SUMMARY REPORT
of the
NATIONAL BIODEFENSE SCIENCE BOARD
Teleconference
October 28, 2011
3:00–4:00 p.m., EDT

VOTING MEMBERS PRESENT

Patricia Quinlisk, M.D., M.P.H., *Chair*
Georges C. Benjamin, M.D., FACP, FACEP(E), FNAPA, Hon FRSPH
Ruth L. Berkelman, M.D.
Stephen V. Cantrill, M.D.
Jane Delgado, Ph.D., M.S.
David J. Ecker, Ph.D.
Daniel B. Fagbuyi, M.D., FAAP
John D. Grabenstein, R.Ph., Ph.D.
Kevin A. Jarrell, Ph.D.
Thomas J. MacVittie, Ph.D.
John S. Parker, Major General (Retired), M.D.
Betty J. Pfefferbaum, M.D., J.D.
Patrick J. Scannon, M.D., Ph.D.

EX OFFICIO MEMBERS PRESENT

Rebecca S. Daley, Policy Advisor, Office of International Health and Biodefense, U.S. Department of State (*designated by Kerri-Ann Jones, Ph.D.*)
Bruce Gellin, M.D., M.P.H., Director, National Vaccine Program Office, Office of the Assistant Secretary for Health, U.S. Department of Health and Human Services
Rosemary Hart, J.D., Special Counsel, Office of Legal Counsel, U.S. Department of Justice
Carole Hudgings, Ph.D., Senior Advisor to the Deputy Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health (*designated by Hugh Auchincloss, M.D.*)
Franca R. Jones, Ph.D., Senior Policy Analyst, Chemical and Biological Countermeasures, Office of Science & Technology Policy, Executive Office of the President
Peter Jutro, Ph.D., Deputy Director, National Homeland Security Research Center, U.S. Environmental Protection Agency
Ali S. Khan, M.D., M.P.H., RADM, U.S. Public Health Service, Assistant Surgeon General and Director, Office of Public Health Preparedness & Response, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services
George W. Korch Jr., Ph.D., Senior Science Advisor, Office of the Principal Deputy, Office of the Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services
Randall L. Levings, D.V.M., Scientific Advisor, National Center for Animal Health, U.S. Department of Agriculture

Richard A. Martinello, M.D., Veterans Health Administration, Office of Public Health and Environmental Hazards, U.S. Department of Health and Human Services (*designated by Victoria J. Davey, Ph.D., M.P.H.*)
Vincent Michaud, M.D., M.P.H., Office of the Chief Health and Medical Officer, National Aeronautics and Space Administration (*designated by Richard S. Williams, M.D.*)
Diane Poster, National Institute of Standards and Technology, Department of Commerce (*designated by Michael D. Amos, Ph.D.*)
Bonnie Richter, Ph.D., Director of the Office of Illness and Injury Prevention Programs, Office of Health Safety and Security, U.S. Department of Energy (*designated by Patricia R. Worthington, Ph.D.*)

STAFF OF THE NATIONAL BIODEFENSE SCIENCE BOARD

Leigh Sawyer, D.V.M., M.P.H., CAPT, U.S. Public Health Service; Executive Director
MacKenzie Robertson, Program Analyst
Jomana F. Musmar, M.S., Program Analyst, Contractor

CALL TO ORDER AND CONFLICT OF INTEREST RULES

Leigh Sawyer, D.V.M., M.P.H., CAPT, U.S. Public Health Service; Executive Director

CAPT Sawyer called the meeting to order at approximately 3:00 p.m. and called the roll. She reviewed the guidelines for Federal advisory boards, as well as conflict of interest guidelines.

WELCOME, AGENDA OVERVIEW, AND GOALS

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

Dr. Quinlisk welcomed the National Biodefense Science Board (NBSB) members and other participants and reviewed the agenda for the meeting (see Appendix A). She said the primary goal of today's meeting is to discuss and vote on the report with recommendations of the Anthrax Vaccine (AV) Working Group (WG).

