



Presidential Commission
for the Study of Bioethical Issues

TRANSCRIPT

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1 DR. GUTMANN: So we will hear now from Dr. John
2 Parker. Welcome.

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

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

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

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

23 Dr. Parker, we are privileged to have you. Thank
24 you for joining us to discuss the National Biodefense

1 Science Board's work.

2 SESSION 3: THE NATIONAL BIODEFENSE

3 SCIENCE BOARD REPORT

4 DR. PARKER: Thank you very much. Good morning.

5 I'm John Parker, and I'm Chairman of the Defense Science
6 Board.

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

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

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

22 You can all read. I'm not going to read these
23 things. This is to give you a background of who did what
24 and why.

1 We got a letter from the Assistant Secretary of
2 Preparedness and Response, Rear Admiral Nicole Laurie, and
3 this is the task that she gave the Board.

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

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

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

19 We were asked to look at several excursions and we
20 came up with two options, conduct a pre-event or don't
21 conduct a pre-event study, and the Board recommended that
22 we would move forward and submit to the Secretary that we
23 should have a pre-event study so that we know about the
24 safety aspects of the vaccine in children. It doesn't give

1 us any efficacy aspects, except that we would have an
2 ability to look at the immune component of what protects an
3 adult and see if we can raise that level in the children.

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

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

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

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

22 The NBSB has always been concerned with the
23 protection of our pediatric population which is our youth
24 ages zero to 17 years of age. The concern has transcended

1 all of our work since the Board was initially commissioned
2 more than four years ago.

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

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

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

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

22 We all want a better vaccine. There's no question
23 about that, but we live today and we have what we have. If
24 something happened tomorrow, we must use it.

1 I talked about the government plan for vaccinating
2 the adults and giving antibiotics to the adults, giving
3 antibiotics to the children, and with some parental
4 permission to give the vaccine to the children and then an
5 aliquot of those children that would have gotten the
6 vaccine would have been closely monitored as a subgroup for
7 reactivity and safety, the others would be monitored by
8 their private physician.

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

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

24 The Board wanted the United States Government to

1 be able to tell parents that the vaccine has been studied
2 and safe for children at the time of the event. We cannot
3 do that now.

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

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

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

23 Should an event happen, we need to safely protect
24 the children and at the same time sustain the credibility

1 of the United States Government through the Department of
2 Health and Human Services. This credibility is sustained
3 by the United States Government being able to say we tested
4 the vaccine in pediatric populations and this is the result
5 or the United States Government must be able to say we
6 tried to test the vaccine and, after thorough scientific,
7 academic, and ethical reviews, the final recommendation was
8 that we should not do a pre-event study because the risk of
9 the event was less than the potential risk to children
10 should we have to use the vaccine.

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

14 DR. GUTMANN: Thank you very much, Dr. Parker.
15 Could I begin with a question and then open it up for
16 members of the Commission? It's a very thoughtful
17 presentation, and we have to thank you and the Board for
18 all the work you've done prior to our deliberating about
19 this.

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

23 DR. PARKER: That is correct. Now let me just
24 give you just a little insight.

1 DR. GUTMANN: That was just my pre-question but go
2 ahead.

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

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

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

20 Is that something that you, your Board discussed,
21 because I'm not saying that they would be the exclusive
22 children tested because that would push it too far in the
23 other direction perhaps, but if the people who are in favor
24 of this would feel that it was the right thing to do to

1 volunteer their children, that would send a very strong
2 signal about the confidence in the rightness of doing this.

3 Can you comment on that?

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

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

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

22 DR. GUTMANN: Raju?

23 DR. KUCHERLAPATI: Thank you. Thank you for the
24 report.

1 So I was wondering whether it is possible to
2 extrapolate from the data from these very large populations
3 of adults that have been vaccinated and not only from
4 anthrax vaccination but other studies that have been done
5 in the past and can we put a measure about the level of
6 confidence that these vaccines would be safe or how safe
7 they would be in children?

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

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

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

24 DR. GUTMANN: Just to get out, could you say a

1 little bit more about the reactivity we see in adults? And
2 then Anita.

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

17 DR. GUTMANN: Thank you.

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

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

22 DR. PARKER: Yes, and the reactivity about anthrax
23 vaccine has been hyped a little bit because, if you really
24 spread it out on a chart and you looked at reactivities of

1 most of the vaccines that we give, it's equatable.

