TRANSCRIPT

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Meeting 9, Session 3
May 17, 2012
Washington, DC
DR. GUTMANN: So we will hear now from Dr. John Parker. Welcome.

John Parker is Chair of the National Biodefense Science Board. Dr. Parker is also the Senior Vice President of Corporate Development, Chief Medical Officer, Chairman of the Institutional Review Board, and Technical Fellow at Science Applications International Corporation.

Prior to SAIC, Dr. Parker was the Commanding General of the U.S. Army Medical Research and Materiel Command at Ft. Detrick, Maryland, where he was responsible for medical research, product development, technology assessment, and rapid prototyping of medical material.

Dr. Parker has served as Special Assistant to the Secretary of Defense for Medical, Chemical, and Biological Defense and was Deputy for Medical Systems in the Office of The Assistant Secretary for Acquisition, Logistics, and Technology.

He has had leadership responsibilities in disasters, such as the Beirut bombing, Chernobyl, the Berlin Disco bombing, USS Stark recovery, and the management and resolution of the 2001 anthrax letters incident.

Dr. Parker, we are privileged to have you. Thank you for joining us to discuss the National Biodefense
SESSION 3: THE NATIONAL BIODEFENSE
SCIENCE BOARD REPORT

DR. PARKER: Thank you very much. Good morning.
I'm John Parker, and I'm Chairman of the Defense Science Board.

Members of the Commission and Chairman Dr. Gutmann, thank you very much for giving me the opportunity to speak on behalf of the National Biodefense Science Board and talk to you and report on our recommendation on this vital issue concerning medical countermeasures and the safety of our nation's children.

This slide presentation is meant to convey the scope of the task that was given to the National Board. The Board accepted the task. We convened an Anthrax Working Group. We held public meetings, all our work is open to the public, and workshops, inviting all relevant stakeholders.

We listened to expert testimony within and outside the United States Government. We wrote many drafts and deliberated heavily on the final recommendations.

You can all read. I'm not going to read these things. This is to give you a background of who did what and why.
We got a letter from the Assistant Secretary of Preparedness and Response, Rear Admiral Nicole Laurie, and this is the task that she gave the Board.

The Board accepted the task and we formed a working group and we decided that we would investigate these particular issues and I will tell you that the Board does have a say as to whether they will accept a task or not. That's part of a great piece of the deliberation.

The United States Government has a plan and in the event of a release of anthrax spores, the current plan is that we will give antibiotics to the adults and we will vaccinate them with three doses of anthrax vaccine.

The reason for the combination of the anthrax vaccine and the antibiotics is there's deliberative research with nonhuman primates that demonstrate antibiotics alone do not clear us of the anthrax spore and that, even after a reasonable length of antibiotics, those spores could vegetate and reinfect the host.

We were asked to look at several excursions and we came up with two options, conduct a pre-event or don't conduct a pre-event study, and the Board recommended that we would move forward and submit to the Secretary that we should have a pre-event study so that we know about the safety aspects of the vaccine in children. It doesn't give
us any efficacy aspects, except that we would have an
ability to look at the immune component of what protects an
adult and see if we can raise that level in the children.

We debated the ethical and regulatory implications
on how best to obtain valid safety and immunogenicity data
about the anthrax vaccine as part of a post-exposure
prophylaxis for children.

The Board included some of the presenters that are
here today as part of our working groups. Because of the
sensitivity of the involvement of children in research, our
recommendation voiced our desire to have other focused
experts, like yourselves, formally review and address these
issues from an ethical perspective.

As a result, the Secretary has asked you, the
Commission, for ethical advice on the development of
medical countermeasures for children, including anthrax
vaccine post-exposure prophylaxis in children, as part of
your review.

To frame the problem and the elements of our
deliberations with more resolution than I presented in the
slides, I want to mention a few facts.

The NBSB has always been concerned with the
protection of our pediatric population which is our youth
ages zero to 17 years of age. The concern has transcended
all of our work since the Board was initially commissioned
more than four years ago.

If we as a nation are exposed to any weapon of
mass destruction, all of our medical countermeasures will
involve children and other special populations.

The NBSB was not tasked with the evaluation of the
threat and that's very important. It is recognized by the
United States Government as a threat and the Department of
Homeland Security and the National Command authorities have
the responsibility to determine that fact.