REMARKS FROM THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE (ASPR), U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS)

Nicole Lurie, M.D., M.S.P.H., ASPR

Dr. Lurie thanked the Board for taking on the challenging issue of how best to protect children in the event of an anthrax attack. She thanked the AV WG co-chairs in particular for their thoughtful work in developing the report and also thanked all those who participated in the process by providing comments and testimony. She reiterated the task to the Board to compare the advantages and disadvantages of studying anthrax vaccine in children in the absence of an anthrax attack.

Dr. Lurie underscored that protecting children is very important. Many of the Board's ex officio members could not attend the start of this meeting because they are attending the inaugural meeting of a pediatric/obstetric integrated product team—a group of Federal officials across the Public Health Emergency Medical Countermeasures Enterprise

(PHEMCE) who will advise on protecting pregnant women and children. She concluded that she knows the task of addressing the use of anthrax vaccine in children was not easy, and she repeated her thanks.

Dr. Quinlisk added her thanks to the AV WG, its co-chairs, and the NBSB staff for the incredible amount of work they had done for this report.

AV WG REPORT: *CHALLENGES IN THE USE OF ANTHRAX VACCINE ADSORBED (AVA) IN THE PEDIATRIC POPULATION AS A COMPONENT OF POST-EXPOSURE PROPHYLAXIS (PEP)*

Daniel Fagbuyi, M.D., FAAP, Chair, and John S. Parker, M.D., Major General (Retired), Co-Chair, AV WG, NBSB

Dr. Fagbuyi said the AV WG agreed that the development of the report would center around three pillars:

- Protecting children
- Addressing the issue of anthrax vaccine testing in an open, public process, which it did through a stakeholder engagement process, working with subject matter experts, involving public health authorities and other entities that care for children, engaging the media, and providing opportunities for public comment
- Thoroughly considering and discussing ethical and legal issues

To gather input for the report, NBSB sponsored a public stakeholder engagement workshop on July 7, 2011, with public and private entities to discuss ethical and legal issues, among others. At the NBSB public meeting in September, the AV WG presented a draft of the executive summary and received additional input from the Board and the public, which informed the draft report presented today.

Dr. Parker added his thanks to the ex officio members who provided outstanding insight into the report. He also noted that it is likely that 26 percent of any population exposed to anthrax spores as the result of an attack would be children. While we are confident we can care for adults exposed to anthrax, many pieces of data are missing for the pediatric population, he said, and the scope of the question merited lengthy and thorough consideration, discussion, and debate.

The report recommends the following:

> The Department of Health and Human Services (HHS) should develop a plan for and conduct a pre-event study of AVA in children, to include a research investigational new drug application (IND). HHS should submit the study protocol to one or more investigational review boards (IRBs), and comply with the 21 CFR 50.54/45 CFR 46.407 federal review process. This recommendation should be revisited if new anthrax vaccines or other therapeutic countermeasures become available.

Dr. Fagbuyi added that the AV WG believes that a national-level review board should

consider any plan to study AVA in children and look more deeply into ethical, legal, regulatory, and safety issues.

Discussion

Patrick Scannon, M.D., Ph.D., reinforced that the AV WG discussed the difficulty of trying to conduct a clinical trial of AVA and get needed information during or after an anthrax event, and that set the stage for the recommendation. Thomas MacVittie, Ph.D., acknowledged that the issue is controversial, and he anticipated that similar dilemmas will arise in seeking medical countermeasures for radiological/nuclear threats. He said the issue is a matter of weighing risk against benefit.

John Grabenstein, R.Ph., Ph.D., said all the IRBs and research ethics panels that he has been involved with since for almost 20 years recognize that children are a vulnerable population and there are special requirements in place to protect them. He said his decision about the recommendation came down to whether he would rather know the response to the vaccine before being confronted with offering it to many thousands of children. Dr. Grabenstein said we should write a good study protocol and give parents a goodly amount of time to weigh the pros and cons and decide whether to enroll their children.

Kevin Jarrell, Ph.D., noted that collecting data on AVA in children in advance will allow public health authorities to administer AVA more safely and more effectively in the event that it becomes necessary to administer the vaccine to children. When he considered the relative risks, he was in favor of a pre-event study. Dr. Jarrell added that the Board and the AV WG did a good job of weighing all sides of a difficult issue, and he supported the conclusions of the AVWG.

