

UNITED STATES OF AMERICA

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ARMED FORCES EPIDEMIOLOGICAL BOARD

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MEETING

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TUESDAY, MAY 21, 2002

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GAITHERSBURG, MARYLAND

The Board met at the Gaithersburg Marriott Hotel
9751 Washington Boulevard, Gaithersburg, Maryland, at
1:10 p.m., Dr. Stephen Ostroff, presiding.

BOARD MEMBERS:

STEPHEN M. OSTROFF, M.D., President

LINDA ALEXANDER, Ph.D.

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KEVIN M. PATRICK, M.D.

GREGORY A. POLAND, M.D.

CAROL RUNYAN, Ph.D.

DENNIS F. SHANAHAN, M.D.

ROBERT E. SHOPE, M.D.

LtCOL. RICK RIDDLE, USAF

AFEB Executive Secretary

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COL. J. GUNZENHAUSER, MC, USA
CAPT. K.W. SCHOR, MC, USN
CAPT. ALAN J. YUND, MC, USN

FLAG STAFF OFFICERS:

RADM (Sel) STEVEN HART, MC, USN
ADM. RICHARD WYATT

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P-R-O-C-E-E-D-I-N-G-S

(1:10 p.m.)

DR. OSTROFF: Welcome back. It's nice to see the entire Board together in session and, as I mentioned this morning, the format for this meeting is somewhat unusual in that the tradition of the Board is usually to go through the Preventive Medicine updates at the beginning of the meeting, but based on the way the schedule worked out we had to defer those presentations until tomorrow morning. And it's great that we have so many Board Members in attendance.

Let me introduce Adm. Wyatt from the Surgeon General's office, and also it's good to see Adm. Hart again in attendance. I think what we'll do before we get started is if we could just go around the room and have everyone introduce themselves at the table, since not everyone was together this morning.

CAPT. YUND: My name is Jeff Yund, and I'm a Preventive Medicine Officer with the Navy Surgeon General.

CAPT. SCHOR: Hi. I'm Ken Schor, from the Headquarters Marine Corps.

LtCOL. FENSOM: I'm Col. Maureen Fensom, Liaison Officer.

MAJ. BALOUGH: Brian Balough, Joint Staff

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1 Health Services Support Division.

2 DR. HAYWOOD: Julian Haywood.

3 DR. RUNYAN: Carol Runyan, University of
4 North Carolina.

5 DR. ALEXANDER: Linda Alexander.

6 DR. PATRICK: Kevin Patrick, San Diego
7 State University.

8 DR. NESS: Roberta Ness, University of
9 Pittsburgh.

10 CAPT. SMITH: Jack Smith, Principal
11 Director for Clinical Program Policy and Health
12 Affairs.

13 RADM. HART: Steve Hart.

14 DR. WYATT: Richard Wyatt, Office of the
15 Surgeon General and NIH.

16 LtCOL. RIDDLE: Rick Riddle, Executive
17 Secretary for the Armed Forces EPI Board.

18 DR. OSTROFF: Steve Ostroff, Board
19 President, from the Centers for Disease Control and
20 Prevention.

21 MS. EMBREY: Ellen Embrey. I'm the
22 Designated Federal Official to the Board, and Dr.
23 Winkenwerder's Deputy for Force Health Protection and
24 Readiness.

25 DR. IACONO-CONNORS: I'm Lauren Iacono-

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1 Connors. I'm with the Center for Biologics Evaluation
2 and Research at the FDA.

3 DR. BERG: Bill Berg, Director of the
4 Hampton, Virginia Health Department.

5 DR. POLAND: Greg Poland, from Mayo
6 Clinic, Rochester.

7 DR. GRAY: Greg Gray, University of Iowa.

8 DR. HERBOLD: John Herbold, University of
9 Texas, School of Public Health.

10 DR. MORRIS: Glen Morris, University of
11 Maryland.

12 DR. CLINE: Barney Cline, Tulane
13 University.

14 DR. MALMUD: Leon Malmud, Temple
15 University.

16 DR. SHANAHAN: Dennis Shanahan, Carlsbad,
17 California.

18 DR. FORSTER: Jean Forster, University of
19 Minnesota.

20 DR. CATTANI: Jacqueline Cattani,
21 University of South Florida.

22 DR. CAMPBELL: Doug Campbell, from Durham,
23 North Carolina.

24 CDR. LUDWIG: Cdr. Sharon Ludwig, from
25 Headquarters, U.S. Coast Guard.

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1 CAPT. BROWN: David Brown, British Liaison
2 Officer for Gulf and Deployment Health, standing in
3 for my Army colleague, Col. Mike Staunton.

4 DR. OSTROFF: Thank you very much. This
5 afternoon we have a number of presentations which
6 focus on vaccine and therapeutic issues related to
7 biological weapons threats, and not all of you were in
8 attendance this morning in the classified briefings,
9 but as I pointed out, if you turn to Tab 5, there is a
10 very specific directive from Department of Defense
11 which was developed in 1993, which requires us on an
12 annual basis to review the threat list. And if you
13 turn to page 6 of that document, it very specifically
14 says that the AFEB, in consultation with the DOD
15 Executive Agent and the Secretaries of the military
16 departments, annually will identify to Health Affairs
17 vaccines available to protect against validated
18 biological warfare threat agents, and recommend
19 appropriate immunization protocols. And this issue
20 has certainly taken on greater urgency than it has in
21 previous years because of everything that's transpired
22 within the past year and the fact that there are
23 potentially new vaccine issues which weren't available
24 in recent years, especially those related to smallpox.
25 And so there is a lot to be discussed during the

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1 afternoon session and the remainder of the meeting.

2 Our first presentation will be by LtCol.
3 Debra Schnelle, who is the Medical NBC Staff Officer
4 at the Office of the Surgeon General, and she will
5 begin this session and present the question to the
6 Board and the status of the current risk matrix. Col.
7 Schnelle.

8 LtCOL. SCHNELLE: Good afternoon. It's
9 always an honor and a privilege to be asked to address
10 this distinguished body, and the issue I'd like to
11 bring to your attention is an issue I've been working
12 on since I last spoke with you in May of '01. Next
13 slide, please.

14 (Slide)

15 The question you are being asked to
16 consider is to provide recommendations on vaccines and
17 immunizations required to address the validated BW
18 threats. This question addresses the more fundamental
19 question of does our medical readiness correspond and
20 address the current BW threat. Next, please.

21 (Slide)

22 I'll touch on briefly where we've been, a
23 sense of where we are now especially in the light of
24 9/11, and then talk a bit about an emerging concept
25 that I'd like to present to you for your review and

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1 analysis, and then i'll summarize statements being
2 recommended by the Biological Medical Advisory
3 Committee of NATO. Next, please.

4 (Slide)

5 As your Chair recognized, Department of
6 Defense Directive direct all of us to participate in
7 this exercise in reviewing the vaccines and
8 therapeutics against BW threat agents, and in '99 this
9 body recommended that a medical risk assessment be
10 conducted of the BW threat list. Last May, we
11 presented to you the product of that work and we
12 presented an integrated approach, it's an intelligence
13 assessment and a medical risk assessment of the BW
14 threat list. Next.

15 (Slide)

16 I'll just briefly review that project for
17 those of you who might not have been present at that
18 time. Again, our concept was to integrate the two
19 different assessments. Next, please.

20 (Slide)

21 We convened two separate panels, one a
22 body of military subject matter experts and one a body
23 of scientific subject matter experts, to integrate the
24 operational effectiveness measures and the BW threat
25 assessment measures. Next, please.

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1 (Slide)

2 And next?

3 (Slide)

4 I'm sure this chart will be even more
5 readable on your small handout, but essentially this
6 is the scoring in accordance with the operational
7 measures defined and weighted by the military panel of
8 the agents on the BW threat list. This is to include
9 some of the agents of the scientific panel simply we
10 are deeply interested in scoring and evaluating as
11 well. Next, please.

12 (Slide)

13 This is the same data presented as a bar
14 chart. The bar at the top represents the maximum case
15 of -- maximizing every criteria in the worst case
16 possible, so all bars underneath that reflect a
17 relative assessment compared to the maximum worst
18 case. Next, please.

19 (Slide)

20 And this is the product that we presented
21 to you last year. Again, I'm sure that it's perfectly
22 readable both in your handouts and on the screen, but
23 essentially, again, on top is the intelligence
24 assessment of the threat from, on the right, low to
25 high -- this is top, left -- the reds included, of

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1 course -- and on the vertical axis we have the medical
2 risk assessment. Next, please.

3 (Slide)

4 So, as I understand it, this body endorsed
5 this method and this product in September '01.
6 Unfortunately, for some reason I now can't remember I
7 was unable to attend, it's widely applied and
8 informally used by many different headquarters. I had
9 a briefing sent to me of some subordinate unit in the
10 Air Force Seventh PAC Fleet who was using the product.
11 This is good. And I have personally presented in
12 several different meetings and received some very
13 useful feedback on it.

14 But one of the meetings, a meeting with
15 Dr. Seth Caras (phonetic) at the National Defense
16 University in July, actually made me relook and re-
17 evaluate this. We've always known that this was only
18 a first step in a more in-depth method. But what Dr.
19 Carus asked is how does this apply to address the
20 other aspects of the medical threat? And my first
21 thought was, "I don't know, this is just a task for
22 me, I wasn't going to change the world with the task,
23 I just did the work", but I went off and thought about
24 it, and actually the events of 9/11 proved quite
25 illuminating. Next, please.

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1 (Slide)

2 Concurrent with my meeting with Dr. Carus,
3 the QDR was ongoing, and it was directing a shift from
4 threat-based planning and concept to capability-based
5 concept. Of course, we had the events of 11 September.
6 Shortly thereafter, the GAO released a report in which
7 their first recommendation was that "DOD had not yet
8 addressed the gap between the validated BW threat and
9 the current level of medical readiness". And the
10 Surgeon General's Office was tasked to perform a CBRN
11 hazard analysis by May '02, which is the concept I'm
12 basically presenting to you in draft form today.
13 Next, please.

14 (Slide)

15 This is the traditional definition,
16 according to military doctrine -- joint publications
17 from the staff doctrine -- of threat, vulnerability
18 and capability. Threat is essentially defined as the
19 combination of the enemy intent and capability. The
20 intelligence community assesses intent by review of
21 the enemy doctrine. They assess the enemy capability
22 by review of the enemy's possession of the means to
23 produce the BW agent, to weaponize the BW agent, and
24 to deliver the BW agent. This is the classic military
25 doctrine.

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1 When we assess the capabilities of our own
2 forces, we are led to understand, ideally, our
3 vulnerability -- what particular agent combination of
4 delivery system, weaponization and agent are we most
5 vulnerable to -- and then, in theory, we would then
6 develop the appropriate capability to address that
7 vulnerability.

8 I think the events of 9/11 and QDR
9 direction that was already emerging prior to then
10 illustrates that we need to have a broader
11 understanding of these three concepts in order to
12 fully address the threat. Certainly, no one
13 identified box-cutters as the specific threat that
14 exploited the vulnerability of people's assumptions
15 about the nature of highjacking, and to expect that we
16 would be able to identify all possible asymmetric
17 scenarios is perhaps unrealistic. Next, please.

18 (Slide)

19 Before we go any further, let's address,
20 or at least summarize, the different approaches to
21 defining the BW threat or the NBC threat, in general.

22 There are many different lists available. If you look
23 at the international community, I think NATO is
24 currently operating under, in different stovepipes,
25 three different BW threat lists. There are different

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1 requirements, but none of them really address the full
2 spectrum of the CBRN threat.

3 For one thing, the list failed to rule out
4 -- because Soman (phonetic) is not listed as a threat
5 in the Korean peninsula, can you thus assume that it
6 is not present? No. It's only positive
7 reinforcement. If the intelligence community tells
8 you Soman is present, then you certainly have to
9 prepare for it, but they will not tell you it is not
10 present, so you still have to prepare for it.

11 And, also, the listing of threats and
12 their analyses reinforces the concept that we have to
13 plan simultaneously for every single threat and
14 address each of them individually. Next, please.

15 (Slide)

16 The Chairman's BW Threat List was
17 primarily developed to support acquisition, although I
18 am anecdotally told that it was developed by people in
19 the Army Surgeon General's Office of Health Affairs
20 and the Joint Staff because, without a directive and a
21 Threat List, they couldn't emphasize the need for
22 anthrax immunizations. So, first, they did the
23 directive, then they did the threat list, then they
24 got anthrax immunization. I have no idea whether
25 that's true or not, but it makes a great story. And,

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1 of course, last year we developed a medical risk
2 assessment of that same list.

3 The Canadian, U.K., U.S. Trilateral Group,
4 more informally known as CANUKUS CBR MOU -- that would
5 stand for CHEM/BIO/RAD Memorandum of Understanding, I
6 believe -- have also done an international task force
7 to assess and prioritize the BW threat. And, of
8 course, CDC has developed their own Critical
9 Biological Agent List, which you can find on their Web
10 site. Next, please.

11 (Slide)

12 I think one of the flaws in the threat
13 list is the it tries to be all things to all people.
14 Certainly, the acquisition people need guidance on
15 what is the appropriate vaccine or antibiotic to
16 develop, but the strategic policy people also need to
17 know how to orient our preparations in order to
18 address our long-term national military strategy. And
19 speaking as someone who works primarily at the
20 operational level, I need to know how to prioritize,
21 plan, and focus my efforts. In case it's not
22 perfectly obvious to everyone, we cannot do everything
23 at the same time with the current staffing, and since
24 I don't see millions of people rushing to join my
25 headquarters, we're going to have to prioritize and

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1 focus.

2 And, finally, the CINC representatives
3 repeatedly tell us that they need to have more
4 concrete guidance so that they, in turn, can be more
5 effective in addressing potential threats in their
6 area of operation. Next, please.

7 (Slide)

8 So we reviewed this definition already.
9 Next.

10 (Slide)

11 At this point, especially for those of you
12 who are not privileged to receive the DIA presentation
13 on the BW threat, I'd like to just emphasize the
14 breadth of the BW threat. As we sated earlier, you
15 have to account for all possible agents. Then you
16 have to account for all possible delivery systems, and
17 you have to account for all possible scenarios or
18 targets of interest. It is not always obvious to the
19 nonmedical audience that you don't need a fancy, high-
20 tech, long-range missile system to deliver a BW agent.

21 One of the most devastating possible scenarios is
22 infecting a few volunteers with smallpox and sending
23 them out to spend a lot of time in airport hubs in the
24 U.S. Pre-9/11, this would have been inconceivable.
25 Who would volunteer for such a thing? Well, evidence

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1 would indicate they might not have been volunteers,
2 anyway. Next, please.

3 (Slide)

4 In addition to each of these hazards, you
5 also have a breadth of their application ranging from
6 naturally occurring endemic disease to a massive
7 weaponized military saturation of the battlefield
8 through use of a BW-weaponized agent, and all
9 possibilities in between. So we have a diversity of
10 hazards and we have a diversity of their employment.
11 Next, please.

