE NATIONAL BIODEFENSE SCIENCE BOARD

Leigh Sawyer, D.V.M., M.P.H., CAPT, U.S.P.H.S., Executive Director
Erin Fults, Scientific/Technical Writer
MacKenzie Robertson, Program Analyst
Brook Stone, M.F.S., LTJG, U.S.P.H.S., Program Analyst

CALL TO ORDER, ADMINISTRATIVE MATTERS, AND CONFLICT OF INTEREST RULES

CAPT Leigh Sawyer, D.V.M., M.P.H., Executive Director, National Biodefense Science Board (NBSB)

CAPT Leigh Sawyer welcomed the board, the *ex officio* members, and the public to this public conference call to discuss the H1N1 virus. Eighty-one participants were on the call in addition to those present in the conference room. She noted that the NBSB is governed by the Federal Advisory Committee Act. Most NBSB work is performed by working groups, whose findings have been presented to the entire Board. She then reviewed Conflict of Interest rules, which apply to the Board. Those members of the public who wished to speak were asked to queue up with the assistance of the conference call administrator. CAPT Sawyer also noted that Dr. Jean Smith was available on the phone to speak on immunization practices if there are questions about the Advisory Committee on Immunization Practices.

CHAIR'S REMARKS AND AGENDA OVERVIEW

Patricia Quinlisk, M.D., M.P.H., Chair

Dr. Patricia Quinlisk began by stating that this was a very important meeting on the H1N1 virus. The purpose was to learn how the Board can respond to concerns and questions about the virus.

OPENING REMARKS

RADM William C. Vanderwagen, M.D., ASPR, U.S. Department of Health and Human Services (HHS)

RADM Vanderwagen spoke abut the current status of the transition at HHS. The results of this meeting will be important for HHS Secretary Kathleen Sebelius, as she is actively involved in the 2009 H1N1 influenza situation. Secretary Sebelius wants the NBSB to provide expert review, consideration, and recommendations vis-à-vis difficult choices in the face of a less-than-robust science base. So, the input from this meeting will be that much more important due to the group's experience and knowledge.

The NBSB is pursuing an active approach in dealing with this situation. Some issues arose in Wave 1 of the epidemic and the Board is now thinking ahead to Wave 2. RADM Vanderwagen noted that the first two case reports were sent to the World Health Organization (WHO) on April 18 and he acknowledged that a lot has happened since then. RADM Vanderwagen evaluated the national response as appropriate thus far, and noted that there are logical, rational next steps. Most people know what happened with the swine flu in 1976 and 1977 and this time, RADM Vanderwagen said, HHS needs to know whether to move forward or "get off the freeway," providing support but not pursuing monomaniacal decisions. RADM Vanderwagen observed the need for a national and international approach. While putting domestic considerations first, he noted that Secretary Sebelius is extremely mindful of the global realities, and she will consider those concepts as well.

Dr. Quinlisk thanked RADM Vanderwagen for his support of the Board. RADM Vanderwagen said that he is extremely pleased that a longtime friend has been nominated to assume his role, Dr. Nicole Lurie, as the next Assistant Secretary for Preparedness and Response (ASPR). RADM Vanderwagen will continue in the position as ASPR until Dr. Lurie's confirmation.

OVERVIEW OF THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES H1N1 VACCINE STRATEGY

For the first topic, Dr. Robin Robinson, Director, Biomedical Advanced Research and Development Authority (BARDA) talked about vaccine strategy. Dr. Robinson began by explaining that the strategy has been in place since 2004. There are three different but inter-related phases that will occur, informing decisions going forward.

In the vaccine development phase, researchers are identifying new vaccine candidates. This requires isolation of the virus, which first goes to a center or lab. In this case, the samples went to the Centers for Disease Control and Prevention (CDC). The next step is to replicate the virus. Virus strains are currently made in two ways: traditional replication and the reverse genetics method. Manufacturers then make master seeds and begin study of the vaccine candidates. In clinical studies, they look at antigens, safety, dosage, adjuvant use, and related considerations. For the H1N1 virus, the virus reference strains will go from World Health Organization (WHO) to manufacturers worldwide, as well as to other labs investigating a vaccine for the virus.