Scenarios spoken of previously of an anthrax spore
release have been run and analyzed as part of our national
preparedness efforts. These excursions have demonstrated
that a very large population could be at risk. One such
scenario theoretically exposed over 7.2 million people to
the anthrax spore and that you have to think about that, 25
percent of those are children.

The accepted standard of treatment that I already
talked about is 60 days of antibiotic and three doses of
the anthrax vaccine and I alluded to the research that said
why the combination's important.

We all want a better vaccine. There's no question
about that, but we live today and we have what we have. If
something happened tomorrow, we must use it.
I talked about the government plan for vaccinating the adults and giving antibiotics to the adults, giving antibiotics to the children, and with some parental permission to give the vaccine to the children and then an aliquot of those children that would have gotten the vaccine would have been closely monitored as a subgroup for reactivity and safety, the others would be monitored by their private physician.

The anthrax vaccine is safe in adults. There's been over 10 million doses delivered to about 1.2 million people, mostly in the Armed Forces. There was very good follow-up and monitoring and reporting and, if you read the studies, there are a lot of associated, associated reactions and other things, including one death, but no direct connectivity to the vaccine itself.

We wrestled with the question is it ethical to give children a vaccine that is untested for safety? We explored the protections and reviews to perform a research study involving children. We recognized that there were few drug or vaccine studies involving children across the drug and vaccine domain, and we wanted to reduce the unknown risk to children by studying the safety of the vaccine in a pre-event scientifically-controlled situation.

The Board wanted the United States Government to
be able to tell parents that the vaccine has been studied and safe for children at the time of the event. We cannot do that now.

Under most circumstances, a drug only approved for the adult population by the FDA is given to a child by a very specific prescription by the individual's private practitioner. Generally off-label usage of drugs and vaccines, especially when we know little of its safety, cannot be dispensed by broad policy.

There are respectable sectors of the public who do not believe in the threat, do not believe the vaccines can be safe and effective, and that under no circumstances should children be involved as research subjects, except on a 1:1 basis. For example, a child with cancer being offered a chance for palliation of cure.

It is clear to me and others on the Board that the facts speak loudly. If there is a threat of anthrax release, the Government says yes, and we will need to treat our population in a post-exposure mode with antibiotics and vaccines which we know is safe for adults. We must strive for that same degree of surety regarding the safety of the vaccine for our children.

Should an event happen, we need to safely protect the children and at the same time sustain the credibility
of the United States Government through the Department of Health and Human Services. This credibility is sustained by the United States Government being able to say we tested the vaccine in pediatric populations and this is the result or the United States Government must be able to say we tried to test the vaccine and, after thorough scientific, academic, and ethical reviews, the final recommendation was that we should not do a pre-event study because the risk of the event was less than the potential risk to children should we have to use the vaccine.

The Board is confident that the Commission will help us and our nation deliberate this very complex issue, ensuring safe medical countermeasures for our children.

DR. GUTMANN: Thank you very much, Dr. Parker.

Could I begin with a question and then open it up for members of the Commission? It's a very thoughtful presentation, and we have to thank you and the Board for all the work you've done prior to our deliberating about this.

So you and the Board are strongly supporting safety, having safety trials for a children's vaccine, correct?

DR. PARKER: That is correct. Now let me just give you just a little insight.
DR. GUTMANN: That was just my pre-question but go ahead.

DR. PARKER: Yes. This wasn't easy, and up until this particular task, we've always had unanimous vote on the Board to accept the recommendation. This recommendation was not accepted unanimously. We had one vote in dissent of the recommendation.

But to answer your question directly, because of how our charter is and everything else, yes, the Board feels that we should study this vaccine.

DR. GUTMANN: So I always like to consider the strongest case for the side and so I want to ask you would -- so in my mind, the strongest case for something where there's a possible catastrophic risk, low or uncertain probability about it, and some risk with no direct benefit to children and their parents who are intimately connected to them, would be if the community that's most supportive of moving this forward would volunteer their own children for being part of the test.

Is that something that you, your Board discussed, because I'm not saying that they would be the exclusive children tested because that would push it too far in the other direction perhaps, but if the people who are in favor of this would feel that it was the right thing to do to
volunteer their children, that would send a very strong
signal about the confidence in the rightness of doing this.

Can you comment on that?