12 (Slide)

13 As stated earlier, almost all of the lists
14 have these weaknesses. All agents are treated
15 equally, thus, leading to the chronic cry of, "Yes,
16 Ricin is a high threat, but who cares". And, finally,
17 it does not allow people to rule out possible threat,
18 and neither does it account for the unknowns. I was
19 not able to be present for the DIA brief this morning,
20 but their briefing as of last year addressed only
21 state actors, not nonstate actors. The threats
22 presented by terrorists or nonstate actors who are
23 able to procure BW agent delivery systems is not
24 typically a part of the briefing, although it may have
25 been this morning. Was it? Yes? Oh, good. I

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1 wouldn't have been surprised if it was. But the
2 tracking of the transfers between state actors and
3 nonstate actors is very, very difficult. Next,
4 please.

5 (Slide)

6 So the concept I'd like to present to you
7 is sort of a picture of where we need to be, and I
8 will be perfectly honest and tell you this is not
9 fully fleshed out yet, so please feel free to offer
10 your comments. Next, please.

11 (Slide)

12 The basic concept is to analyze using
13 existing analytical tools chem/bio/rad/nuke hazards as
14 they are actualized as events in a quantitative way so
15 that we can then assess the order of magnitude of the
16 required medical capabilities for an effective
17 response. I was actually able to say "actualized" as
18 an event in that sentence, so I'm proud of that
19 particular presentation, but this definition has
20 shifted. In fact, the more we work on this project,
21 the more we become convinced that the title "Hazard
22 Analysis" is actually quite misleading, since our work
23 and our analysis spans from the identification of the
24 hazard all the way up to the definition of "medical
25 response strategies", so we're in search of a good

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1 title at the moment. Next, please.

2 (Slide)

3 We see the same chart that we addressed
4 before, but each of these concepts has been broadened.

5 The outbreaks of the threat must include not only
6 enemy intent and capability, but the risk from the
7 CBRN hazard in becoming an event. The damage that
8 results from that event is expressed as an aspect of
9 the vulnerability, as is the normal operating
10 functions of the unit or system. So, vulnerability is
11 an assessment of potential damage to your system and
12 an assessment of the normal operating conditions of
13 that system.

14 Finally, the capability must address an
15 aggregate of your facilities, expertise, personnel and
16 resources, your competency which is your capability of
17 applying those resources in a way that allows you to
18 execute a specified course of action. Next, please.

19 (Slide)

20 We based our thinking on diverse sources.

21 The Medical Risk Assessment was a primary source,
22 And I do not mean to deride of our work on the Medical
23 Risk Assessment, it is more like renovating your
24 house. You do all the hard work of renovating your
25 dining room and it looks gorgeous. And it is at that

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1 point that you realize that your living room really
2 looks like crap. So, by taking the step for with
3 Medical Risk Assessment that we took, I think it shed
4 light on many different aspects of our thinking about
5 medical response, threat and capability, and that
6 thinking has continued since that time.

7 We've also incorporated the guidelines
8 from the World Association of Disaster and Emergency
9 Medicine where they tried to establish an intellectual
10 framework for defining, assessing and evaluating
11 medical responses to disasters, to all disasters, on
12 an even playing field.

13 And one of our first challenges was
14 understanding that all of these terms are used
15 interchangeably and very confusingly. I was actually
16 in a meeting fairly recently where we were trying to
17 define how to improve the Army's capabilities to
18 address chem/bio/rad/nuke. And in that meeting, the
19 word "capability" was used to refer to detectors,
20 medical surveillance, and NBC as well. So there was a
21 great deal of confusion. In fact, I even look back on
22 our Medical Risk Assessment project and see that our
23 criteria of operational effectiveness combined
24 measures that I would now see as characteristics of
25 the hazards and measures that I now see are actually

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1 medical capabilities. So, even in that early work,
2 there was some confusion about the difference between
3 hazards and capabilities. Next, please.

4 (Slide)

5 We use primarily a NATO medical planning
6 guide for NBC battle casualties. It's informally
7 known as AMED P8. The AMED refers to Allied Medical
8 Publication, not to Army Medical Department, and a
9 modeling simulation tool that applies that concept and
10 produces outputs, quantitative outputs called NBC
11 CREST. Next, please.

12 (Slide)

13 So the concept of threat now embodies the
14 hazard risk and the event, and, as earlier stated,
15 this is a very, very broad spectrum since you have
16 many diverse agents, many diverse ways that they can
17 become actualized in event, and you have to address
18 them all. Next, please.

19 (Slide)

20 Vulnerability is an assessment of the
21 damage, disruption of your normal operating
22 conditions, and a measure of the impact of that
23 damage, both severity and extent. Next, please.

24 (Slide)

25 And capability has to encompass specified

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1 course of action or potential courses of action,
2 competency, and an aggregate of facilities, expertise
3 and resources. It's very misleading to conceive of a
4 capability as being a particular widget or object, or
5 a particular thought. It's actually much more
6 complicated and harder than that in that you're going
7 to have to make decisions about the application of
8 diverse resources and personnel. Next, please.

9 (Slide)

10 Hazards can be defined in terms of their
11 characteristics, and we actually did a fairly good job
12 of both defining and scaling, as in waiting or
13 evaluating these characteristics, with the Medical
14 Risk Assessment project. Next, please.

15 (Slide)

16 Events are more difficult to define, and
17 we found ourselves always taking bouncing back between
18 event and damage, event and damage, which just
19 illustrates how confused all our thinking is. So,
20 typically, we refer to an event when we talk about
21 scenarios, but I would like to offer that we need to
22 define the event much more narrowly, much more
23 specifically, and at this point I'm relying on the
24 definition set forth by the World Association of
25 Disaster and Emergency Medicine, really fondly known

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1 as WADEM nowadays. So we look at events from their
2 scope, from the perspective of their scope, their
3 duration, and their onset, in the hope, the original
4 hope -- which still persists -- is that if we define
5 them in these general ways, we can find a consistent
6 way of evaluating a wide, broad diversity of events in
7 a way that allows us to get a handle on all of that
8 diversity. Next, please.

9 (Slide)

10 Damage, in particular, is broader than the
11 increased morbidity and mortality that medics
12 frequently focus on. It also looks at the compromised
13 functions of our food and water supply system,
14 facilities, communication, transportation, and so
15 forth. Unless you think that's an unnecessary
16 addition, let me remind all of us that only five
17 people died from the anthrax letters, and yet the
18 impact was much greater. We had denial of buildings,
19 we had disruption to our productivity, and so forth
20 and so on. This will be, in many ways I think, the
21 hardest part to define in a way that's both
22 operational, measurable, observable, and yet allows
23 continuity of definition across not only the chem/bio
24 field, but also in comparison with volcanoes and other
25 natural disasters. Next, please.

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1 (Slide)

2 Emerging from all of this work
3 simultaneous, which led to a lot of confusion, was an
4 emerging understanding of what the medical NBC
5 capability should be. None of these capabilities
6 listed up here are exactly shocking or radical in
7 their concept. In fact, almost every one of us in
8 this room could have composed a short list of what we
9 thought the capabilities were. I would just like to
10 suggest, however, that could we at least agree on the
11 list so that we could move forward and address more
12 significant questions, aside from always arguing over
13 what they might be. Next, please.

14 (Slide)

15 As stated earlier, I would suggest that a
16 medical response is even more global application of
17 diverse capabilities to address a particular event.
18 You can have many different kinds of actions --
19 planning, preventive, mitigation, recovery. They can
20 be ongoing, simultaneous, congruent, and so forth.
21 Next, please.

22 (Slide)

23 What I'd like to do now is show you some
24 initial products of this hazard analysis project.
25 Next.

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1 (Slide)

2 If I go back and relabel the Med Risk
3 Assessment as being on of the initial products, we
4 revisit those charts. Next.

5 (Slide)

6 One of the first lists or products in the
7 hazard analysis -- and at this point, the institute of
8 Defense Analysis was critical in helping with all the
9 modeling and the thinking and the analysis -- was a
10 prioritization of CBRN events. This list was actually
11 roughly produced on September 18th. For me
12 personally, it allowed my office to focus on the
13 highest potential, the highest impact risk.
14 Surprisingly enough, use of chemical warfare agents is
15 not very high on that list, and yet it was one of the
16 things most talked about in those first couple of
17 weeks. Next, please.

18 (Slide)

19 This is an interesting chart, and I'm
20 sorry it didn't blow up more, but essentially what it
21 is is percent of the total casualties from five or six
22 biological agents. So this is not percent of the
23 exposed population, this is percent of the total
24 casualty load.

25 Some interesting items here, first of all,

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1 for most of the BW agents, they present very sharply,
2 very sharp increase in casualties on Day 3, and the
3 presentation of these initial casualties pretty much
4 stops by around Day 8 or Day 9. The entire load of
5 casualties is going to present between Day 3 and Day
6 9. When you understand that some of the numbers
7 associated with those peaks are on the order of
8 hundreds of thousands, that is an astonishing result.
9 Next, please.

10 (Slide)

11 This gives you some idea of the casualty
12 loads, and this should be an anthrax chart, and the
13 highest peak there -- this is casualties per day in a
14 metro area that I would not otherwise specify -- so we
15 see that on Day 4 we're looking at, in that day,
16 appearing into our medical system, 45,000 casualties.

17 Next, please.

18 (Slide)

19 This is a smaller scale event, BOT TOX, I
20 believe, in another unnamed metro area, and again we
21 see -- I can't exactly read the numbers, but they're
22 on the order of 5,000 casualties. Next, please.

23 (Slide)

24 Given those initial charts and a rather
25 global scale analysis of these different events, IDA

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1 was actually able to give us the capability of
2 predicting on the first day of casualties appearing,
3 the ultimate scope of the event. When you're talking
4 about an event that's going to unroll in seven days,
5 you will not have time to figure out what your medical
6 response should be. If you have to wait until then to
7 figure out your medical response, this is not a good
8 thing. So, you want as soon as possible to know the
9 total package of medical capabilities you need to
10 bring to bear.

11 So, if on the first day you realize you
12 have a problem -- and remember that very steep curve,
13 so it will all appear for many of the agents on one
14 day, smallpox being the obvious exception -- if you
15 have on the order of 25,000 casualties on that first
16 day, you already know you're in Event 5 or 6 at least,
17 and then as soon as you get an agent identification
18 you can modify that, it might have been 5, or it had
19 been 6, or had been seven. At that point of time, you
20 would initiate the medical response package equivalent
21 to those assessments at that time. If the event turns
22 out to be much smaller, this is not a bad thing.
23 Hopefully, though, these are credible maximum events,
24 and so it would not be significantly an overwhelmingly
25 larger. Next, please.

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1 (Slide)

2 Again, this is just an example. The NBC
3 CREST modeling and simulation tool using the Joint
4 Readiness Clinical Advisory Board protocols for
5 treatment of BW casualties allows the simulation tool
6 to assess the personnel and bed resources required
7 from chem/bio casualties.

8 We quickly see that for some scenarios we
9 need on the order of 40,000 physicians, which is not
10 possible or doable, so we will almost certainly, in
11 the event of one of these maximum credible events, be
12 driven into suboptimal treatment protocols. Next,
13 please.

14 (Slide)

15 We are also lucky in that that particular
16 model produces line item inventory control number
17 detail of the equipment and supplies. And CDC and I
18 have just recently discussed this. Probably very
19 unlikely that this will have any major radical changes
20 to the CDC national pharmaceutical stockpile, but it
21 would be an interesting cross-check to see if any
22 secondary supplies or equipment items emerge out of
23 this analysis that were not obvious. Next, please.

24 (Slide)

25 So, some of the insights we're trying to

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1 capture from this work is instead of talking about,
2 for example, how do we address the SEB threat, we can
3 ask ourselves, in general, the threat from SEB is
4 essentially the threat presented by any sudden and
5 short event with a large-scale casualty load, and then
6 we can plan our medical responses to that general
7 category of event as opposed to tailoring it
8 specifically for SEB.

9 Again, slow and short events, such as
10 Tularemia, Anthrax, and plague, tell us that our
11 window for medical response is very short. And
12 smallpox, of course, all this introduces exceptions to
13 all this thinking.

14 In a recent meeting, when you work through
15 some of the scenarios for smallpox -- and these are
16 the scenarios worked out in partnership between DHHS
17 and DOD -- if you are willing to assume global mixing
18 of populations in a global first world environment,
19 the delayed presentation of smallpox means that you
20 can do restriction of movement measures, which many
21 people are discussing in great depth, may not be as
22 effective as we thought. For example, let's say a
23 confirmed case of smallpox appears in Atlanta. If
24 you're the Garrison Commander at Ft. Lewis,
25 Washington, does it do you good to quarantine your

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1 facility at that point? Chances are, it is completely
2 possible that within your facility, within your
3 installation, someone was exposed to the same source
4 of smallpox.

5 Certainly, we need to initiate isolation
6 measures in terms of limiting spread between known
7 contacts, but in terms of massive restrictions of
8 movement of otherwise unknown contacts or unknown
9 potentially exposed people, it might not be effective
10 at all. Next, please.

11 (Slide)

12 This was the scale chart I referred to
13 earlier. In the immediate days post-9/11, people
14 seemed to generically apply the Tokyo Sarin case as
15 being the measure of the chem/bio threat. And as you
16 can see on this chart, chem/bio threat is what I would
17 call a BN2 event, not on my radar screen in terms of
18 advance planning. Next, please.

19 (Slide)

20 One of the other analytical tools
21 developed by the Institute of Defense Analysis -- and
22 we already clearly see that this chart needs to be
23 modified -- is that categories of events, in this case
24 specified by particular chem/bio agents -- really
25 require different medical response strategies in order

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1 to effectively deal with them. And, again, as stated
2 earlier, we would want to initiate the appropriate
3 strategy as soon as possible in the event, not allow
4 the event to overwhelm us so that we are driven to a
5 particular strategy out of desperation and without
6 forethought. By the way, the distribution system for
7 prophylaxis or antibiotics for BW agent use could
8 serve as the backbone for the distribution system for
9 supplies, medical equipment, and the kits you would
10 send home for at-home care as well. So, the same
11 distribution system, if we thought ahead, could be
12 leveraged for all these different strategies. Next,
13 please.

14 (Slide)

15 This is one of the first products that
16 came out of the analysis, and it is in many ways the
17 most useful. If you have a BW agent release
18 represented by Day 0, and if you have detectors in
19 place that detect the release and if you immediately
20 disseminate the appropriate antibiotics -- this curve
21 is averaged over all bacterial BW agents within the
22 model -- then you can avoid 100 percent of the
23 casualties from the exposed population. This is
24 setting aside extreme cases, side effects, and so
25 forth. If you have a medical surveillance system that

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1 can pick up the spike of 2 to 10 percent of the
2 casualties on Day 3 post-release and you immediately
3 release the antibiotics, you can avoid 71 percent of
4 those casualties. If you wait for clinical diagnosis,
5 you have waited too long.

6 First of all, this chart illustrates the
7 critical importance of medical surveillance.
8 Secondly, from a command operational viewpoint, the
9 chilling thing about this chart is that the decision
10 to release antibiotics will almost certainly have to
11 be made at a point in time when you do not have
12 confirmation of the attack or the agent. To a
13 commander who is facing the potential of worldwide
14 notoriety and releasing antibiotics to U.S. forces,
15 possibly overseas, that's not an easy decision to have
16 to make. It also addresses the issue of you would
17 need to have the antibiotics prepositioned
18 appropriately so that you could release them
19 immediately. Next, please.