Ruth Berkelman, M.D., thanked the co-chairs and the AV WG for their dedication in tackling this challenging issue and the many people who contributed to it through the workshop and public comments. The decision to recommend a pre-event study is extremely difficult, she said. She agreed with the scientific counsel to the AV WG that data are needed, especially data about the safety and immunogenicity of AVA, as plans are made to use the vaccine for children on a large scale if needed. But scientific issues collide with the ethics of testing where there are no safety data in children and no evidence that the testing will provide any benefit to the child, Dr. Berkelman continued. The AV WG has clearly been sensitive to the ethical issues. She suggested HHS conduct a feasibility study to determine under what circumstances parents would be willing to enroll their child in a pre-event AVA study.

It is paramount that the issue receive formal ethical consideration, said Dr. Berkelman, so she proposed that such consideration be included in the recommendation as follows:

> The issue should be referred to a review board to formally address the ethical considerations. This board should include ethicists and public representation. If the ethical considerations are adequately addressed, HHS should develop a plan for and conduct a pre-event study of AVA in children, to include a research IND. HHS

should submit the study protocol to one or more IRBs, and comply with the 21 CFR 50.54 / 45 CFR 46.407 Federal review process. This recommendation should be revisited if new anthrax vaccines or other therapeutic countermeasures become available.

Dr. Quinlisk said she struggled with weighing the risks and benefits of conducting a pre-event study of AVA in children against conducting such a trial when the risk of disease is imminent and the benefits of the vaccine are clear. She said her background influenced her thinking. She did not feel that recommending a pre-event study is an appropriate response to the complex and difficult concerns about the use of AVA in children.

Board members Stephen Cantrill, M.D.; Jane Delgado, Ph.D., M.S.; David Ecker, Ph.D.; and Betty Pfefferbaum, M.D., J.D.; and several ex officio members offered no additional specific comments but generally supported the conclusions and recommendation of the report. Many of them offered thanks to the co-chairs, the AV WG, and the NBSB staff for their hard work on the report and recommendation.

Georges Benjamin, M.D., said he brought the perspective of having served as a health official in Maryland when the anthrax letters were sent to the Brentwood Postal Facility. He and his colleagues pondered the issue and were very concerned about what they would do if children were exposed to anthrax. Dr. Benjamin said the AV WG did a good job of trying to understand the risks and benefits.

Dr. Grabenstein agreed with the spirit of Dr. Berkelman's suggestion and asked whether the Pediatric Advisory Board at the U.S. Food and Drug Administration (FDA) would serve Dr. Berkelman's intent. Dr. Berkelman said she was primarily concerned that the ethical considerations be formally reviewed, whether by an existing or a new group, and that the group should include ethicists and public representatives. Dr. Parker suggested changing the proposed statement from "a review board" to "an appropriate review board."

Action Item
Board members agreed to revise the recommendation as suggested by Dr. Berkelman with the additional change of wording suggested by Dr. Parker.

Public Comments
For a full transcript of the public comments provided at the meeting, please refer to the October 28, 2011, Public Meeting webpage on the NBSB website, available at: http://www.phe.gov/Preparedness/legal/boards/nbsb/meetings/Pages/111028meeting.aspx

Jonathan Newmark of the Joint Program Executive Office for Chemical and Biological Defense at the Department of Defense said his organization is a major purchaser of AVA. If the Board recommends that HHS fund an AVA study in children, he asked, what would such a study look like? Would it involve a reduced schedule or a reduced challenge? He said work is ongoing to reduce the number of doses required. Among children, fewer doses is better, said Colonel Newmark, and he wondered what the

minimum dosage would be to meet the challenge outlined by Dr. Lurie. Dr. Fagbuyi responded that the Board was asked to consider whether a pre-event AVA study should be conducted in children; if HHS decides to conduct such a study, others will consider how to undertake the study.