DR. PARKER: Yes. First of all, thank you for
that question. It was very well framed.

I have several years as an IRB chair, so social
justice and social equality in studies is terribly
important. If we put that aside, we believe, and the Board
did both openly and in individual discussion, discuss your
question and in my background, I've talked with first
responders, I've talked with families in the Special
Forces, and there are groups, there are groups out there
that would want their families protected as much as they
are protected as they do their job in fear of bringing
something home.

However, that doesn't say that -- that's a fact
but it doesn't say that these people have any obligation
that they should be first-comers to volunteer their
children for a study, but I would say that there are
numbers in our population that would like their family
immunized.

DR. GUTMANN: Raju?

DR. KUCHERLAPATI: Thank you. Thank you for the
report.
So I was wondering whether it is possible to extrapolate from the data from these very large populations of adults that have been vaccinated and not only from anthrax vaccination but other studies that have been done in the past and can we put a measure about the level of confidence that these vaccines would be safe or how safe they would be in children?

DR. PARKER: I might not be the right person to answer that because I'm not an immunologist, but if history were a teacher, I can't think of a vaccine or a drug that we've used in the adult population that has been terribly dangerous to a younger population.

I don't know if we're here to argue that extrapolation, whether extrapolation is proper or not, but one of the reasons that I personally, and I think members of the Board would like to see a test with this, we have a vaccine that works. It is abundantly clear it's a reactive vaccine because of the way it's manufactured. It's not what I would call a clear clean vaccine.

I am concerned with the reactivity that it would have in children and would like to know if that reactivity that we see in adults and we do see reactivity in adults, whether that reactivity is harmful to children.

DR. GUTMANN: Just to get out, could you say a
little bit more about the reactivity we see in adults? And then Anita.

DR. PARKER: As with any vaccine, we see reactivity. Now the reactivity that we see with the anthrax injection goes from local redness and tenderness to severe redness and tenderness, malaise, a few people have had fevers, but a lot of people have complained more about the anthrax injection, say, the flu shot or all injections have reactivity, but if you were to gauge the reactivity on this, some people would say, well, this has no more reactivity than a hepatitis B shot but it is a reactive vaccine. That's how it works and I am immunized and, although I didn't return to a doctor to say it hurt or I got reaction, I accepted what I got, but it hurt, I had reaction, but I knew why, and the ultimate result is very, very important to me.

DR. GUTMANN: Thank you.

DR. PARKER: So I don't know how a child at age two will react.

DR. GUTMANN: We understand that. It's just helpful to see what the range of reactivity in adults is.

DR. PARKER: Yes, and the reactivity about anthrax vaccine has been hyped a little bit because, if you really spread it out on a chart and you looked at reactivities of
most of the vaccines that we give, it's equatable.

DR. GUTMANN: Is there a paper you can refer us to that we could post on this on our website, a scientific paper?

DR. PARKER: I'd have to look back and get back to you.

DR. GUTMANN: Okay.

DR. PARKER: I know during the deliberation, we saw a slide presentation that had a number of the vaccines that we're used to with their reactivities.

DR. GUTMANN: It would be helpful for us to know what the state of scientific knowledge on it is.

Anita Allen?

DR. ALLEN: So the treatment protocol was three doses of vaccine and 60 days of antibiotics, and I wanted to ask you about the antibiotics.

People, I think, are maybe a bit more excited about the anthrax vaccine, but I think we should think about the implications of treatment with antibiotics and apparently neither Ciprofloxacin or Doxycycline are typically given to children and yet those are the antibiotics of choice for dealing with anthrax release.

So could you just comment on the implications, including reactivity-type issues, but the implications of
administering antibiotics, in particular, that family of
antibiotics to children?

DR. PARKER: Generally speaking, the stronger
antibiotics are listed as the antibiotics that would be
used to cover all situations but for an example, the
anthrax that was spread in 2001 in the Hart Senate Office
Building was actually sensitive to penicillin.

So in looking at this range of antibiotics from
penicillin to our fourth and fifth generation
Ciprofloxacin-type antibiotics, the drugs that are
stockpiled are those that will probably be most effective,
given a range of sensitivities, if anthrax were used as a
weapon of mass destruction in a terrorist event.

Taking any antibiotic for 60 days is a chore. I
don't know how many of you have tried it. It's difficult
to have the discipline to take the antibiotic each day and
if you don't have a way of disciplining that, you won't
take it every day. It'll tail off after about 30 days.