20 (Slide)

21 In summary, I would like us to try to
22 clarify our terminology by evaluating our BW agents as
23 hazards which, in fact, your Medical Risk Assessment
24 project pioneered. I would like us to examine a broad
25 range of potential BW events instead of marrying any

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1 particular scenario or particular event, and if you've
2 been in meetings with high-ranking, nonmedical,
3 nonchem/bio specialty leaders, you will note that they
4 tend to marry a particular threat, and that's their
5 threat. There's nothing wrong with marrying a threat,
6 but you can't afford to ignore all other threats.
7 And, also, hopefully by clarifying this terminology
8 and analyzing it within a consistent framework, we can
9 assess and prioritize the damage, such as increased
10 casualties, across the entire spectrum. Next, please.

11 (Slide)

12 And then, because I couldn't find any
13 better place to put it in the briefing, I'd like to
14 review these two statements which the BioMedAC is
15 going to formally present to the NATO community in the
16 next six months.

17 First of all is the recognition that
18 effective military planning to address a smallpox
19 threat must be integrated with civil defense planning.

20 This was not exactly shocking and radical news to the
21 NATO community either, but NATO, by its structure, is
22 not always well-integrated across the military-civil
23 line, so this is a reminder for NATO to address that
24 integration issue more strongly.

25 Secondly, the unique aspect of smallpox is

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1 that it is not present in natural form. So the
2 appearance of a confirmed case of smallpox is almost
3 certainly as a result of an illegal act, aside -- and
4 there's a caveat in the original document -- aside
5 from a legitimate accidental release from one of the
6 two facilities identified, CDC and whatever the
7 Russian version now is.

8 Secondly, the most likely scenario will
9 lead to a large number of index cases in many
10 different locations. Most medical planning in general
11 or historical experience with smallpox is not based on
12 multiple index cases with a wide geographic
13 dispersion.

14 And, finally, the BioMedAC recommends that
15 all NATO allies have the capability to immediately
16 vaccinate their forces on the first appearance of a
17 confirmed case of smallpox. They do not specify
18 whether or not that vaccination should be pre-
19 exposure, pre-event, or it should be only at the
20 appearance of the first case, but nonetheless
21 encourage all allies to have the capability to do so.

22 Again, some of this may not seem all that
23 radical except that at this meeting, in the beginning
24 of the meeting, several of the NATO allies said that
25 as far as they were concerned, they did not feel that

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1 their country was a target, and so they did not feel
2 that any undue preparations were needed to protect
3 their military forces, at which point my U.K.
4 counterpart very quietly and gently asked, "Do you
5 have an airport?" And that concludes my briefing.

6 Thank you. Questions?

7 DR. OSTROFF: Thank you for that
8 presentation. Let me open it up to the Board, if
9 there are any comments or questions.

10 RADM. HART: Have we expanded beyond the
11 initial question to the Board?

12 LtCOL. SCHNELLE: Yes, sir. In the
13 earlier discussions, not only do I present the
14 question and present any assessments of the BW threat
15 list, which is why I included the additional
16 discussions on smallpox, but they asked if I had had
17 any additional work since the Med Risk Assessment
18 project, and this is it.

19 RADM. HART: So the product then of this
20 group is to provide recommendations for vaccines and
21 immunization protocols, but the product of what you
22 are doing is going to be well beyond that, is that
23 correct?

24 LtCOL. SCHNELLE: Yes, sir. And since it
25 is not complete, I was not able to use, as a result of

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1 this analysis, a defined answer to that question. But
2 the long-term goal within the next year is that the
3 recommendations from my office on that question would
4 be based within a very consistent analytical framework
5 and thus would be very consistent, and not a matter of
6 personality or personal skills or experience, a
7 framework that you could evaluate from your own
8 prospectus.

9 DR. OSTROFF: I guess my question is, what
10 are you anticipating the final product of this is
11 going to be, and how are you planning to use it in
12 terms of your planning contingencies? I mean, I
13 didn't see much here that others -- as far as the
14 casualty estimates, they are exactly consistent with
15 what everybody else has always shown.

16 LtCOL. SCHNELLE: The key question is can
17 we use from this consistent framework a way -- again,
18 consistently scoping the required capabilities, which
19 requires a great deal of definitions and assertions
20 which are not in this briefing because we are still
21 working on them. But one emerging thought is the
22 statement that given that you define your population
23 at-risk -- and we'll set aside that for now but, say,
24 it's the Washington Metro Area as your maximum
25 population at-risk -- one idea that's emerging from

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1 this analysis is that your planning efforts would be
2 focused that a maximum casualty of 33 percent of your
3 POD, based on several other studies which I won't go
4 into. So that gives you an estimate both of the depth
5 of capabilities you need -- 33 percent of the
6 Washington population at-risk means X-number of
7 casualties, I've got to be prepared to treat X-number
8 of casualties in 7 days, you could do a lot of number
9 crunching at that point. And it also gives you an
10 analysis of the cost-benefit or, similarly, from the
11 perspective of this Board, some of this work
12 reinforces common sense, which is actually quite
13 reassuring. I think it reinforces that we need
14 vaccination for anthrax and smallpox. The question is
15 what is the cost-benefit analysis of vaccine for
16 Tularemia versus medical response to Tularemia. It's
17 my hope that this framework will allow us to answer
18 that question as well. Both are useful. What is the
19 cost estimate on each?

20 DR. OSTROFF: But many of the examples
21 that you are presenting here have to do with exposures
22 to the civilian population, and I think some of the
23 answers concerning the use of vaccines aren't
24 necessarily the same in military populations as they
25 are in civilian populations, so how do you -- I mean,

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1 what the Board is being asked to do is to make
2 recommendations for military populations, and I could
3 see some potential usefulness of a Tularemia vaccine
4 in a military population that I might not necessarily
5 see in the civilian sector.

6 LtCOL. SCHNELLE: I'm not sure I would
7 recommend widespread civilian use of a Tularemia
8 vaccine, certainly, but I'm not sure we can continue
9 to see that a BW agent threat is specific to a
10 deployed force. In fact, the most likely doctrinal
11 use, enemy doctrinal use, of the BW threat is on our
12 civilian population in preparation for military
13 action.

14 RADM. HART: How will you know when you're
15 done, if we don't have -- we sort of lost the
16 question.

17 LtCOL. SCHNELLE: Well, let me recenter
18 myself and get off of the hazard analysis concept and
19 go back to the question. The question to the Board is
20 what vaccines would I recommend that the Board
21 consider for immunization of U.S. forces? Anthrax and
22 smallpox. However, I think the issues of smallpox
23 immunization require an in-depth understand of the
24 impact upon the civilian population.

25 A trivial example is, if you immunize me

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1 and arrange for a 14-day quarantine for my family, or
2 what measures would you take to protect my family from
3 the fact I was vaccinated. So I think smallpox
4 vaccination requires extensive discussion in the
5 context of civilian planning as well. But in terms of
6 addressing the BW threat worldwide, smallpox and
7 anthrax, no question. And then the rest is expanded
8 thinking.

9 DR. OSTROFF: Are there other comments or
10 questions?

11 DR. PATRICK: Just one question. Kevin
12 Patrick. On the medical NBC capability. It seems one
13 of the (inaudible) is the communication capability
14 (inaudible) gather information (inaudible words)
15 needed, and I cannot forget (inaudible words) into the
16 public here, and what has happened. Now, is that one
17 of the four capabilities that you're talking about
18 here in this paradigm hazard analysis?

19 LtCOL. SCHNELLE: Yes, sir.

20 DR. PATRICK: I didn't see it bulleted per
21 se.

22 LtCOL. SCHNELLE: One of the struggles
23 about defining the capabilities -- and it was an
24 exercise with 40 or 50 different people over a period
25 of two days, very similar to your environment now --

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1 is addressing those systemic issues because you can
2 have the widgets, you can have the training, you can
3 have the environment and the facilities, but if you
4 don't have the systemic issues of effective
5 communication, et cetera, et cetera, then it doesn't
6 make much difference.

7 That's why the last one, which is a
8 strange set-apart capability, is competency. We did
9 not deliberately call it training and education
10 because it means far, far more than that. And the
11 longer definition, which I didn't bore you all with,
12 is the ability to gather, interpret and share
13 information rapidly. So, in that broader -- and not
14 well defined at this point in time -- label of
15 competency we're including some of those system
16 aspects of being able to do the job.

17 DR. NESS: Roberta Ness. One of the
18 things that struck me was that you talked a great deal
19 about essentially early detection, containment and
20 treatment, rather than talking about primary
21 prevention, and I think that's kind of what you're
22 hearing in response, is that -- I mean, effectively,
23 your message, if I'm understanding you correctly, was
24 that these early detection and beyond capabilities are
25 going to be very difficult to employ in a timely

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1 fashion.

2 So, therefore, it seems to me that, in a
3 sense, where you're thinking has gotten you to is that
4 you need to be thinking kind of beyond that point. I
5 mean, it seems what the original charge was, which was
6 thinking about primary prevention with respect to
7 immunization, and then, as well, kind of thinking
8 about the early detection capability with respect to
9 surveillance, have almost got to be -- I mean, I would
10 think where you're going to want to be spending all of
11 your time, or a great deal of your time.

12 LtCOL. SCHNELLE: Right. That list of
13 capabilities is essentially an order of priority
14 because if you can prevent or mitigate the event as
15 soon as possible, the overall cost and damage is less.

16 Obviously, much of this work was done shortly after
17 9/11 and our priority was BW on a metro area. That
18 gentleman correctly identified it -- how does this
19 have to do with military forces?

20 In point of fact, the model NBC CREST is
21 specific to military deployed forces, and it took
22 quite a lot of tweaking to apply it to civilian urban
23 areas. So, our thinking was shaped by that immediate
24 priority.

25 Other studies done by the Center for

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1 Health Promotion and Preventive Medicine addressed
2 toxic industrial chemicals, and that it was clear
3 preventive measures in terms of physical security and
4 other measures was critical.

5 DR. OSTROFF: One more, and then I think
6 we'll have to move on.

7 DR. MALMUD: Malmud, from Temple. I'd
8 like to make a statement so that I could understand by
9 your response, if I understood you correctly.

10 No. 1, you recommend that there be
11 immunization for smallpox and anthrax. No. 2, that
12 smallpox, because it is so communicable, would have to
13 be a disease treated not only in the military, but in
14 the civilian population as well in order to make any
15 attempt to contain it, and that this should be done as
16 soon as a single case is detected anywhere in the
17 continental -- in the United States or among our
18 troops. And the third item is that anthrax not being
19 communicable presents a different problem, but that
20 the use of anthrax either in the United States or with
21 our troops stationed overseas would result in the
22 recommendation for immediate treatment for the
23 population exposed as compared to the entire
24 population. Is that a fair summary?

25 LtCOL. SCHNELLE: Yes, sir.

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1 DR. MALMUD: Thank you.

2 DR. OSTROFF: We're going to have to move
3 on, but I have one very specific question for you.
4 There was a memorandum from the Board last September
5 related to the Medical Risk Assessment, which made
6 some recommendations about how that risk assessment
7 ought to be modified. Was that ever done?

8 LtCOL. SCHNELLE: No, sir. I've been
9 waiting for the latest version of the BW Threat List.

10 Again, I didn't see the presentation today, but I was
11 privileged to see an earlier advance copy of the
12 threat list -- not in-depth because the complete
13 threat list is a package of about 100 pages long --
14 and the conclusion of the threat list, I was told, is
15 that the intelligence community concluded that it was
16 not possible to prioritize or assess the threat in-
17 depth. And at that point, in order to update the Med
18 Risk Assessment and apply it against the current
19 threat list, you would need to have a current threat
20 list that went into the detail of the previous threat
21 list. Did they actually present to you a priority
22 ranking of the threat list this year?

23 LtCOL. RIDDLE: Yes, based on the
24 intelligence assessment. The Medical Risk Assessment
25 then takes the countermeasure, the whole package, so

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1 that it better allows you to prioritize a product
2 development acquisition in combination with the
3 intelligence threat list.

4 DR. OSTROFF: Okay. let's move on to the
5 next presentation, and that one will be by LtCol. John
6 Skvorak, and I hope I didn't pronounce that
7 incorrectly. He's the Director of the Medical
8 Biological Research Program, Medical, Chemical and
9 Biological Defense Research Program, at U.S. Army
10 Medical Research and Materiel Command.

11 LtCOL. SKVORAK: Good afternoon, and thank
12 you for inviting us, and that was a perfect
13 pronunciation of my name. I think that the short
14 title of my presentation will be expanded thinking.
15 Could I have the next slide, please.

16 (Slide)

17 What we are going to do today is look at
18 three things -- the program in general, kind of a
19 program overview, spend some time on the product, the
20 emerging products that we have, and then spend a
21 little bit of time on the process, the process that we
22 go through to get these products through the -- or
23 into advanced development and hopefully to procurement
24 and fielding. Next slide.

25 (Slide)

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1 This is a DOD program, by law. All
2 biodefense has been consolidated in the DOD, and
3 oversight of that program is the responsibility of
4 that DOD Board that's pictured there. They are
5 responsible for fiscal and program guidance,
6 coordinating the medical and nonmedical portion of
7 that, and we'll talk about that very briefly, and
8 overall the responsibility for planning, programming
9 and budgeting. By DOD directive, the Army is the
10 Executive Agent for the Chem/Bio Defense program, and
11 management of the program is facilitated through that
12 Joint NBC Defense Board that's shown there.

13 What's most important -- and it's a little
14 bit different than what you have in the slides that
15 are being handed out -- is the two bodies underneath
16 that Board. The JSIG is going away, however, what's
17 really important is there is a body that is
18 responsible for requirements -- for coordinating,
19 integrating and prioritizing our requirements as far
20 as the program goes. The other group, the JSMG, the
21 materiel group, is responsible for coordinating,
22 integrating, planning and programming, and responsible
23 for execution. Again, the Army is the Executive Agent
24 and execution of the Joint Medical/Chem/Bio Defense
25 Research Program is an Army responsibility who

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1 integrates both the DOD portions and the non-DOD
2 portions of that program, or the extra-mural portions,
3 I should say, within the Med/Biodefense program,
4 execution is the responsibility of the U.S. Army
5 Medical Research and Materiel Command, and my office
6 is a staff office of that command. And beneath that
7 command, there are a number of laboratories and we'll
8 look at those very quickly. Next slide.

9 (Slide)

10 We look at our mission -- and this talks
11 about chem and bio, but obviously it's just as
12 applicable for the bio alone -- is to develop medical
13 solutions for military requirements. We want to be
14 able to protect and sustain the warfighter in a bio-
15 warfare environment. And what we think we need to do
16 is to prevent casualties. If we can't do that, to
17 develop treatment protocols or treatments available
18 that will return soldiers or the warfighters to duty
19 as soon as possible, and also to develop far-forward
20 diagnostic capabilities. Next slide.