Manufacturers then take 6 to 8 weeks to produce vaccines for study. There are mix-and-match studies of antigens and adjuvants, and manufacturers want to test all permutations. The hope is that the interim information will be available by mid-September, when, ideally, there will be a better idea of what the vaccine will look like. In parallel, the vaccine manufacturers will have to be able to look at potency and adjuvants, and there will be work on reference strains.

An order signed the morning of the meeting asked three drug companies to manufacture the H1N1 influenza vaccine. The initial funding is $1.1 billion for immediate testing and production, as well as creating supplies of bulk adjuvant for licensed producers of influenza vaccines. The adjuvants will be produced over the summer. Activity in the southern hemisphere, which is entering flu season, will help determine if there is a real need for an immunization program. The decision as to whether or not to have a program will likely be made in late September. However, it takes 9 months to get an immunization program in place, so now is the time to plan for what might have to be done.

The last phase is the actual vaccine immunization program. This summer, planning will occur as if there is a need for a program. ASPR will determine when the vaccine might be available and will monitor the effects of the vaccine, which may involve a large-scale clinical trial. This strategy meets two goals: first, to have the infrastructure in place to deliver 600 million doses in 6 months after a pandemic, and second, to stockpile for those individuals who are in the critical workforce during the event. ASPR is moving ahead with this.

Dr. John Grabenstein asked Dr. Robinson if pediatric studies are planned. There have been multiple meetings at HHS with the CDC, the National Institutes of Health (NIH), and the Food and Drug Administration (FDA) about what clinical trials would be needed and pediatric populations and the elderly are being addressed there. Dr. Ken Dretchen noted that the over-60 population might have immunity to the H1N1 virus and inquired as to whether there was a possibility of dosing them differently. Dr. John Parker added to this, asking if there is an opportunity for an immune globulin, since the over-60 population seems relatively immune to the H1N1 virus, possibly due to their long history of receiving flu shots. Dr. Robinson

responded, indicating that they are examining what happens with different populations after the first dose and how that would affect the vaccine supply. This is something that will be deliberated in the coming months. Dr. Patricia Quinlisk asked what trials will be held in the southern hemisphere. Dr. Robinson noted that there are likely to be trials in South Africa or South America. Dr. Pavia asked if there is a contingency plan for alternative potency tests and Dr. Robinson responded in the affirmative. He noted that there have been issues with hemmaglutinin inhibition tests depending on the type of red blood cells used for the test. Therefore, they are validating assays and doing comparisons.

Another concern is the possibility of mutations in the H1N1 virus. Dr. Robinson said that the hope is that enhanced monitoring will reveal any mutations. Clinical studies will show whether the vaccines can handle virus drift.

THE ROLE OF FEDERAL ADVISORY COMMITTEES AROUND DECISION-MAKING FOR H1N1 VACCINE DEVELOPMENT AND USE

Dr. Bruce Gellin, Director of the National Vaccine Program Office (NVPO) at the Office of Public Health and Science (OPHS), discussed the role of the NVPO and possibilities for the role of the NBSB. There are four different committees that deal with this, not including NBSB. The Advisory Committee on Immunization Practices (ACIP) is looking at whether there should be a vaccine program. At FDA, the Vaccines and Related Biological Products Advisory Committee (VRBPAC) looks at licensure, as well as flu strains to be selected for the coming year. There are some parallels between the groups regarding the clinical trials done by companies and the NIH. The advisory committees will also be exploring the use of adjuvants in a vaccine. ACIP looks at how licensed vaccines are used. They can also investigate unlicensed vaccines if necessary, which may be required in the given the current situation. The National Vaccine Advisory Committee (NVAC) advises on research, utilization, supply, and monitoring. Another group is the Defense Health Board, which advises the military and has a subgroup that looks at vaccines.

Dr. Jean Smith, the Assistant to the Director for Immunization Policy explained the role of ACIP, which provides advice to the CDC Director and HHS Secretary on the use of vaccines licensed in the United States. ACIP holds three public meetings a year at CDC and members vote on the recommendations for use of vaccines. The ACIP has an influenza working group, which deliberates on seasonal flu and the associated vaccines.

Dr. Gellin explained that another advisory group is the Defense Health Board's Select Subcommittee on Pandemic Preparedness, which advises the Assistant Secretary of Defense for Health Affairs. The Defense Health Board reviews the Subcommittee's recommendations and develops recommendations for the Department of Defense (DoD).