Steven Fisher asked that the report clarify on pages 12 and 17 and in footnote 36 that no anthrax vaccine was used by the employees of the Brentwood Postal Facility. Page 31 refers to the use of anthrax spores by terrorists; Mr. Fisher said we know that the terrorist attack that involved the anthrax letters was from the United States and delivered by U.S. citizens. On page 14, the report indicates that AVA has been licensed since 1970; Mr. Fisher asserted that question was raised with Judge Sullivan, and ultimately it was deemed that licensing was completed in 2004. Appendix 9 depicts the current package insert for AVA, and Mr. Fisher said that at the July workshop, he noted that the current package insert is not the same as the original that accompanied the anthrax vaccine. *Please see his comments in the transcript.*

Vera Sharav of the Alliance for Human Subjects Protection said, "U.S. law prohibits trials among children if no direct benefit is expected unless there is a serious threat. There is no evidence that anthrax is a serious problem affecting U.S. children." She continued, "The vaccine carries serious risks. Anthrax is only one of many biological agents, so why is there so much emphasis on it?" Ms. Sharav finalized her comment by saying, "antibiotics are the proven treatment of choice for anthrax exposure, not vaccination." *Please see details of her comments in the transcript.*

Meryl Nass said she would be happy to provide a copy of slides from MILVAX and the Vaccine Healthcare Centers describing the rate of 1–2 percent of serious adverse events following adult AVA. Dr. Nass said the Board was almost unanimous in its support, but the American public commented and is unanimously against the recommendation. She said it was interesting to see how much of an "inside-the-beltway" thing the report is. *Please see her comments in the transcript.*

Steve Krug, a physician and representative of the American Academy of Pediatrics, described his medical practice in Chicago and noted that he is definitely not "inside the beltway." He and numerous other physicians participated in the July workshop. On behalf of the Academy, he applauded the AV WG for its excellent work. Dr. Krug noted that there are ethical issues with a pre-exposure trial as well as with trying to understand how the vaccine would work after something happens. He said members of the Academy support the recommendation, and they do not work for the government. Dr. Krug said there are challenging questions, as several people have pointed out, and technical issues to be considered that are very pertinent. He supported the report's recommendation.

Robert Malone said he is a physician-scientist who specializes in vaccines for biodefense. He agreed with the first commenter: if it is possible for the Board to advocate for investment by the National Institute of Allergy and Infectious Diseases in dose-sparing studies of AVA in pediatric populations, he suspects it will be warranted because of the potential for adverse events.

VOTE ON THE REPORT WITH RECOMMENDATIONS

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

Dr. Quinlisk called for a vote to approve the report with the modified recommendation and to send the report to the HHS Secretary. Twelve Board members voted in favor, and one voted against. The report and recommendation were approved by the Board.

> **Recommendation**
> The Board approves transmitting the report *Challenges in the Use of Anthrax Vaccine Adsorbed (AVA) in the Pediatric Population as a Component of Post-Exposure Prophylaxis (PEP)* to the HHS secretary with the following recommendation:
>
> > The NBSB recommends Option 1, in light of the current HHS plan to follow the ACIP recommendations for the use of AVA for PEP following exposure to *B. anthracis* spores:
> >
> > The issue should be referred to an appropriate review board to formally address the ethical considerations. This board should include ethicists and public representation. If the ethical considerations are adequately addressed, HHS should develop a plan for and conduct a pre-event study of AVA in children, to include a research IND. HHS should submit the study protocol to one or more IRBs, and comply with the 21 CFR 50.54 / 45 CFR 46.407 federal review process. This recommendation should be revisited if new anthrax vaccines or other therapeutic countermeasures become available.

Dr. Lurie emphasized for those outside the Board that NBSB is an advisory body, and its recommendations are not binding. She appreciated the thoughtful and hard work involved in crafting the report and recommendation, noting that today's discussion highlighted how complicated the issue is. The Board's work is helpful and will be considered in the Department's efforts, such as the ongoing AVA dose studies in adults planned for the coming months.

Dr. Lurie assured participants that HHS takes the concerns about further evaluation of ethical issues extremely seriously. She noted that HHS is not yet ready to make a decision and will continue to communicate with the Board going forward. She looked forward to continued work with the Board.