21 (Slide)

22 What I did want to mention, though, is
23 we're going to talk strictly about medical, but when
24 we talk about chem/bio defense, we look at four
25 aspects -- medical that we'll talk about, the

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1 nonmedical or the physical countermeasures --
2 detectors, decontamination, the masks, the suits, that
3 type of protective devices; the intel, and I think
4 we've been talking about that quite a bit as far as
5 what's available, what's out there, who has it, will
6 they use it, how will they use it, those kinds of
7 questions; and then education and training. The
8 medical folks contribute considerably to that, but
9 developing courses and materials that are available to
10 train medical providers in the diagnosis and treatment
11 of bio casualties, and this has gone well beyond the
12 military health care providers and very popular
13 outside military. Next slide.

14 (Slide)

15 The USAMRMC, the Medical Research and
16 Material Command is located at Ft. Detrick. Co-
17 located is the primary lab for the med/bio defense
18 research program, that's USAMRIID, or the Research
19 Institute of Infectious Diseases. Very important to
20 our program as far as DOD labs are both the Walter
21 Reed and the Naval Medical Research Institute in D.C.,
22 or Forest Glen. ICD, the Institute of Chemical
23 Defense is a portion of the Bot Tox therapeutics work.
24 What that slide doesn't show and I think what's
25 really important is through cooperative agreements,

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1 transfer agreements, grants and contracts,
2 contribution to this program is worldwide. Next
3 slide.

4 (Slide)

5 What we aim to do is to do some basic
6 research, identify mechanisms, pathogenesis, immune
7 response to these diseases, and using that type of
8 information develop the countermeasures, the vaccines,
9 the pretreatments, the treatments. We talk a little
10 bit more about models maybe under this program, and
11 I've got some more about that information later, but
12 developing appropriate animal models is a very
13 significant part of the technical approach to these
14 countermeasures. And as I also mentioned, diagnostic
15 systems.

16 (Slide)

17 The next slide is a bit defensive to be
18 perfectly honest. What people are looking for from
19 us, and what we're looking for ourselves and what we
20 are measured by, are those pretreatments, the
21 vaccines, the therapeutics, but we need to remind
22 people that the work that we do, the basic science
23 that we do, also contributes to a number of other
24 products. I mean, the basic science research and
25 discoveries, the maintaining capability that can

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1 respond to emerging threats. Information and
2 education I already mentioned. Expertise that's
3 available within our laboratories is extensive, and in
4 recent times has been tapped considerably. Next
5 slide.

6 (Slide)

7 Hopefully this list looks somewhat
8 familiar from your recent briefing on the threat list.

9 What I did want to mention, though, is under the
10 bacterial threats, within the tech base and the
11 events, develop a program. We are working on the top
12 -- I don't have my glasses on -- glanders, up.
13 Tularemia, however, is strictly in the advanced
14 developers realm. As far as viral threats, we have
15 programs in all the viral threats listed there. And
16 as far as toxins, we have programs in all the -- in
17 the top three that are listed there, and we'll go
18 through these a little bit, not in great detail but in
19 a little bit of detail. Next slide.

20 (Slide)

21 As far as organization of our program, we
22 have three task areas. We look at vaccines,
23 therapeutics and diagnostics. Vaccines and
24 therapeutics are further divided into bacterial, viral
25 and toxin, so we have essentially seven task areas,

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1 the way we look at it.

2 We also have seven -- currently we have
3 seven DTOs. I'm not sure how familiar you are with
4 DTOs, but basically they are -- they work off defense
5 dollars, protected dollars. They have a lot of
6 visibility. What they are are more advanced, more
7 product-oriented areas of research. Generally, DTOs
8 then transfer to the advanced developer, and we'll
9 look at all these again, too, a little bit. What you
10 can see, though, from that list is with the exception
11 of the common diagnostic system, all of those are
12 vaccine or vaccine-related. Next slide.

13 (Slide)

14 This slide provides you our program in one
15 slide, basically. It's pretty much all there. Under
16 diagnostics, just very briefly, the goal is an
17 integrated system, a system being the sample
18 processing, the device, the protocols, the reagents,
19 that are capable of analyzing multiple samples,
20 looking for multiple agents, and to do so rapidly,
21 again, far-forward, far-deployed, and to eventually
22 provide confirmatory analysis.

23 Stepwise, looking at the common diagnostic
24 system as the PCR system, we're moving to the
25 immunodiagnostic system. That's basically to pick up

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1 the toxins that we are unable to find in the common
2 diagnostic system, and eventually get into the
3 integrated system.

4 Under vaccines, they are listed there. I
5 don't think there is much more for me to say other
6 than the underlying ones in brown represent those
7 details, so those are most our advanced efforts. What
8 I think is important to remember is that in the tech
9 base in those task areas we continue to work on the
10 next-generation vaccine. We have an rPA candidate for
11 anthrax, for example, DNA vaccine for anthrax as an
12 alternative or, again, as the generation-after-next,
13 so to speak.

14 Therapeutics: for bacterial therapeutics,
15 we generally are looking at licensed antibiotics as
16 applied to our threat agent, or to investigational
17 antibiotics. With the viral and toxins, since there
18 aren't sort of a stable of drugs out there, a lot of
19 the effort there is looking at collections of
20 compounds and identifying lead candidates through a
21 number of screening type assays.

22 I mentioned the DARPA. It's a five-year
23 program. We have some dollars to look at DARPA
24 transition products. DARPA is generally looking at
25 very immature technology, and with the limited

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1 dollars, limited facilities we have, we put most of
2 our efforts in proven areas, although you can't depend
3 on that completely, but what the DARPA transition
4 dollars allows us to do is to look at, to use the
5 cliché, "out of the box" type of potential answers to
6 some of our problems. I think one of the best
7 examples is if we talk about the bacterial agents,
8 looking at license and investigational antibiotics
9 that are available, under the DARPA program we are
10 looking at a number of unique classes of compounds
11 that may prove to be a next-generation type of
12 antibiotic. Next slide.

13 (Slide)

14 To look at some of our emerging products
15 briefly -- I don't know what the order is, there is no
16 order here so don't read anything into that --
17 recombinant Bot vaccine, it's a pentavalent vaccine,
18 although I think Col. Danley will tell you the advance
19 developer is just moving forward with a Bi-valent AB
20 subtypes of Bot Toxin. I think you probably know how
21 Bot Tox works. And what the vaccine is recombinant
22 protein fragments that are genetically engineered from
23 yeast.

24 The recombinant plague vaccine, our major
25 concern with plague, of course, is aerosolized or

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1 pneumonic plague, however, the vaccine has to, by the
2 requirements document, be effective against the other
3 forms of plague. And this, again, is a recombinant
4 protein vaccine, looking at a fusion of the F1-V --
5 those are two plague proteins -- F1 is a capsular
6 protein and V, I think, is a secreted protein. These
7 are expressed in E.coli. Next slide.

8 (Slide)

9 The next generation anthrax vaccine I kind
10 of mentioned. The recombinant PA from brucellas
11 anthracis, and I think -- I'm sure many of you are,
12 but if you just read a newspaper in the last few
13 months, you've become an expert on anthrax, and know
14 that the spores are easily aerosolized and
15 environmentally very stable.

16 The other on that slide is the multivalent
17 VEE vaccine. This is somewhat different. It's an
18 infectious clone technology, and what we have is an
19 infectious clone that is effective against the 1AV
20 serotype, and it looks as if it provides adequate
21 cross-protection against 1E. There is another
22 serotype that we consider important, and although it
23 is preliminary, it looks like the 1-AB serotype will
24 provide protection against the 3-A. VEE doesn't get a
25 lot of press, however, VEE has a very low infectious

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1 dose. Apparently, it is readily made and frozen, and
2 we're talking about an aerosol exposure which although
3 VEE has a very, very low mortality especially in the
4 age group of the military population with aerosol and
5 respiratory exposure, the incidence of encephalitis
6 seems to be much greater. Next slide.

7 (Slide)

8 The recombinant SEB again, another
9 recombinant vaccine, produced and expressed in E.coli.

10 SEBs are superantigen toxins, act quite rapidly.

11 Brucella: Of the ones we talked about so
12 far, brucella is probably the least mature of the
13 vaccine candidates we have. To be effective against
14 brucella -- suit, melitensis and awardis (phonetic).

15 It's a modified live, or live-attenuated brucella
16 Melitensis oral vaccine candidate. Again, this is
17 another one that doesn't have -- get a lot of press.

18 It has a low infectious dose, very, very low
19 mortality, more incapacitating or debilitating. Next
20 slide.

21 (Slide)

22 Certainly, the least mature of our vaccine
23 candidates, one of our new DTOs or proposed DTOs is
24 for Ricin. And I'm not sure if Ricin fits into a talk
25 to an Epidemiology Board, being a plant-derived toxin,

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1 however, it is a very abundant toxin and has a very,
2 very rapid onset of signs after aerosol exposure.

3 I sort of short-changed the antibiotics
4 and the diagnostics just based on what I thought this
5 audience wanted to hear. Although as I showed in that
6 list of the DTOs, the vaccines are certainly the --
7 have been the priority within the program, we are
8 shifting toward therapeutics in our new DTOs. Two of
9 the new DTOs are both based on therapeutics, and
10 certainly if you look at the funding, there is the
11 shift toward therapeutics.

12 DR. OSTROFF: Can I interrupt you for one
13 quick question?

14 LtCOL. SKVORAK: Certainly.

15 DR. OSTROFF: When you have listed on there
16 FY02 planned, what does that mean because this is
17 FY02? For a lot of these products you have FY02
18 planned. Does that mean you're going to have a
19 product in FY02?

20 LtCOL. SKVORAK: Oh, I kind of skipped
21 over that because I wasn't sure how significant that
22 was to you. No. As I go along in this briefing a
23 little bit more -- in fact, I think the roadmap comes
24 next -- well, why don't we just go there. Can we go
25 to the next slide?

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1 (Slide)

2 We're governed by or operate under the DOD
3 acquisition framework, and within that there are
4 milestones A, B and CAD. CAD stands for Component
5 Advanced Development. And that first bullet I had
6 under many of those products refer to the acquisition
7 milestone status. And I think before when we had the
8 Component Advanced Development decision review is
9 planned for fiscal year '02, and that should match
10 what you see up on that slide. So, no, that doesn't
11 mean you're going to have a product, what that means
12 is under the Defense acquisition strategy, we're
13 moving one step closer. A CAD is specifically taking
14 one of those vaccine antigens and saying we think this
15 is it, we think this is the one we should be able to
16 move forward. We want to go to the phase where we can
17 file for an IND and, among other things, put it into
18 Phase I and find out if, indeed, we do have a safe
19 product.

20 DR. OSTROFF: Thank you.

21 LtCOL. SKVORAK: And along with that, that
22 slide probably shows -- it's probably one of the more
23 important charts that I have for you. I don't have
24 any way to brief this, although this, again, gives us,
25 as I just explained, our roadmap for getting these

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1 products to the soldiers. Next slide.

2 (Slide)

3 I will leave the advanced development
4 products to the advanced developer, and will just move
5 to the next one.

6 (Slide)

7 Future trends. We in some way are working
8 in all of these areas, but these are the things that
9 we feel within the program are going to be
10 considerably significant as time goes by. Genetically
11 engineered threats. We live in an age where these
12 microbes are engineered to defeat our defense
13 mechanisms and to impede our diagnostic mechanisms.
14 That's one thing we have to address.

15 Immunotherapy. We do have a limited
16 amount of work into the immunodiagnostics -- not
17 immunodiagnostics, but immunotherapeutics as
18 pretreatment and also as stimulators for vaccines,
19 quicker immunity, that kind of thing, and multiagent
20 vaccines, again, we do have, in fact, a DTO that's
21 going back through a tech base. The idea is to
22 produce a delivery mechanism which can deliver a
23 number of vaccine antigens at one time. A concept
24 would be, for example, words), that kind of thing.
25 Next slide.

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1 (Slide)

2 And I think I've said all I need to say
3 about DARPA. Next slide.

4 (Slide)

5 This charts the process part, as I
6 mentioned already. Why don't we just go right ahead
7 to the next slide.

8 (Slide)

9 That's the DOD acquisition management
10 framework, and I'm certainly not going to try to
11 explain all of this, but it is something which we have
12 to work under, and it's important to have some
13 introduction to that. A real acquisition program
14 doesn't start until you get to Milestone D, but that
15 framework starts with a milestone, and what I'd like
16 to do is go to the next slide which shows pretty much
17 how we work.

18 (Slide)

19 You know, that's very linear where in
20 medical product development of vaccines and
21 therapeutics is very iterative. And what I think this
22 slide shows is that a lot of the work that we do
23 happens before we reach that Milestone A with the
24 basic science work -- I can't read it -- this is the
25 discovery part, this is very basic science,

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1 characterizing the agent and agent interaction, and
2 begin to identify potential vaccine and antigen
3 components. As we mature, we develop scientific
4 steering committees. These steering committees, we're
5 starting to have them develop product development,
6 hoping that it will be more efficient as far as moving
7 these things forward, but they again would be
8 responsible at the laboratory and science levels. And
9 we are doing is defining animal models, looking at
10 assays, as we continue to mature and become closer to
11 a concept for a vaccine, we developed an ITP -- and I
12 won't go through that -- but their responsibility is
13 to manage the product in transition.

14 As we move further along, we get into the
15 pre-IND phase, looking at efficacy studies and, again,
16 looking at manufacturability of our chosen candidates,
17 and looking at assays. And, finally, after that CAD
18 which we feel is very important because that's where
19 the work of the tech base, our work and the advanced
20 developer begin to merge, and that's as we move to an
21 IND in a Phase I clinical trial, also the development
22 of GNP lots, and to develop the assays that we're
23 working towards. After that, that product will
24 essentially leave our responsibility and move to
25 control by the advanced developer. Next slide.

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1 (Slide)

2 That pretty much says what I just said,
3 but in considerably more detail as far as the FDA
4 licensure process. Nothing ever lines up as nicely as
5 it does on paper, but that's the idea. Next slide.

6 (Slide)

7 One thing that's been provided to us, our
8 technology readiness levels, which provide us just
9 another way of communicating between acquisition
10 activities on maturity of the product, we've had to
11 convert these two to fit our medical products. What I
12 think these most beneficial for is for us to compare
13 competing components as far as moving them forward in
14 the acquisition process. Next slide.

15 (Slide)

16 And things have changed for us in a way,
17 although we haven't felt it too greatly since
18 September 11th, but it looks like we're going to be
19 facing a much more broadened mission focus. DOD
20 Chem/Bio Defense program will plan a program for
21 research and development across all validated mission
22 areas, which will include force protection and
23 consequence management. In one of the first slides,
24 when I talked about mission, I said we respond to
25 military -- provide solutions to military

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1 requirements. We're going to expand our mission to
2 looking at other requirements.

3 One example of this is bio-
4 counterterrorism research program. There's a few
5 bullets about that. It's an interagency research
6 program. Again, the second bullet shows that the
7 focus is national security, law enforcement, public
8 health.