RADM Vanderwagen noted that after the meeting the NBSB will want a more formal document from which Dr. Quinlisk and the Board can work. There are major adjuvant and antigen manufacturing decisions to make in light of the H1N1 epidemic, and the NBSB needs to stay informed. Significant data points will have a lot to do with what the vaccine looks like, but the epidemiological information will help decide whether to proceed. With so many advisory committees working on the flu, it is important that the NBSB not waste time recreating some of the detailed work already done by other groups, nor cross over into the territory of another advisory group.

The NBSB will be able to help clarify the situation and the current environment, which will help aid the Secretary of HHS and others in making their decisions.

Dr. Pavia noted that significant thought has been given to the crucial decisions about the use of adjuvants in an influenza vaccine, and whether adjuvants are needed for immunity or cross-protection. Another crucial question is whether or not the United States should be responsible for producing extra adjuvant and antigen to help other countries, and whether this is even an appropriate question for the Board to consider. RADM Vanderwagen acknowledged that the science data will be very important, but a more appropriate question for the Board would be how much we should focus on an antigen-sparing strategy, since sparing antigen increases the global availability of the antigen. Secretary Sebelius is focused on domestic issues but also wants to understand the global picture, and antigen-sparing strategy is one element that factors into this.

Dr. Gellin said that antigens will be initially looked at on the clinical level and the aggregate data might need to come before the Board because it will affect global antigen capacity. A lot of individuals and groups will have opinions on the use of adjuvants, and the question arises as to what will be the best way to ensure appropriate input. The adjuvant decision is one that will be driven by data, but the answer may not be clear, and will undoubtedly require extensive evaluation. It will be important to harmonize the roles of the various advisory groups so the Secretary does not get conflicting or competing recommendations. The NBSB, with its wide range of expertise, should consider how to facilitate synergies and is encouraged to work with other groups addressing these issues. Looking forward to its June meeting, the NBSB should consider pulling in members of the different groups to determine effective roles, goals, and strategies.

Dr. Grabenstein observed that there had been a great model collaboration in assessing smallpox vaccine safety surveillance data (when the Armed Forces Epidemiological Board and the ACIP formed a joint working group), and this could serve as model for the current influenza situation. Dr. Gellin noted that NVAC is probably poised to look at most of this and that the NBSB could best serve by evaluating some of the larger decisions to be made. Dr. Grabenstein pointed out that there are also state level data, liability, and compensation programs to consider.

It was suggested that a transparent master list of all the things that can go wrong be developed, with each advisory committee providing input. Authority and funding to administer a vaccination program are important factors, as well as monitoring vaccine use in patients. This needs to go beyond medical surge. If there is a second wave, there will be a lot of issues not fully addressed and it is important to consider how committees will make decisions if confronted with these issues.

Dr. Quinlisk asked about the use of other vaccines, beyond H1N1, and how they might work into these decisions. Dr. Gellin responded that a working group of the ACIP on a pneumococcal vaccine is currently addressing this issue. Dr. Smith elaborated, explaining that the group is actively considering vaccine in a pandemic setting, has a draft document, and will add another half day to their June meeting for a presentation on this topic. Dr. Gellin noted that it is important to determine if this is about the stockpile or an immunization program. There have

been investigations into the emerging epidemiology of influenza and secondary infections; it is important to see if this is covered by existing programs. Dr. Pavia added that collaboration between CDC and the Infectious Disease Society of America (IDSA) has begun to look at the bacterial complications of influenza surveillance, the possible need for a staphylococcal vaccine, as well as stockpiles of antibiotics and other drugs. It is crucial to collect a variety of different opinions. Dr. Pavia said that in 1976 there may have been too much "group think," so, in the present situation, it is crucial to collect a variety of different opinions and viewpoints to help prevent a repeat of history. Dr. Grabenstein agreed, stating that an interest in harmony should not be at the expense of truth. Dr. Quinlisk added that in light of the rapidity of decisions needed for swine flu, it is not clear how the NBSB can advise when the decisions are at that pace. Dr. Robinson said that the questions will come to the Board and ASPR will keep the NBSB posted on issues the Board can and should be addressing. Dr. Grabenstein sees it as a wave spreading down the road, requiring quick decisions up front to provide the appropriate people with the appropriate information. The reality is that there must be strategic decisions made in the next three months.