NBSB FUTURE TOPICS FOR 2012

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

Dr. Quinlisk summarized six topics raised during Board meetings on which the Board could focus its future efforts:

- 2012 PHEMCE Strategic and Implementation Plan (CAPT Sawyer said Dr. Lurie is considering the best mechanism for getting the Board's input, and a formal presentation may be coming.)
- Planning for unknown threats
- National strategy for development of diagnostics
- E-health or social networks and communication issues, particularly around responses to events
- Integrating the countermeasures research portfolio
- Community resilience in the face of a disaster or attack

Discussion

Dr. Fagbuyi felt that planning for unknown threats is germane to the Board's work, interesting, and important and has implications for adult and pediatric populations in different areas (e.g., urban and rural). He supported it as a priority topic, followed by consideration of the 2012 PHEMCE Strategy and Implementation Plan.

Dr. Parker agreed that planning for unknown threats and the 2012 PHEMCE plan are important. He added that there has been much discussion about building resilience among the American public, and he favored writing a Board report on that topic. Peter Jutro, Ph.D., agreed but added that the discussion of resiliency should go beyond medical considerations.

Dr. Quinlisk said the comments would be taken into account, and the Board would discuss future topics further at its next meeting.

WRAP-UP AND ADJOURNMENT

Leigh Sawyer, D.V.M., M.P.H., CAPT, U.S. Public Health Service; NBSB Executive Director, and Patricia Quinlisk, M.D., M.P.H., Chair, NBSB

CAPT Sawyer announced that the next in-person meeting of the Board is scheduled for January 12, 2012, in the Washington, DC, area. Meeting information will be posted on the NBSB website, in the *Federal Register*, and through the NBSB e-mail distribution list. CAPT Sawyer thanked NBSB staff MacKenzie Robertson and Jomana F. Musmar, M.S., for their hard work.

Dr. Quinlisk adjourned the meeting at 4:01 p.m.

Appendix A – Agenda, NBSB Public Teleconference October 28, 2011

NBSB NATIONAL BIODEFENSE SCIENCE BOARD

PUBLIC TELECONFERENCE
OCTOBER 28, 2011
3:00 p.m. to 4:00 p.m. ET

Questions please email: nbsb@hhs.gov

NOTE: Because this is a teleconference and will be transcribed, please identify yourself when speaking.

3:00 p.m. – 3:10 p.m.	**Administrative Matters** **Call to Order and Conflict of Interest Rules** *Leigh Sawyer, D.V.M., M.P.H.* *Executive Director, National Biodefense Science Board* *CAPT U.S. Public Health Service* *U.S. Department of Health and Human Services* **Agenda Overview and Goals** *Patricia Quinlisk, M.D., M.P.H.* *Chair, National Biodefense Science Board* **Remarks** *Nicole Lurie, M.D., M.S.P.H.* *Assistant Secretary for Preparedness and Response* *Rear Admiral U.S. Public Health Service* *U.S. Department of Health and Human Services*
3:10 p.m. – 3:35 p.m.	**Anthrax Vaccine Working Group Report** **"Challenges in the Use of Anthrax Vaccine Adsorbed (AVA) in the Pediatric Population as a Component of Post-Exposure Prophylaxis (PEP)"** *Daniel Fagbuyi, M.D., FAAP* *Chair, Anthrax Vaccine Working Group* *National Biodefense Science Board* *John S. Parker, M.D., Major General (Retired)* *Co-Chair, Anthrax Vaccine Working Group* *National Biodefense Science Board* **Discussion**
3:35 p.m. – 3:45 p.m.	**Public Comment**

3:45 p.m. – 3:50 p.m.	**Vote on the Report with Recommendations** *Patricia Quinlisk, M.D., M.P.H.* *Chair, National Biodefense Science Board*
3:50 p.m. – 4:00 p.m.	**NBSB Future Topics for 2012** *Patricia Quinlisk, M.D., M.P.H.* *Chair, National Biodefense Science Board*
	Discussion
4:00 p.m.	**Wrap Up and Adjourn** *Patricia Quinlisk, M.D., M.P.H* *Chair, National Biodefense Science Board*

Please refer to the NBSB website for further information, available at
http://www.phe.gov/Preparedness/legal/boards/nbsb/meetings/Pages/default.aspx