9 And the last slide that I'm going to talk
10 about is the next one.

11 (Slide)

12 We have a stable of slides that we choose
13 these from, and I argued that this slide, rather than
14 do challenges and opportunities, these are the facts
15 of life, but I think it is, again, important as far as
16 moving our products forward that you have an
17 understanding. Of course, we want FDA approval, and
18 what that encompasses, of course, is showing safety in
19 animals and in humans, and showing efficacy in animals
20 and humans, however, with our products, with both the
21 med and chem products, efficacy in humans is not
22 possible. What the FDA has is the so-called two-
23 animal rule, that allows us, if we can show efficacy
24 in two animal models and develop a surrogate marker,
25 as I mentioned earlier that the developing animal

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1 models is extremely important within our program,
2 along with a couple of other requirements as far as
3 having probably a more complete understanding of past-
4 agent interactions, that we can get these products FDA
5 approval. That's all I have. Thank you

6 DR. OSTROFF: Thank you. I think we have
7 time for one or two questions before we move on to the
8 third presentation, since we are a bit behind. Yes.

9 DR. LEMASTERS: This may be a simple
10 question, but why are the locations all on the East
11 Coast rather than throughout the U.S.? It seems like
12 that would limit your medical responsiveness to the
13 nation.

14 LtCOL. SKVORAK: Well, I'm not exactly
15 sure what the definition of medical responsiveness is.
16 We're the S&T program. We're looking at the basic
17 development of a product that is actually, if you look
18 at that roadmap, pretty far from fielding. I mean, I
19 don't know why all these labs are on the East Coast,
20 other than historical answer to that. But, again,
21 like I said, through the contract of mechanisms, we
22 certainly deal with across the United States and
23 certainly many international partners.

24 DR. OSTROFF: Other questions? I have one
25 quick on, which is, have you changed or accelerated

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1 anything that you're doing as a result of last fall's
2 events?

3 LtCOL. SKVORAK: Certainly, there's a new
4 emphasis on priorities, and, you know, for us to do
5 that, it requires more than -- it requires dollars,
6 space and people. And we haven't seen any large
7 changes along those lines. There's always the
8 argument to -- when you look at our program and I
9 showed you that sort of modified threat list and said
10 we are doing these four and these three and these
11 five, the argument comes up, why don't you just do
12 three of those or five of those, and take all of your
13 dollars, people and facilities and focus them on
14 those.

15 We generally argue against that just
16 because of the capabilities that we've developed, that
17 they go across-the-board. We haven't been asked to do
18 that, but that, I think, would be the only way
19 currently that we could redirect our efforts or
20 refocus our efforts based on those recent events.

21 COL. EITZEN: Could I add a comment to
22 that question? Ed Eitzen, from USAMRIID. We have
23 tried to see if we can accelerate some of the products
24 that are closest to transition -- for instance, the
25 rPA anthrax vaccine and the F1-V plague vaccine. But

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1 I will tell you that we have had no -- not a nickel
2 increase in core funding for our research program
3 since 9/11. We are on the same funding slope that we
4 were on prior to 9/11, which is a slow increase over
5 the POM, over the next five years, but not much of an
6 increase.

7 It's sort of a hurry-up-and-wait. We
8 could accelerate some of this basic and applied
9 research and get to the same choke point as far as
10 trials.

11 DR. OSTROFF: And then getting to final
12 products, that will move us on to the next
13 presentation.

14 DR. MS. EMBREY: The Office of Homeland
15 Security also, I think, granted DOD some significant
16 amount of money to do some contingency planning in
17 certain cities which combines detection technologies
18 with some movement of advanced research at the very
19 end of the cycle. And to that end, they have been
20 looking at various ways to accelerate work on smallpox
21 vaccine, next-generation, as well as anthrax.

22 DR. OSTROFF: Thank you. Let's mo on to
23 the last of the set of presentations for this
24 particular session, and that is Col. Danley, who is
25 the Product Manager for the Joint Vaccine Acquisition

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1 Program, or JVAC, a traditional presentation before
2 the Board. Thank you for coming again.

3 COL. DANLEY: Thank you very much for
4 inviting me. In light of what was said by the two
5 previous speakers, I think, I think I'll change the
6 title of my program to "And then the miracle occurs".

7 (Laughter.)

8 For those of you who were here during the
9 Gulf War, when we realized that there was a biological
10 threat, there was a rapid infusion of money and a
11 great deal of, for one thing, saying we need to
12 mitigate this threat, meaning "vaccines now". It's 12
13 years later, and we're just starting to produce and
14 license an anthrax vaccine.

15 So, I'm going to be emphasizing to you
16 that when we talk about making vaccines, that this is
17 a long process, this is an expensive process, and it
18 is a process with risk involved in it, but that we're
19 really coming to grips with these issues, and while
20 we're trying to come to grips with these events we
21 have had the 9/11 event, the anthrax letters and,
22 again, we see a massive infusion of money and a lot of
23 harrumphing and saying "We need to solve this problem
24 now", and without recognizing that the limitations
25 from a cost schedule performance have not changed. In

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1 other words, you can have it fast or cheap in two
2 months. Next slide.

3 (Slide)

4 In 1994, an office was stood up called the
5 Joint Program Office for Biological Defense. Its job
6 was to field detectors that would be developed, and to
7 get the licensed product for defense vaccines that
8 were being developed at Ft. Detrick. The Joint
9 Vaccine Acquisition Program grew out of the Joint
10 Biological Defense Program.

11 We are now in the year 2002 looking at a
12 Program Executive Office. The Program Executive
13 Office was dictated by a reorganization in the Army
14 who put all of its Program Management Offices under
15 PEO, so there is a new Program Executive Office that
16 would deal with both chemical and biological defense,
17 and it's very possible that this office will become a
18 Joint PEO. The decision is pending, which means now
19 all services would play in this process, which is
20 really what Congress was envisioning from the get-go -
21 - that is that no service would have its own unique
22 chem/bio defense program, we would have a program
23 common to all of the services. And in light of what's
24 happening with homeland defense, this sort of decision
25 is gaining more and more support. Next slide.

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1 (Slide)

2 This portion of the organization is still
3 in flux -- that is, the PEO, who it reports to. What
4 I want to point out is that this organization, the
5 Joint Vaccine Acquisition Program will become the
6 Chemical/Biological Defense Medical Systems Program.
7 under that we will have a group called MITS that will
8 include chem defense as well as a diagnostic piece
9 that I'd like to talk about at the end of my
10 presentation, a program that makes the reagents that
11 are used both in the diagnostic and detection side of
12 the house. Under the JVAP, we will have the classical
13 program that I'm going to be talking to you about
14 today, as well as the AVA, Drugs and Therapeutics.

15 Now, with respect to Drugs and
16 Therapeutics, I want to point out that we have not had
17 a program for developing and fielding the drugs and
18 therapeutics -- that is antiserum or nonspecific
19 immune stimulators. This is the first year that we've
20 gone into the Pentagon and said, "We need money to do
21 this", and we are planning money for the year -- for
22 the Fiscal Year 2004" -- in other words, two years
23 from now. And I want to point out to the Board, for
24 those not familiar with the funding differences
25 between Health and Human Services and the Department

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1 of Defense, I have to plan two years from now for the
2 products that will be going into advanced development,
3 into the FDA's licensure approval process, and I do
4 not have a Secretary in my Department who can go up to
5 Congress and say, "Give me \$850 million this year".
6 He may go up and ask for money to fight wars, but in
7 terms of medical products, I go through a very classic
8 program where I have to program out two years from now
9 and hope that those products are there for me to
10 invest in. Makes it somewhat difficult. Next slide.

11 (Slide)

12 Joint Vaccine Acquisition Program, as I
13 mentioned, was developed as a chartering acquisition
14 program for the advanced development and FDA licensure
15 of vaccines. I want to impress upon those of you who
16 are not familiar with this program, that prior to the
17 Gulf War we did not license biodefense vaccines. The
18 only licensed vaccine was the smallpox vaccine and the
19 anthrax vaccine, which were commercial products that
20 had a market for those. All of the vaccines that we
21 made at that time were IND products. There was a
22 somewhat casual agreement with the FDA that we would
23 hold those products, and that we could use them
24 without informed consent in case of a catastrophe.
25 The catastrophe was the Gulf War. That approach was

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1 evaluated and rejected. We used informed consent. We
2 still have problems. We're still suffering from those
3 problems with the accusation that we were using
4 experimental vaccines on our forces. At that point,
5 it was decided that our vaccines would need FDA
6 license.

7 Now, let me just say that Health and Human
8 Services is making a decision, we believe, to perhaps
9 pursue this IND approach -- that is, don't license
10 vaccines for the public, use them as INDs because they
11 would be used under an emergency or contingency
12 approach. If that's their decision, that's fine. The
13 Department of Defense has to stay the course and get
14 our vaccines licensed to ensure that what we give our
15 forces are approved products. That means more money,
16 more expense, and more time. Next slide.

17 (Slide)

18 We were established in about 1995. It
19 wasn't until 1997 that we developed a prime contract
20 to a single company, DynPort Vaccine Company, to act
21 as the company that would take these new products and
22 get them licensed. The approach that this company was
23 to take was to go out and use the commercial
24 marketplace to get these vaccines licensed and
25 produced. Our requirement for these vaccines was

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1 very, very small. You cannot go out and make as much
2 vaccine as we want, it's defined, and the definition
3 for most of the vaccines was a relatively small amount
4 of vaccine. So, using small vendors, small
5 manufacturers, existing clinical trials organizations
6 to take our products through to licensures appeared to
7 be a valid approach.

8 Now, in light of what's been said in the
9 newspaper recently about a government-owned
10 contractor-operator vaccine production facility, I
11 have no strong feelings one way or the other about
12 that, but let me point out to you again that producing
13 the vaccine is the easy part. Making them is easy.
14 It is getting them licensed that is the hard part, and
15 maintaining that licensure over time. Next slide.

16 (Slide)

17 I want to point out that we look at
18 vaccines as a system. When people talk about
19 vaccines, I get a kick out of what I read in the
20 newspaper because industry is coming forward and
21 saying, "Look, we've got a vaccine", and when they're
22 talking about that vaccine, they're generally talking
23 about that antigen up there in some sort of
24 formulation. If it's a recombinant protein, it's
25 generally an aloid, and that is the easy part to do.

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1 The hard part with most of our vaccines right now is
2 in that issue of assays. We cannot reduce the number
3 of anthrax vaccination shots because we don't have
4 surrogate markers of immunity against anthrax. We
5 will not develop a new anthrax vaccine to replace the
6 original anthrax vaccine until this issue is resolved.

7 And this issue right now resides with Center for
8 Disease Control, and that study is about two to three
9 years away from being completed.

10 As I mentioned, regulatory compliance is a
11 critical issue. We are working with the Food and Drug
12 Administration. We have improved relationships in
13 terms of their assistance in helping us and our
14 manufacturer getting our products through to
15 licensure. But we have to look at all of these issues
16 when we think about how we're going to formulate a
17 product, not the least of which is logistics because
18 if your products have to go overseas, we don't want
19 something that is stored in the minus-20-degree
20 Centigrade, and how we formulate or how that logistics
21 piece, of course, impacts on formulation which, of
22 course, impacts on regulatory compliance. Next slide.

23 (Slide)

24 So here are our challenges. It used to be
25 that I always started off with this top one, but

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1 clearly it is the second bullet which has come to
2 light. That is to say that we are no longer making
3 products simply for the Department of Defense. The
4 excellent work that's been done in Medical Research
5 and Materiel Command specifically at USAMRIID in
6 developing new vaccines impacts on our nation. These
7 are the vaccine candidates that are not just the DOD
8 vaccine candidates, but they are the vaccine
9 candidates that our nation will rely upon, and
10 recombinant protective antigen against anthrax is a
11 classic example.

12 So, what has happened is that while we've
13 been kind of cooking along trying to make these
14 vaccines for the DOD, Health and Human Services walks
15 in and says, "We need a smallpox vaccine". A program
16 that I have invested \$20 million in suddenly gets
17 equipped by an HHS program worth \$850 million. And
18 the question becomes, "DOD, why are you doing this?"
19 And it's a very good question. It's a very legitimate
20 question. So we have to look right now at how we're
21 making our investments and products that historically
22 we've worked on, but that are being eclipsed by
23 larger, more extensive investments by Health and Human
24 Services, and we are working with them in that regard.

25 Domestic and international partners

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1 addresses that as well. I see my colleague from
2 Canada, Maureen Fensom is over there. We've recently
3 completed a project arrangement to co-develop smallpox
4 vaccine, and that has to be done in the context of a
5 bigger requirement. We want a common vaccine for
6 North America, perhaps for all of the Americas,
7 because disease has no boundaries. And so we are
8 looking to not only exploit smallpox at this time, but
9 plague, anthrax, and other vaccines as well.

10 Before 9/11, limited industrial base was
11 an issue. We had small businesses. Since 9/11 in the
12 larger investment by Health and Human Services, we're
13 starting to see some major vaccine manufacturers enter
14 into this business. Next slide.

15 (Slide)

16 I want to point out, as was mentioned to
17 you, that our job is to integrate the DOD process and
18 the FDA process because the DOD process determines our
19 funding and the milestones that justify additional
20 funding as products progress. So, what we've done
21 here is basically laid out a simple plan that shows
22 that our products -- our vaccines do go through a
23 standard development process that's industry standard,
24 and this does take time. There's no shortcuts in the
25 development of DOD vaccines. Next slide.

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1 (Slide)

2 This is another iteration of the slide
3 that John showed you that says we take that process,
4 we apply technology readiness levels that have been
5 defined by the DOD -- the way we do business, using
6 integrated product teams, the milestones that have
7 been identified, and then, of course, this teeny, tiny
8 little line up here which is our funding line. And,
9 again, the nature of our funding compared to our
10 colleagues in Health and Human Services is quite
11 separate, quite different. We get our money busted
12 down into little pieces and parts, depending upon the
13 maturity of the product, and our ability to make that
14 money available depends upon that product's maturity.
15 So, again, we program for the money, and the we hope
16 that that product is going to be mature enough to
17 accept that money. If we get out of sync, then our
18 product and our development program is at-risk. Next
19 slide.

20 (Slide)

21 These are the products that we currently
22 have fully funded -- smallpox vaccine and Vaccinia
23 Immune Globulin, Tularemia vaccine, and a Bi-valent
24 Botulinum vaccine. In general, we anticipate that
25 making a recombinant vaccine, protein vaccine with a

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1 single protein in it is about a \$60-80 million effort.
2 With a product like Tularemia where you've got a live
3 attenuated bacterial vaccine, that's going to be more
4 expensive, and the reason for that is that when folks
5 were making this vaccine, which is one of the only BD
6 vaccines that was tested in humans against live
7 challenge and worked, the vaccine nature of the
8 attenuation has never been defined, and the surrogate
9 markers of immunity have never been defined, and we
10 have had to go back now and recreate and redo all of
11 this work that really represents a changed posture by
12 the Food and Drug Administration in terms of what they
13 require for getting a product licensed. so, what used
14 to work back in 1950 -- that is, feet up, feet down,
15 or people survived and were healthy, or didn't survive
16 and were healthy -- those processes have been eclipsed
17 by modern technology. So we have to maintain our
18 program and keep up with new requirements at the same
19 time.