Dr. Smith believes that the public needs to understand that there are also people outside the government helping make these decisions. With the smallpox vaccine, people felt decisions were made in isolation. Dr. Gellin suggested taking this as a lesson learned. He said one way to prevent this is to facilitate lots of dialogue, and take in information and issues of pertinence from the ground level.

Dr. Patrick Scannon said that the time for these advisory groups to work together is now, as opposed to waiting for the situation to change. Today was an important first step in understanding other groups and the Board's interactions with them, rather than waiting for an emergency situation. Dr. Gellin added that this may be an opportunity to ensure representation from other groups and to work with others to refine some of the pertinent questions. Dr. Pavia noted that the agenda for the June meeting on H1N1 keeps shifting, so they need to put in some careful thought. The NBSB needs real clarity about what the decisions will look like, where advice will come from, and where they want to share information. They also need to pursue certain types of outside input that might not otherwise come to them as well as formalize the roles of the different advisory groups. There is a lot to do to clarify the agenda.

There also exist gaps in pandemic preparedness beyond vaccine issues. For example, the Secretary will need to plan for what to do while Congress is in recess and there is a growing concern in regard to the readiness of alternate care facilities and triage sites. It is also important to educate clinicians, because vaccine stocks could be exhausted through inappropriate use. There are a lot of issues to address beyond vaccine use and development.

RADM Vanderwagen remarked that antiviral distribution could function better. It needs to be determined who will attend to vaccines versus other countermeasures, and their relative distribution. It is impressive that 25 percent of the Tamiflu stock was out the door within 36 hours of the announcement of the H1N1 virus. But, downstream, there will be fewer assets to address the issues. Visibility and the level of information available locally are important elements in successful epidemic planning.

Dr. Gellin is aware of no advisory boards that specifically deal with public risk communications, education, and the like. Dr. Quinlisk agreed, stating that communication can be one of the most critical things in responding to a pandemic. Dr. Gellin added that there needs to be understanding of how people deal with information. For example, the principals of schools that closed maintained that the CDC told them to close when in fact the CDC had merely offered guidance. People did not make the distinction between recommendations and directions. The NBSB could address messaging through public meetings. There should be a document that could be an educational tool for the next wave and this is something that should be discussed further.

PUBLIC COMMENT AND DISCUSSION

Peter Carrasco of the World Health Organization wanted to know if there were concerns about simultaneous administration of the seasonal vaccine and the H1N1 vaccine. Dr. Gellin responded that they want to keep the vaccines separate. On the ground, people might follow the recommendations differently. This is something to consider, on top of the existing schedule. Dr. Robinson added that there is a big concern about logistics. An understanding if the population's immunity will be important, especially if they have received previous vaccines. WHO is getting questions on this. It will be a big item to watch unfold in South America's winter, but it will be faced in the north eventually. Clinical trials will be necessary to determine how to immunize for both H1N1 and seasonal flu.

Susan Chu, from ReadyMoms Alliance, referenced a study about antibodies that had been published last year, regarding Guillain-Barré syndrome. She wondered whether there is relevance between the study and the use of adjuvants. Because a recombinant vaccine is close to licensure, they do not need to wait and can start clinical trials in June and the vaccine can be made rapidly. She asked if there has been any effort to test the feasibility of this. Dr. Robinson said that there must be a robust adverse event monitoring system. A working group is looking into this to see if it can be picked up as quickly as possible. The current approach is working with the manufacturers already known from a regulatory standpoint. Adjuvants licensed outside the United States will also be reviewed. Dr. Robinson added that the recombinant vaccines are interesting, as Ms. Chu noted, and there are currently contract negotiations on a recombinant vaccine.

WRAP UP AND ADJOURN; CHARGE TO THE PANDEMIC INFLUENZA WORKING GROUP

RADM Vanderwagen concluded by noting that NIH has moved to get the best discussion from many experts. The issue is how to assure good expert overview of the process and the group felt the best way to get recommendations to the Secretary was to go through NBSB.

Dr. Pavia requested that the group contact him via e-mail if they had anything to say about the upcoming June meeting on H1N1. Dr. Quinlisk said they will continue working on this topic, covering a variety of critical issues. She appreciated the work done by the various advisory committees. Dr. Quinlisk informed the group that the next meeting of the NBSB is scheduled for September 24-25.