So the idea of just antibiotics, we're talking
about a behavioral question and how people react to taking
antibiotics.

DR. GUTMANN: So I'm a little mystified by that
because it's not only a chore, right? People have serious
reactions for that length of time of taking antibiotics and
there's a question of the build-up of resistance to antibiotics in a population, correct? I mean, those are two different questions but I just want you to expand. To say it's a chore makes it sound like it's only a question of whether people will actually take it, have the discipline to take it, but there are more issues than that, medical issues about taking antibiotics for that long.

DR. ALLEN: To be specific, I mean, if you talk about diarrhea, about yeast infections, about allergy, allergic reactions. So what are the implications of these sorts of -- as applied to children, too. How do we think about that, that side of it, the antibiotic side as opposed to the anthrax side?

DR. PARKER: Well, this is an important question and this crosses a lot more domains than just medical countermeasures.

When you take antibiotics for a prolonged period of time, you can have abdominal bloating. You have all the things that you talked about. You might not eat properly because you might be nauseated or you might have -- there's all sorts of complications of taking antibiotics for a long period of time, including changing the flora and perhaps creating opportunities for other types of infections, as you said, yeast infections, etcetera.
The reason in this particular case that 60 days of antibiotics, plus the vaccine, is given is based on some very good nonhuman primate trials and I don't know how many people have taken antibiotics for a long time. I took Doxycycline for a long period of time because I had a large number of labs that did malaria research and so I was on and off long periods of Doxycycline and I can tell you I didn't enjoy it. I did not enjoy it.

DR. MICHAEL: Thanks, General. I was going to just also point out that there's a recent -- actually, in this week's New England Journal that describes the long-term impact of using drugs, like the fluoroquinolone class, of which Cipro and Levo are both, as well as Zithromycin and certainly in the elderly populations, there's a significant increased risk of cardiovascular mortalities with prolonged treatments and these are very common drugs that are obviously used in hospital as well as outpatient practices.

So just the idea that the government response is going to be 7.1 million people in one scenario with a quarter being children with a prolonged exposure to antimicrobials of these classes, I think as we debate the risk of looking at a subgroup of individuals that might be willing to be volunteers in a study, pre-event, and then
contrast that with what looks like to be the default plan, which is to go forward and treat millions of Americans in such a scenario with antimicrobials and concomitant vaccination, I think, at least to me, it leaves significant amount of concern about going into that kind of scenario without having a bit more information about what the long-term impacts are, not just for antimicrobials, *C. difficile* infection, resistance, all the things that we've talked about, but also what the real implications are about the impact of vaccination in children when we simply have no experience.

So at least to me, I mean, I'm a scientist, also a clinician, an internist, not a pediatrician, but it leaves me a lot of pause.

DR. PARKER: I'm glad we are thinking people. It gives us all great heart and we're dealing with a particular type of a scenario with anthrax spores and I think Alex might speak better to this than I, but there's the initial plume and the initial exposure and we're treating those people but there's another part of how long does it take to clean up all those spores, and one of the reasons for the antibiotics plus the vaccine is that the fact that these spores will settle down but as we walk around or the wind moves, there's a re-aerosolization of
these spores and hence an opportunity to reinfect.

So what we're doing after an event is not only

treating people immediately for their post-exposure but
giving them some resilience as we decontaminate the area.

DR. GUTMANN: I want to thank you, but I'm going
to just put a pause on this so we can all welcome a very
special guest.

[Session interrupted by a visit from Secretary
Sebelius. Please see notes from the “Distinguished Speaker”
session for a transcript of Secretary Sebelius’s remarks.]

DR. GUTMANN: With that preface, I'm going to turn
it -- Jim has a question. So we're back in business.

DR. WAGNER: We probably only have a few more
minutes to grill you before the roundtable and I hope
you'll be staying for the roundtable.

I just wanted to clarify, is it indeed the case
that the Board assumed that the risk of an event -- the
Board passed no judgment on the risks of an event, just
assumed that the risk of the event is non-zero, and then
answered the -- made their recommendations subject to that.
I guess for our Commission, is that something -- is that
the same place we are comfortable starting from?
DR. PARKER: Your assumption's correct. We did two things upfront. Did not debate the threat. We accepted the threat laid down by the people that are paid well beyond my level to analyze and prioritize our threats. The risk of that threat, I believe if they do have any sort of a number, it is greater than zero, or it's not a threat. But the absolute risk was not debated because we assumed that that went along with the threat.