20 From a cost standpoint, the biggest
21 driver, the biggest change to our programs, and the
22 ones that are put in the greatest deal of jeopardy
23 right now are the number of subjects that we've got to
24 enter into our clinical trials. When we originally
25 wrote the contract for these vaccines, we anticipated

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1 perhaps 3,000 subjects to get our vaccines licensed.
2 Right now, we're up in the neighborhood of 10,000
3 subjects, pushing toward 20- or 30,000 subjects. And
4 if you say that a subject is costing you \$2-10,000,
5 depending on the nature of the vaccine, we can
6 suddenly have an increase in our program of \$10
7 million at the drop of a hat. Next slide.

8 (Slide)

9 I want to talk about the fact that we have
10 a contingency stockpile. These are old vaccines that
11 were manufactured at the Salk Institute that we have
12 maintained. After the Gulf War, there was an effort
13 to write emergency protocols that will allow us to use
14 these contingency vaccines, or stockpile vaccines, IND
15 vaccines, in case of an emergency. That effort really
16 didn't go anywhere until after 9/11. Since 9/11,
17 there's been an effort both in the Department of
18 Defense and CDC to write the emergency use protocols,
19 and protocols are now being completed for smallpox
20 vaccine, Botulinum, Immune Globulin Botulinum vaccine
21 and post-exposure the use of anthrax vaccine.

22 We still have this question of whether
23 some of these other vaccines that we are currently
24 stockpiling should also have emergency use protocols,
25 and the question becomes, if we don't have a reason

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1 for these vaccines or to use these vaccines, then why
2 are we saving them? Are we creating a false sense of
3 security? Without those protocols and without these
4 vaccines being tested, they are simply taking up
5 freezer space. Next slide.

6 (Slide)

7 Again, I want to point out the fact that
8 we've successfully negotiated a product arrangement
9 with Canada under the CANUKUS MOU. We look at this as
10 being a very promising way forward for creating
11 interoperability between our forces. As has been
12 pointed out to me in the recent deployment to
13 Afghanistan, that Canadian forces were fully
14 integrated with U.S. forces. We have that kind of
15 integration. We really need to have medical products
16 that are licensed in both countries and can be used
17 with a great deal of assurance. Next slide.

18 (Slide)

19 To reiterate the point I made earlier that
20 this is a long, complex and very expensive and
21 regulated process. Our prime contractor is in place
22 and is working very successfully right now in using
23 existing technologies and industry, biotech industry
24 out there, to meet our requirements. Next slide.

25 (Slide)

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1 Let me talk a little bit about JBAIDS.

2 Next slide.

3 (Slide)

4 JBAIDS is an effort to put into the field
5 a rapid diagnostic capability for biological agents.
6 Of course, the technologies we're looking at right now
7 are nucleic acid identification, PCR, and of course
8 antigen antibody. Next slide.

9 (Slide)

10 We are looking at NDI, nondevelopmental
11 items, commercial off-the-shelf items. We are
12 planning to have a flyoff in July between
13 approximately nine bidders who have systems that they
14 believe meet our requirements. We will award a
15 contract that allows us to procure about 400 of the
16 devices, but it would also be a contract that awards -
17 - that would allow the contractor to develop the
18 actual kits themselves, and the protocols for handling
19 samples. We recognize that as we start out that these
20 processes and products will not be FDA licensed, but
21 that's what we will be moving towards so that
22 initially when we field these devices they will not be
23 diagnostic devices, they would be detectors or samples
24 that would come into a laboratory, such as
25 environmental samples. Next slide.

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1 (Slide)

2 These are some of the criteria. We're
3 looking for small units, units that weigh under 40
4 pounds so that they can be hardened and taken to the
5 field, but we also want systems that are sensitive
6 enough to pick up pathogens in different kinds of
7 samples that would be coming into the laboratory, and
8 to try to provide results as early as possible -- that
9 is, within an hour or less of receiving those samples,
10 recognizing, as Col. Schnelle pointed out, that
11 following exposure we can interdict with drugs,
12 antibiotics and antivirals, and reduce or eliminate
13 the possibility of frank infection. Next slide.

14 (Slide)

15 This is our schedule. We hope to have a
16 contract award here in the first quarter of FY03.
17 Next slide.

18 (Slide)

19 We have block development for this
20 product. The first block will include biological
21 warfare agents that are bacteria and viruses. Block 2
22 will address the toxins. Now, the reason we busted
23 things up that way is that currently technology favors
24 detecting small numbers of agents using nucleic acid
25 identification. That doesn't always work when we

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1 start dealing with toxins. So, what we're hoping will
2 evolve over time is a common platform and a common
3 approach for looking at all biological warfare agents.

4 Next slide.

5 (Slide)

6 I want to point out for this group.
7 however, the following, and again getting back to the
8 business side of science, the Biological Defense
9 Program cannot fund the development of infectious
10 disease kits. So when we do JBAIDS, we will not be
11 developing kits for malaria, for diarrhea, for
12 leishmaniasis, that that will have to be funded
13 independently through the Infectious Disease Program,
14 but that we can and are standing by to integrate with
15 the Infectious Disease Program to come up with common
16 tests that use the platform that is selected for
17 diagnostics.

18 That completes my presentation. I welcome
19 your questions. Thank you.

20 DR. OSTROFF: Thank you, Colonel. Let me
21 start by asking essentially the same question that I
22 asked to the previous presenter, which is, can you
23 give us some idea of whether or not things have
24 changed as a result of last September, or are you
25 still pretty much going on in the same pace and

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1 fashion that you have been?

2 COL. DANLEY: Very good question, very
3 complicated question. Obviously, after 9/11, we
4 started putting together information papers and
5 requests for additional funding to accelerator our
6 program. We told our prime contractor, "Pull the
7 stops out. Tell me how you can cut time out of your
8 schedule". They gave us plans. We put in
9 requirements for additional funding.

10 Some of that funding, particularly to
11 accelerate the production of Vaccinia Immune Globulin,
12 was put into the Title IX, which is currently sitting
13 in OSD Comptroller. We hope that that \$40 million
14 will be released. You're shaking your head, ma'am, I
15 don't like that.

16 But let me point out to you folks
17 something about the smallpox vaccine. You know,
18 you're making 200 million doses of vaccine plus
19 another 300 million doses that are sitting there. You
20 have no Vaccinia Immune Globulin to administer this
21 vaccine with. You're going to have to use Sunofovir
22 (phonetic). The only VIG that currently exists is in
23 the DOD stockpile, and we're desperately seeking
24 funding so that we can manufacture all that VIG into a
25 new -- or all that sera into new Vaccinia Immune

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1 Globulin to support both the DOD and our nation, and
2 provide some sort of interim safety net until CDC gets
3 their big program up and running. These are the kinds
4 of things that drive us nuts, it's not the things that
5 are hitting the newspaper that are the critical
6 issues, there are these little nitnoid things out
7 there that are driving us crazy, that keep us from
8 realizing success that we need.

9 DR. OSTROFF: I appreciate the difficulty
10 of your job. Please don't take anything that I say
11 personally, but we were sitting here comparing the
12 milestone chart to what was presented last year and,
13 if anything, it looks like there's been some slippage.

14 COL. DANLEY: Absolutely. Absolutely.

15 DR. OSTROFF: And so we're not
16 accelerating, we're actually slowing down.

17 COL. DANLEY: Right, and part of that has
18 to do with this funding issue. As I said, we
19 originally had planned, when we did our smallpox
20 vaccine, to have about 3,000 candidates. That number
21 has gone up to 10,000. Now, to pay for that kind of a
22 study, I've got to take the money that I've got and
23 move it elsewhere. So, some of our programs have, in
24 fact, slipped.

25 By the same token, some of our programs

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1 will accelerate if we get this additional funding
2 we're anticipating. We, for instance, have
3 recombinant PA going into two Phase I clinical trials
4 this fall. That's a year ahead of schedule. And
5 we've done that because we've been about to work with
6 the CDC getting these trials started. While that will
7 help us get a new anthrax vaccine potentially
8 developed, the long pole in the tent there is the
9 surrogate markers of immunity that have to be
10 identified and accepted by the Food and Drug
11 Administration. We're approximately six months ahead
12 of schedule right not with smallpox and VIG, if we get
13 the funding that we're anticipating.

14 DR. OSTROFF: Other questions from the
15 Board.

16 DR. BERG: Bill Berg. You said that
17 you're heading toward 10,000, maybe as many as 20,000,
18 volunteers to test these vaccines. I assume these are
19 active duty military personnel?

20 COL. DANLEY: The first Phase I trial that
21 we'll be doing is the University of Kentucky on our
22 smallpox vaccine. Historically, we have not chosen to
23 use military personnel for clinical trials for the
24 simple reason that we do not want to give the
25 impression of any coercion in the selection of our

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1 candidates, nor do we want to create a sense that they
2 are getting picked. Now, that was sort of post-Gulf
3 War, and in the midst of the Gulf War illness issue.

4 Since 9/11, again, we're seeing a change
5 in the way people perceive vaccines in a very positive
6 way and, in fact, what we're finding is that our
7 military wants desperately to be involved in clinical
8 trials, and that the population as a whole is becoming
9 more receptive to their participation in clinical
10 trials.

11 DR. BERG: Aside from the cost, do you
12 have any concern as to whether you can find that many
13 volunteers?

14 DR. BERG: No. Actually, right now what
15 will happen, I think, what the FDA has implied to us
16 but hasn't spelled out for us, is that they will allow
17 us to do a small Phase III clinical trial of about
18 7,000, and then they are going to want a Phase IV
19 trial. Now, a Phase IV, they would license the
20 product. We would administer the product, and then
21 track those individuals over time. Now, they've not
22 spelled out these Phase IV trials. This was mentioned
23 at the pre-IND meeting. I'm sure it will be spelled
24 out for us in the future.

25 DR. BERG: Thank you.

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1 DR. OSTROFF: I guess we've eaten a bit
2 into our break time, and I'd like to move on to the
3 break, but I must confess that I'm a little
4 disappointed that there hasn't been more of a concept
5 that things changed dramatically last fall, and that
6 for a lot of these items we really do need better
7 interventions than we currently have available not
8 only in the civilian sector, but also for the military
9 populations, and I don't get the sense that there's an
10 attitude of this being sort of a Manhattan Project for
11 many of these products because -- I mean, we're going
12 to be sitting here five years from now basically in
13 the same place that we are right now, and I guess it's
14 a question for higher levels than you, but what's it
15 going to take to get this sort of jump-started?

16 COL. DANLEY: Well, I think Ed's got a
17 comment, and if he doesn't say it, I will, sir.

18 (Laughter.)

19 DR. OSTROFF: And the answer has to be
20 more than money.

21 COL. EITZEN: I would challenge the
22 assumption that there is not a sense among us who are
23 working in the field that things changed after 9/11
24 significantly. We feel a great sense of urgency to
25 get these products out, but -- running at full

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1 throttle, we've gone forward in the research program,
2 and without more money, space, people. In fact, since
3 9/11, because of the diagnostic work -- over 30,000
4 samples, we've run over 260,000 assays will be run at
5 USAMRIID in response to the operational requirements
6 of the anthrax (inaudible). We have actually had to
7 shift at times, especially last fall with the crisis,
8 researchers from some of our other research divisions
9 to diagnostics, to handle that operational workload in
10 the midst of the crisis. So, we understand that we
11 need to move forward with a lot of these
12 countermeasures, but, again, we cannot do it without
13 more money, people, lab space.

14 Now, I will add one factor which hasn't
15 even been brought up today, which actually is making
16 the most significant challenge that we in the tech
17 base face over the next couple of years, and that is
18 that DOD and the Army are coming forward with some
19 very, very stringent security requirements for all the
20 laboratories in the Department of Defense and the Army
21 that handle these select agents, and the cost of those
22 requirements just from what we have from the Army so
23 far, is looking for just my lab alone, at around \$7
24 million a year. And for the DOD requirements, some
25 that have been released in draft, are going to be much

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1 more costly and stringent than that. \$7 million a
2 year is 15 percent of our core budget. So, what that
3 means is that if I end up and there's no funding that
4 is for the increased security programs that we're
5 going to have to have, then we perceive (inaudible).
6 So, if I have to take that (inaudible) over the next
7 two or three years, that almost means cutting the
8 division out of USAMRIID, that's how significant the
9 cost is.

10 So, I'm being very frank here that I would
11 tell you that we appreciate the urgency that we need
12 to respond to the nation and throughout the DOD, but
13 we cannot do it without the resources necessary to do
14 it.

15 DR. OSTROFF: Well, I think -- let me just
16 say for the Board that I'm really very concerned and
17 dismayed by what I'm hearing, and I'm trying to figure
18 out how we on the Board can be helpful to you and to
19 the Department to try to get this raised to a higher
20 level of concern. I can't imagine that this isn't a
21 concerning issue for the Department of Defense, but
22 the sense of urgency seems to be somewhat muted.

23 MS. EMBREY: Well, I would say that
24 everyone feels a sense of urgency. I think that the
25 fact that we're engaged in a war on terrorism, we're

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1 trying to prosecute that war. We are trying to focus
2 on intelligence, improving the intelligence that we
3 have, improving information about the nature of the
4 threat, and enhancing and expediting technologies that
5 will alert us to the presence of those agents so that
6 we can deal with the issues. That has been the most
7 pressing focus. Medical research, in its basic to its
8 advance, has not been the beneficiary of a lot of the
9 money thrown at the problem.

10 I think the Board could help us in that
11 respect, but at the same time it occurred at the end
12 of the last fiscal year, and the Congress had already
13 had in its hand our '02 budget, and the supplemental
14 has gone to executing Operation Enduring Freedom, some
15 operational real concerns, and it hasn't trickled down
16 to the core research effort. So, I don't think that
17 it's a lack of requirement, I think it's we haven't
18 had a chance to institutionalize the whole system to
19 address the research end and the medical end. I think
20 we need to do that, and I think, you know, if you have
21 any insights on that it would be helpful to us.

22 DR. OSTROFF: All I can say is it's been
23 frustrating to be asked every year to make
24 recommendations concerning vaccines for use in
25 protecting the troops when there aren't any vaccines

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1 to recommend. And so it becomes an exercise in sort
2 of circular logic, to some degree, because these
3 products never seem to be coming out of the pipeline
4 at the other end.

5 DR. POLAND: Steve, I guess I might make
6 one comment. I sit on the Institute of Medicine's
7 Committee on Infections of Military Relevance, and of
8 course the vaccine issue is inseparable from that, and
9 that report was just signed off on last week and has
10 now gone for outside review, and then will be
11 published shortly.

12 I guess to reiterate what probably most of
13 the Board already knows, it simply boils down to "no
14 money, no mission". I mean, to so hamper these
15 programs by the paucity of funding given the mission
16 and enlarging mission of what they've been given to do
17 is a demoralizing impossibility. And I think this
18 report will, in part, point that out and, in part, be
19 corollary with measures that have already been
20 recognized that need to be undertaken. So, I think
21 our criticism should be muted and recognize that it is
22 a frustration for everybody, but there are valid
23 attempts, I think, to correct it.