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

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

7 DR. GUTMANN: Okay.

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

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

13 Anita Allen?

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

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

23 So could you just comment on the implications,
24 including reactivity-type issues, but the implications of

1 administering antibiotics, in particular, that family of
2 antibiotics to children?

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

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

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

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

22 DR. GUTMANN: So I'm a little mystified by that
23 because it's not only a chore, right? People have serious
24 reactions for that length of time of taking antibiotics and

1 there's a question of the build-up of resistance to
2 antibiotics in a population, correct? I mean, those are
3 two different questions but I just want you to expand. To
4 say it's a chore makes it sound like it's only a question
5 of whether people will actually take it, have the
6 discipline to take it, but there are more issues than that,
7 medical issues about taking antibiotics for that long.

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

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

17 When you take antibiotics for a prolonged period
18 of time, you can have abdominal bloating. You have all the
19 things that you talked about. You might not eat properly
20 because you might be nauseated or you might have -- there's
21 all sorts of complications of taking antibiotics for a long
22 period of time, including changing the flora and perhaps
23 creating opportunities for other types of infections, as
24 you said, yeast infections, etcetera.

1 The reason in this particular case that 60 days of
2 antibiotics, plus the vaccine, is given is based on some
3 very good nonhuman primate trials and I don't know how many
4 people have taken antibiotics for a long time. I took
5 Doxycycline for a long period of time because I had a large
6 number of labs that did malaria research and so I was on
7 and off long periods of Doxycycline and I can tell you I
8 didn't enjoy it. I did not enjoy it.

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

19 So just the idea that the government response is
20 going to be 7.1 million people in one scenario with a
21 quarter being children with a prolonged exposure to
22 antimicrobials of these classes, I think as we debate the
23 risk of looking at a subgroup of individuals that might be
24 willing to be volunteers in a study, pre-event, and then

1 contrast that with what looks like to be the default plan,
2 which is to go forward and treat millions of Americans in
3 such a scenario with antimicrobials and concomitant
4 vaccination, I think, at least to me, it leaves significant
5 amount of concern about going into that kind of scenario
6 without having a bit more information about what the
7 long-term impacts are, not just for antimicrobials, C.
8 difficile infection, resistance, all the things that we've
9 talked about, but also what the real implications are about
10 the impact of vaccination in children when we simply have
11 no experience.

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

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

1 these spores and hence an opportunity to reinfect.

2 So what we're doing after an event is not only
3 treating people immediately for their post-exposure but
4 giving them some resilience as we decontaminate the area.

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

8

9 [Session interrupted by a visit from Secretary
10 Sebelius. Please see notes from the "Distinguished Speaker"
11 session for a transcript of Secretary Sebelius's remarks.]

12

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

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

18 I just wanted to clarify, is it indeed the case
19 that the Board assumed that the risk of an event -- the
20 Board passed no judgment on the risks of an event, just
21 assumed that the risk of the event is non-zero, and then
22 answered the -- made their recommendations subject to that.
23 I guess for our Commission, is that something -- is that
24 the same place we are comfortable starting from?

1 DR. PARKER: Your assumption's correct. We did
2 two things upfront. Did not debate the threat. We
3 accepted the threat laid down by the people that are paid
4 well beyond my level to analyze and prioritize our threats.
5 The risk of that threat, I believe if they do have any sort
6 of a number, it is greater than zero, or it's not a threat.
7 But the absolute risk was not debated because we assumed
8 that that went along with the threat.

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

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

20 DR. WAGNER: I just think that's critical for us
21 to establish and imagine how we think. Obviously if the
22 risk of -- I think it is obvious. If the risk of event is
23 greater than the risk of an untested deployment or an
24 untested response and the risk of an untested response, in

1 turn, is greater than the risk of testing, that gives us a
2 pattern.

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

6 DR. FAGBUYI: Yeah.

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

9 DR. FAGBUYI: Fagbuyi.

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

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

20 DR. FAGBUYI: In regards to the antibiotics.

21 DR. GUTMANN: Here.

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

24 I think we were talking about the risks of

1 antibiotics.

2 DR. GUTMANN: Yes.

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

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

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

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

22 But one thing that I did want to ask you, though,
23 is you said there was one dissenter and I was wondering
24 what the issues were with the dissenter?

1 DR. PARKER: Would you say -- I'm sorry.

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

4 DR. GUTMANN: What were the issues?

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

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

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

23 But if we live in Kansas, a tornado or a drought
24 may surely out walk any threat that we talk about in these

1 erudite kind of situations.

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

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

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

16 (Applause)