But in that same context, we all recognized that it's a risk to the nation but when you boil the nation down to an individual, that risk does change. So the probability of any one of our children being involved is much less than the national risk, but we don't know what those numbers are.

Yes, we did discuss that but we -- putting that aside, though, that if there is a risk and it happens to an area of our country and any children or adults are involved, that's 100 percent for those people, so we made our recommendation on the basis of that.

DR. WAGNER: I just think that's critical for us to establish and imagine how we think. Obviously if the risk of -- I think it is obvious. If the risk of event is greater than the risk of an untested deployment or an untested response and the risk of an untested response, in
turn, is greater than the risk of testing, that gives us a pattern.

DR. GUTMANN: Let me just read something from the public, members of the public, actually. Do I have Dr. Fagbuyi?

DR. FAGBUYI: Yeah.

DR. GUTMANN: Did I actually pronounce your name correctly?

DR. FAGBUYI: Fagbuyi.

DR. GUTMANN: Okay. Let me read what -- it's really a response, in some sense, to my question. "The Medical Director of Children's National Medical Center, so antibiotic side effects in children include nausea, vomiting, diarrhea, fungal infections, Stevens-Johnsons Syndrome; challenges to children with special needs, G-tube, kids with allergies to medications, resistance risk all can preclude use of antibiotics."

That's important extension. Did you want to add anything to that, briefly?

DR. FAGBUYI: In regards to the antibiotics.

DR. GUTMANN: Here.

DR. FAGBUYI: Sorry. Thank you. Not that I need a mike, but...

I think we were talking about the risks of
antibiotics.

DR. GUTMANN: Yes.

DR. FAGBUYI: With this whole 60-day regimen, it's not something to kind of wink at, and as my colleague John Parker had mentioned, that this is a chore. But I think under that word was the details of what you asked with regard to allergic reactions. Stevens-Johnson Syndrome is not something to play with. It's also life threatening, also. So there are other things that can preclude the use of antibiotics in compliance with 60 days.

DR. GUTMANN: That's what I was asking. I just wanted the notion of it being a chore made it sound like it was simply a question of people's will to continue taking it, but it's significantly more than that.

Alex, did you want to say something briefly and then I'm going to wrap?

DR. GARZA: Right. Very briefly. First, thank you, General, for your service to the country, too. I don't think we say that enough of our Armed Forces people. I too am a recipient of the vaccine so, you know, maybe we can commiserate over our arm soreness later.

But one thing that I did want to ask you, though, is you said there was one dissenter and I was wondering what the issues were with the dissenter?
DR. PARKER: Would you say -- I'm sorry.

DR. GARZA: You said when you took the vote, they're usually unanimous, you did have one dissent.

DR. GUTMANN: What were the issues?

DR. GARZA: What were the issues of the person who is dissenting?

DR. PARKER: I'm really not in a position to speak for the individual. It's not in the manner of the Board to interrogate someone who has a vote that is not in concert with the rest. We don't have an ability for a minority to form an opinion. But I do know the individual pretty well and I think in all honesty this member looked at the risks of the event, looked at the absolute need of having this safety data and the idea of involving children in this particular research and that member just couldn't put that together for a "yay" vote on the recommendation.

The other thing that that brings up is, you know, when people talk about threat, you and I who are in the business, and Dr. Michael, who are constantly in the business or constantly in the weapons of mass destruction defense business, it's a big deal and all of these things become threats.

But if we live in Kansas, a tornado or a drought may surely out walk any threat that we talk about in these
erudite kind of situations.

But, yes, one of the wonderful things about the Board is that there is no coercion. We don't water board and we don't ask people why they -- unless they want to express it, why they feel a certain way. So I was very comfortable with the individual saying, no, to the recommendation.

DR. GARZA: Don't misinterpret my question. I was really wanted to make sure that there wasn't something that we hadn't thought about before.

DR. GUTMANN: Your presentation and your response to questions has been marvelous and we really do thank you and realize that we have a tall order coming in deliberating on the basis of what your Board did. So on behalf of everybody, thank you, very, very much.

(Applause)