24 DR. PATRICK: Steve, perhaps I've missed
25 it, but is there a process by which this is being

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1 articulated with the initiatives of Homeland Security
2 rubric? I mean, it may be a very dumb question, but
3 in what way is Homeland Security factoring into these
4 very issues -- research issues, pipeline issues, those
5 kinds of things? Where are those dots being
6 connected?

7 MS. EMBREY: There's a Medical Policy
8 Coordinating Committee that Governor Ridge has
9 established for the interagency to address medical
10 issues, and there is also another coordinating
11 committee to address research in broad spectrum as
12 applies to a lot of different problems. Frankly, they
13 haven't done much.

14 DR. PATRICK: I'm wondering if there's an
15 opportunity for the AFEB to coordinate with our
16 counterpart body in that particular -- I just suggest
17 that, and I don't know the ways in which that might be
18 done, but it certainly seems, or at least my
19 understanding is, that there are new resources being
20 infused into the Homeland Security Initiative, and if
21 there were some way to bring those people up to speed
22 about the fact that here is a very rich, but long-time
23 developed pipeline, that took a long time to develop,
24 and it's going to continue to take a long time to
25 bring products to fruition, rather than reinventing

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1 the wheel, there ought to be some synergy potentially
2 brought to bear by applying resources. But, again, in
3 the world of politics, perhaps that's a naive
4 suggestion.

5 DR. OSTROFF: Admiral?

6 RADM. HART: I can understand why you
7 would think that a naive suggestion, and in some ways
8 this is paradoxical. The amount of money being made
9 available for biodefense would seem like it would be
10 distributed such that we would maximize all the
11 avenues of getting products to market. The paradox
12 is, for my thin slice of how I see it is, it has had
13 almost a detrimental effect on the funding in the
14 military medical R&D produced products because, if you
15 see a billion or whatever going over for biodefense in
16 an institution of such high reputation like the NIH,
17 you assume that we'll let them do it. So, it becomes
18 a matter of maybe a couple of things, but as far as
19 the Board's role, we have still an issue of awareness,
20 of education of what military R&D has done and can do,
21 and there is a perception even within our own
22 military, our own line officers, of why should we give
23 \$20, \$50, whatever, million to military medicine R&D
24 instead of just buying torpedoes with it because HHS
25 can provide what we need. So, there's an education

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1 program that's still at work, and all this money
2 becoming available is a bit of a paradox with what
3 effect it's had on us.

4 DR. OSTROFF: For those on the Board who
5 may not be aware that there's -- I think the exact
6 amount is \$1.8 billion that NIH will be putting out
7 for basic and applied research for all of the Category
8 A agents, and that will probably be going out I think
9 either later this year or early next year.

10 DR. PATRICK: But then the policy question
11 becomes how to leverage that against the kind of
12 research that we just heard about, and how to build in
13 the authorizing language. NIH gets this
14 reauthorization every year. I mean, it isn't as if it
15 happens on a perpetual basis. And how to find ways in
16 which we can raise this visibility -- those of us who
17 do NIH research, there will be a bunch of people with
18 a lot of bright ideas, and they'll pretend like
19 they're reinventing the wheel.

20 DR. OSTROFF: And I guess the question
21 that I would ask is what degree is DOD involved in
22 helping them spend it wisely.

23 RADM. HART: Yes, good question, and we
24 are very much trying to align with NIH, and NIH is
25 receptive to that. If it is approached correctly, it

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1 appears to be a mutual benefit. So the logical
2 strategy is, well, let's align with these people that
3 have the expertise and maybe deeper pockets, and we
4 can both benefit.

5 COL. DANLEY: Let me just say that our
6 prime contractor, DynPort Vaccine Company, is teamed
7 with other companies to bid both on the smallpox
8 vaccine contracts that HHS let, and will team with
9 other vaccine manufacturers to bid on the next-
10 generation anthrax vaccine. So, while we're doing
11 things in a government sense of -- certainly we can't
12 influence who HHS selects, but our prime contractor
13 can take the intellectual property that DOD has
14 provided and developed through the Biodefense Program
15 and make it available to Health and Human Services,
16 and use their funding if they so choose to fund it, to
17 forward these products.

18 So, I think we can attack this at several
19 different levels, and that's the flexibility that we
20 now have in our program that we haven't had in the
21 past.

22 DR. OSTROFF: One more comment from Ed.

23 COL. EITZEN: We have over the last
24 several months had ongoing discussions with NIH and
25 NINAD (phonetic). Dr. Falci (phonetic) actually came

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1 up to USAMRIID and we briefed him on our tech base
2 program, and his comment to me after the briefings
3 was, "You're already, 40, 60, 80 percent there with
4 what we plan on doing, why should we reinvent the
5 wheel? We need to work together". And that was music
6 to our ears. We're hoping that we can use some of the
7 NIH's abilities and finance to augment our programs,
8 but I think Dr. Falci understands very clearly the
9 tasking at issue, and the key part of the tasking at
10 issue is the ability to do animal studies for efficacy
11 under contaminant conditions. There's only two
12 laboratories in the country that have any capacity to
13 do that appreciably, and that is USAMRIID and Battelle
14 in Ohio, CDC to a lesser extent. But that's the choke
15 point in the research for finding efficacy
16 (inaudible). So we need to work with the NIH since
17 that's the way things appear to be going at this
18 point.

19 DR. OSTROFF: Let me have Adm. Wyatt make
20 a comment, and then I'll let Ms. Embrey close.

21 ADM. WYATT: As I listen to this
22 discussion, I'm reminded of the long history of this
23 Board, and refer back to a presentation that I think
24 many of you and I heard by Ted Woodward within the
25 fairly recent past. And it strikes me as the kind of

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1 collaboration that you're raising, the kind of joint
2 efforts that you're bringing about as a result of
3 simply having this discussion, the Board is therefore
4 doing its work. And I'm pleased to hear the reports
5 of evidence of those kinds of joint discussions,
6 including the visit by Dr. Falci and others, because
7 it seems to me that that's exactly where the Board is
8 moving and where it should move.

9 MS. EMBREY: I just wanted to advise that
10 Secretary Rumsfeld and Secretary Thompson have met and
11 discussed the establishment of a national long-range
12 vaccination council. The idea of it is that it would
13 be established at the Cabinet level, probably in the
14 Office of the President, Executive Office of the
15 President. It would be staffed by outside-government
16 experts. It would be staffed by epidemiologists from
17 other infectious disease experts from HHS and DOD and
18 other agencies that have a need and requirement, the
19 purpose of which is to do exactly what is not being
20 done, which is to coordinate and prioritize needed
21 vaccines in the nation's interest, whether that's
22 national security or pediatric or whatever it is,
23 because our pharmaceutical companies don't seem
24 incentivized to produce them. And it seems that this
25 is an idea that has caught fire. There is a pending

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1 Executive Order to establish it. There is also
2 alternative Plan Bs and Cs that include structures to
3 deal with developing a series of GOCOs, but that is
4 not perceived as the way to go. They prefer having a
5 truly high-level recommendation to the President that
6 says we are not getting to where we need to in these
7 important areas, and we need to move forward, and it
8 would be based on sort of a presidential level AFEB.

9 DR. OSTROFF: Well, we'll try to the best
10 of our ability to help move things along. And, with
11 that, let's take a ten-minute break so that we can try
12 to move back onto schedule. Thank you.

13 (Whereupon, a short recess was taken.)

14 DR. OSTROFF: The next presenter with the
15 question to the Board is Dr. Sal Cirone, who is going
16 to be talking about the Use of Investigational New
17 Drugs in the Combatant Theater for Force Health
18 Protection. Sal?

19 DR. CIRONE: Thank you very much for this
20 opportunity to address the Board on this question. If
21 I could have the next slide.

22 (Slide)

23 This is the question to the Board.
24 Request that the AFEB review the existing Joint
25 Operational Requirement documents, progress on

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1 specific efforts to obtain new indications for
2 existing therapeutics, and acquisition status of
3 biologics for both treatments and prophylaxis, against
4 the current prioritized list of biowarfare agents, and
5 make recommendations on the current status of
6 requirements and suggested priorities. Next.

7 (Slide)

8 This is the background. I presented to
9 the Board last year, but I will quickly go through the
10 background again. In May of '98, Title 10, U.S. Code
11 1107, indicated some changes as far as INDs are
12 concerned to the Department of Defense. 1107
13 basically made two changes. One of them said that the
14 Department of Defense, in particular military
15 operations, intends to provide INDs to service
16 members. It will let them know prior to providing
17 those INDs that they are going to do that, what they
18 are, why they are doing it, pros and cons, and
19 anything else that the Food and Drug Administration
20 would want us to tell them, to put it in writing, and
21 to put that piece of paper notifying them in the
22 medical records. In addition, 1107 says if you want
23 to waive informed consent, only the President of the
24 United States can waive informed consent.

25 September of '99, Executive Order 13139

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1 was signed by President Clinton, basically agreeing
2 with Title 10, U.S. Code 1107, and basically saying it
3 is the policy of the Department of Defense to use FDA
4 approved drugs. However, if an FDA approved is not
5 available and there is an IND which would be the
6 appropriate countermeasure for a chemical/biological
7 infectious disease outbreak or concern in contingency
8 operations, then you would use the IND, but use it
9 under the strict controls and rules of the FDA.
10 Basically it went on to say that if you wanted to
11 waive informed consent, only the Secretary of Defense
12 could make that request to the President of the United
13 States, and in doing so they would have to meet some
14 specific requirements, standards and criteria that the
15 FDA would provide in requesting a waiver of informed
16 consent from the President.

17 A couple of days after that Executive
18 Order, the FDA made a change to 21 Code of Federal
19 Regulations 50.32(d), which basically put forth 18
20 conditions, standards and criteria that would be
21 required before the Secretary of Defense requested a
22 waiver of informed consent by the President. Next.

23 (Slide)

24 In March of 2000, the Assistant Secretary
25 of Defense for Health Affairs, at that time Dr.

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1 Clinton, asked the AFEB for recommendations on
2 treatment for six biowarfare agents.

3 In August of that year, the AFEB provided
4 the recommendation for prophylaxis and treatment for
5 those six biowarfare agents. Unfortunately, a number
6 of those indications were off-label.

7 Going back to 1107, if they are off-label,
8 a requirement exists to notify troops in the
9 contingency operation, let them know what's happening,
10 and if you wanted to have a waiver of informed
11 consent, only the President could do that.

12 I briefed the Board in August of 2001.
13 Next slide.

14 (Slide)

15 And this is a summary of what I said
16 during that brief. I think what is interesting is
17 what has probably occurred since that brief, and that
18 was, (1) we've been working very hard to get some
19 contingency IND protocols for high-threat agents; (2)
20 we've asked the Army Surgeon General who is Executive
21 Agent, to develop some implementation guidance so that
22 the CINCs in the services would know how to utilize
23 these INDs in a contingency operation; and the third
24 thing that we did was try to work with industry to get
25 those items that were not on-label as indications be

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1 approved by the FDA for those indications. Next
2 slide.

3 (Slide)

4 We met with PhRMA and asked them if they
5 would go to the various pharmaceutical organizations
6 that were responsible for the various drugs. Next.

7 (Slide)

8 The only one that responded was Bayer.
9 One of the AFEB recommendations was ciprofloxacin, a
10 prophylaxis and treatment of tularemia and plague.
11 Bayer put together a package, went to the FDA asking
12 for indications on the ciprofloxacin label. The FDA
13 came back and said we need nonhuman primate studies.
14 A problem existed as who had the wherewithal to do the
15 nonhuman primate studies. Bayer said, "We can't do
16 that, can you help us". I think Col. Eitzen indicated
17 there's only two places in the United States that have
18 that capability. They told Bayer what those two
19 places were. In order to get into DOD, I don't have
20 the authority to just tell DOD they have a POM process
21 with a budget for things, and we had to get into the
22 cycle so that we can identify something as requirement
23 so they can have it demonstrated so it can be part of
24 a POM process, part of the POM cycle, so that research
25 can go forward. Next slide.

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1 (Slide)

2 We called the Food and Drug Administration
3 and said we didn't get any response because
4 ciprofloxacin is generic, and there's 20 or 30
5 different firms that have Doxycycline, and none of
6 them are interested in spending all the money that
7 would be necessary to get it listed as a prophylaxis,
8 even though it is listed as a treatment for a large
9 number of the biowarfare agents.

10 So we went to the FDA and said is there a
11 way that it's possible to get Doxycycline listed for
12 prophylaxis, and basically they said no, you have to
13 do the nonhuman primate studies because there's a
14 great difference between prophylaxis and treatment.
15 The treatment may say to use this product for 10 or 14
16 days, prophylaxis may be for 60 days, as we saw with
17 ciprofloxacin, Doxycycline and penicillin as a
18 treatment and prophylaxis for anthrax, and in order to
19 use it in a way that's different from the label, we
20 really need to see the testing first. Next slide.

21 (Slide)

22 That brings us to the question. How do I
23 get Department of Defense to assist us to get the
24 research done so that these drugs which are currently
25 used by our commanders in the field, that have a five-

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1 day bubble-pack for ciprofloxacin, they've got
2 Doxycycline, they've got penicillin out in the field.

3 I think, if you remember Col. Schnelle's slide, the
4 Commander has about three days to make a decision if
5 he thinks that he has a biowarfare situation, to make
6 a decision whether he's going to treat the troops. He
7 is probably not going to have a confirmatory diagnosis
8 that it is one agent versus another. So if he decides
9 to go ahead and treat, if it's anthrax, he's in good
10 shape because on the label it says for suspicion of
11 anthrax, and it's for both prophylaxis and treatment,
12 so you can treat the individual that has been
13 diagnosed and he can use it prophylactically for all
14 the other troops in his arena. If it's tularemia,
15 plague, brucella, it's off-label. So, it may be
16 effective, we don't know, we haven't been infected, et
17 cetera, but certainly he will be in trouble with the
18 Food and Drug and the Congress because we will have
19 violated these requirements.

20 And so that's why what we're really trying
21 to do is to get a joint requirement document which
22 would say that there is a requirement for the use of
23 therapeutics for biowarfare agents so that we can get
24 in the queue with all the other requirements that
25 exist out there for this problem, for which you get in

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1 the queue and hopefully you get some point and get the
2 dollars necessary to do the research and get these
3 stated as indications so that we can properly have the
4 commanders in position where they can treat the
5 troops, and the medical officers in the field in a
6 position where they can make recommendations that are
7 appropriate and within the label. Thank you.

8 DR. OSTROFF: Thank you. I think what
9 we'll do is go on to the next presentation, and then
10 have discussions at the end of the presentations. The
11 next presenter is Mr. Rick Prouty, the Medical
12 Integrator for the Joint Service Integration Group,
13 and he's going to give a presentation about the
14 current Joint Medical/Nuclear/Biological/Chemical
15 requirements.

16 MR. PROUTY: Thank you, sir, and I'd like
17 to also offer my thanks to the Board for giving me the
18 opportunity to come and represent the user community
19 on what they do as part of the NBC defense process.

20 If Col. Danley synopsisized his briefing in
21 one phrase, I'll try to do the same thing with mine.
22 We're kind of in a "build it and they will come" kind
23 of mode. We are given the responsibility in the Joint
24 Service Integration Group currently, through a body
25 called the Medical Program Subpanel, that for lack of

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1 a better analogy is the Surgeon's Office, if you will,
2 for the Joint Service Integration Group, to advise the
3 users in the development and the crafting of a
4 requirement document that sets the stage for the
5 developmental community to use as their benchmark for
6 performance, efficacy, safety and other considerations
7 for the products being produced. Next slide.

8 (Slide)

9 And, as such, we have the opportunity as
10 well as the responsibility to assure that we craft a
11 program that has all the components that are necessary
12 to protect, as it stands right now under our mission
13 directive, fighting forces, and as we all have talked
14 about already, the expansion of that responsibility
15 for DOD, Homeland Security arena, and other venues of
16 consequence management and force protection as they
17 develop through national policy administration. Next
18 slide, please.

19 (Slide)

20 Here is the agenda I've set up for you.
21 Some of the issues and the particulars of the programs
22 have been discussed already by some of the other
23 presenters, including the advanced development side,
24 so I'll give you a template you can use as a
25 reference, but I won't spend a lot of time on

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1 describing the particular programs, and I'd like to
2 finish up and addressing the issue that Dr. Cirone
3 presented to you, that he's also presented to the user
4 community as well, and I'll try to explain to you some
5 of the changes that have happened post-September 11 in
6 the user community that are really the basis for some
7 of those changes. Next slide, please.

8 (Slide)

9 This is the construct of the Medical
10 Program Subpanel. It was a directive by the Deputy
11 Assistant Secretary of Defense for Chem/Bio Matters at
12 that time. This proposes to put the medical piece
13 into the chem/biodefense requirements process.
14 Heretofore, it was purely a nonmedical organization.
15 It mandated that the Commander of the AMED Center and
16 School in San Antonio be the chair of that
17 organization, and each of the services provide a
18 general officer or a general officer representative as
19 a principal, and a supporting action officer from each
20 of the services to work medical requirements in the
21 Chem/Biodefense program. What's difficult to read at
22 the bottom is, their charter also embraces a number of
23 user representatives and stakeholders not only from
24 the user community, but from the developmental
25 community, as active participants in this process so

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1 that requirements are not generated in a vacuum, and
2 the user community doesn't create favor where targets
3 for the developmental community, that they actually
4 are in-tune and abreast of what technology has
5 afforded, and also to ensure that there is a synergy
6 between the developer and the user as well, so that
7 these programs have a good target and benchmark, but
8 also are ready when their time is most advantageous.
9 Next slide, please.

10 (Slide)

11 Looks like boldface didn't work out very
12 well here, but the Medical Defense Requirements
13 Development process started out, as I mentioned
14 before, after the Joint Service Integration Group was
15 put together, a couple of years behind that, and it
16 was done with an effort of assessing what NBC
17 requirements throughout each of the services were
18 doing independent of each other, trying to decide
19 whether they would pick out ones where there was
20 synergy that could be capitalized on and to meld these
21 into joint multi-service or DOD programs.

22 A recommendation was put to the Medical
23 Programs Subpanel for their endorsement to try to
24 figure out the best strategy for prioritizing the
25 efforts that were already in place. Heretofore, the

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1 Army, as the Executive Agent for Medical Material
2 Development, was the generator of all chem/biodefense
3 requirements as well, and the other services merely
4 signed off to them as joint interest participants
5 because the dollars flow into research facilities, for
6 the most part, and all the developmental efforts were
7 vested in the Army.

8 At the development of the Chem/Biodefense
9 Program where each of the services' dollars supporting
10 that effort were fenced into a joint pot of money, and
11 each of the services in turn were prohibited from
12 developing in their support for acquisition and
13 actually purchasing chem/biodefense programs out of
14 their own POMs, it was restricted to the
15 chem/biodefense program dollars. Interjecting the
16 medical piece into this process was just the next
17 step.

18 There were some programs that were
19 premature. The requirement documents had already been
20 crafted and were at later stages of development.
21 Those programs were left alone. Another group of
22 programs were reassessed and had to be reorganized and
23 rewritten into the new Chairman of the Joint Chief of
24 Staff instruction guidelines and format to support the
25 acquisition programs changes that had been made since

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1 the initiation of some of the earlier requirements,
2 particularly vaccines. And a third group were ones
3 that were immature, where requirements had been
4 crafted and developed as future capabilities, but
5 there were candidates in the tech base, the pipeline
6 through Defense technology objectives that were going
7 to mature and presented themselves as active
8 candidates for advanced development, that would
9 support the crafting the requirement document and get
10 the program into the advanced development stage. Next
11 slide.

12 (Slide)

13 As I mentioned before, prior the JSIG
14 stand-up, the Army was the principal lead on this,
15 Now it's a fully vested joint program that has active
16 participation from each of the services. The
17 individuals have been either recommended by their
18 Army, Navy, Air Force and Marine Corps principals to
19 the JSIG side, or also at the advice of the Surgeons
20 General of the respective services.

21 The JSIG Medical Program Subpanel is the
22 integrator of these requirements. Again, in the
23 chem/biodefense arena, it's a one-service/one-vote
24 type of initiative. I think it was alluded to earlier
25 that there's a challenge and there's a competition, if

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1 you will, within the chem/biodefense arena, that
2 medical programs compete against nonmedical programs.

3 Do they need a detector for biological warfare
4 agents, or do you need a therapeutic? It comes out of
5 the same pile of money.

6 Well, I would tell you that the question
7 has been asked of the previous presenters about what
8 change has happened since September 11th, and I think
9 the most significant change in the requirements
10 generation process and also echoed in the Defense
11 Planning guidance, has been a change from a threat-
12 based type of capability or program, to a pure
13 capability basis. It's not a threat-based program,
14 it's a capability-based program. And that, for
15 instance, if the best way to remediate the effects of
16 a biological warfare agent is a vaccine, no one will
17 ever get ill. That's where the effort was prior to
18 9/11. Now it's realized that maybe those things can't
19 reach fruition in a time frame that the user wants, so
20 you've got to have other arrows in your quiver. You
21 need a therapeutic, you need a prophylaxis, and there
22 was a supposition to some degree that because of the
23 physician-patient relationship with therapeutics and
24 associated with therapeutics, that this would be
25 carried more in the administration of therapeutics

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1 those individuals that would have succumbed to a
2 biological agent attack.

3 Well, since then, Dr. Cirone has pointed
4 out that that's been assessed in a mass casualty
5 situation that would be generated from a weapon of
6 mass destruction initiation, but that relationship
7 doesn't exist once it's amassed. So, just reliance on
8 that one-to-one relationship for a therapeutic support
9 issue doesn't pass muster at this particular juncture.
10 So that's changed the focus of how the requirements
11 community is looking at ways to remediate the problem
12 and protect their soldiers, in this case those
13 individuals under their responsibility. Next slide,
14 please.

15 (Slide)

16 This goes into detail of the analysis
17 process we used. I think we can pass that, I've
18 covered that pretty thoroughly already. Next slide,
19 please.

20 (Slide)

21 These are the current programs that have
22 requirement documents that support them. Every year,
23 the requirement community gets together and looks at
24 capabilities and requirements that are based on an
25 analysis of shortfalls in the existing system, and

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1 they look at the tech base to see what transitioning
2 technologies are available and use that to support
3 prioritization of a capability previously manifested
4 in programs that are used to support the POM bills
5 that the services undergo for the Chem/Biodefense
6 Program. It's a standard POM. On the on-years it's a
7 six-year program, on the off-years it's a five-year
8 program. We're in a full POM this year, so we are
9 currently in the process of developing the '04 to '09
10 POM. The basis is the President's budget from the
11 previous year, and everything outside the President's
12 budget competes as over guidance issue supported or
13 unfunded requirement. The process is not unchanged
14 with the other POM processes. The thing that affects
15 Chem/Biodefense Program are those dollars that are
16 salted in by other agencies and other initiatives that
17 change the ebb and flow of efforts that are made.
18 Monies that come in pre-POM have no effect on what
19 program is in the outyears.

20 So, the challenge that the developmental
21 community has, as Col. Danley articulated, is they
22 have to look at when science is going to be able to
23 hit a target POM and budget those dollars by the color
24 of money, if you would, to reach actualization and
25 when they're going to be able to do an FDA approved

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1 product. And if it slips, as you mentioned, it
2 becomes at-risk because it doesn't get executed
3 because there are rules about executing those funds.
4 So funding is a very key point to this process, but
5 funding at the right time at the right place is even
6 more critical.

7 The ones that are highlighted in blue,
8 down to about Q-fever, I believe, are all biological
9 programs. The other ones are programs to support the
10 chemical defense side. And I won't spend a lot of
11 time on addressing those. Next slide, please.

12 (Slide)

13 As we flip through these things, the way
14 this is set up is a description of the system,
15 performance requirements of that system, the
16 capabilities that are articulated usually in efficacy,
17 and also the protective factors associated with them,
18 and then the status of the requirement document. A
19 question was asked earlier about milestones. The
20 acquisition process requires that certain performance
21 happens at different time lines that are described as
22 milestones. An approved requirement document is
23 required -- and I say by "approved", it has to be
24 signed off by the Acquisition Decisions Board of each
25 of the services that were participating in the program

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1 have to be available at Milestone B transition. A
2 program cannot go into advanced development -- let me
3 rephrase that -- it can't go into procurement until it
4 has that Milestone B transition process. That's a
5 marriage between the requirement, the user
6 representative, and also the developer as well, to
7 make sure this program is ready to transition forward.

8 The problem that the medical community has
9 in this arena is FDA approval, which isn't required
10 until transition from Milestone C, which is before
11 they go into full-range production. And they have to
12 have A and B certified as well as the efficacy and
13 safety standards that have been applied by the FDA.

14 And it's a sliding scale, which makes it unique to the
15 acquisition process. It's not a clean transition from
16 Milestone A to Milestone B to Milestone C because
17 requirements of the FDA may push it back into an
18 earlier stage. It changes the requirement with the
19 color of money, and if they have a program in that
20 flex point, that puts the program in jeopardy as well.

21 Again, very regulatorily administered, and that all
22 will develop following along those funding lines.

23 We can kind of flip through these pretty
24 quickly. These are just, again, descriptions of the
25 same program that we've seen from the advanced

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1 development stage. You won't see any S&T programs
2 articulated in here because the user community only
3 prioritizes mature technologies in the details that
4 are going to transition to a requirement document,
5 from one that already has a requirement document
6 written for it. Next slide, please.

7 (Slide)

8 (Slide)

9 (Slide)

10 (Slide)

11 (Slide)

12 (Slide)

13 By the way, these are again priority on
14 the priority list. These are not the empirical
15 priorities, these are the medical priorities as they
16 stand. So you saw anthrax at No. 1, smallpox is No.
17 2. Of the programs that fall into this program,
18 that's the transition position on the current priority
19 list. Next slide.

20 (Slide)

21 I apologize, that got stuck in there.
22 That's a chemical program. That's a protection base
23 to prevent the effects of chemical warfare.

24 (Slide)

25 This is the JBAID system that Col. Danley

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1 addressed. One of the paradigms that exists -- it's
2 an over-used term in the chem/biodefense arena -- is
3 the nonmedical community hazard prioritization in the
4 contamination avoidance arena which further detection
5 devices fall into because they want to be able to
6 detect and treat, that's the phrase that they use --
7 again, going to that capabilities-based assessment,
8 what the medical community has convinced them to do is
9 that if you want to detect on one hand and you don't
10 have the capability to treat once you've detected it,
11 it's not a full capability-based issue. And the light
12 kind of goes on sometimes, which is a pretty basic
13 analogy of that. And they are really starting to
14 support that, and these programs have done very well
15 in competition with their nonmedical counterparts.
16 Right now, there are 72 programs that are prioritized
17 in the chem/biodefense priority list. All the medical
18 programs, with one exception, are 33 or above. One of
19 the vaccine programs is down below that line
20 significantly because of some slippage in the fast
21 transition capability, it's gone back to the tech
22 base. Next slide, please.

23 (Slide)

24 These are some capabilities for future
25 requirements. It's hard to see in blue, but the third

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1 from the bottom is staphylococcal enterotoxin vaccine,
2 which is a newly transitioning capability that Dr.
3 Linden's office, where Col. Skvorak works, has come up
4 with a good candidate, and there's a meeting scheduled
5 to take place to craft out the shell of the
6 requirement document for that program going into
7 advanced development.

8 The latter one is a new capability that
9 was presented by Dr. Cirone to the Medical Program
10 Subpanel here about a month and a half ago, and it is
11 for post-exposure chem-prophylaxis/therapeutics for BW
12 agents.

13 Presently on the priority list, chem
14 therapeutics for biological warfare agents, not
15 prophylaxis by chem therapeutics, is the No. 1 CD
16 defense medical capability on the priority list. But
17 as I mentioned before, because of the philosophy of
18 the Medical Program Subpanel and the nonmedical
19 community after advice was that the therapeutic issue
20 was almost minding itself, and that there were
21 approved therapeutics for each of the biological
22 warfare agents because most all of them occur
23 naturally in some manner, shape or form, and they
24 already had an FDA approved product to be applied
25 against that.

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1 Well, that since has changed and has now
2 changed the fact that we have to come up with a way to
3 support the developmental community doing the efficacy
4 tests that are being required by the FDA to put those
5 products in the arsenal, if you will, of the physician
6 as an on-label application not only for the
7 therapeutic aspect of it, but equally as important in
8 some instances as the post-exposure prophylaxis to be
9 used to buy time for confirmatory analysis or
10 identification of that product for that warfare agent,
11 and then the subsequent treatment that may be
12 required. Next slide, please.

13 (Slide)

14 This is kind of an outline for some of the
15 components of the requirement document that the user
16 community is trying to address in drafting this
17 requirement for the use of the developer. Protection
18 needs to follow across those regimens that are there,
19 and the products that support that may be different
20 candidates. One of the challenges that we have in the
21 user community is building the requirement document in
22 such a way that it's not generic in nature and that
23 you want one over the world requirement with a
24 multitude of different capabilities because FDA is
25 going to ask you what requirement are you placing this

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1 product against and you give them a capstone
2 requirement, it may not meet their needs because the
3 application policies and procedures may be different
4 for each of the candidates that may be put before the
5 FDA for approval. So we have to be able to build it
6 in a way that will support the capability, but also
7 not limit the developer what products or what
8 candidates they choose to support that utilization.

9 And, again, the key to this thing is FDA
10 approval. The user community has also realized that
11 there are stages prior to FDA approval that having
12 something that may be available for IND application
13 with the approved policies in place to support that
14 use isn't an 80-percent solution per se, but it
15 certainly gives the commander in the field you any
16 capability that they wouldn't have if FDA approval was
17 the empirical answer and nothing short of FDA approval
18 would be supported by anybody in the developmental
19 community. So, you can't change the thought
20 processes, FDA approval certainly is the goal. It's
21 the key performance parameter for all the requirements
22 -- in other words, it has to have them at the end of
23 this processes, but the development to get to that
24 point also may provide an important capability in a
25 contingency application.

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1 These therapeutics and prophylaxis that
2 are going to be developed are not going to be at the
3 expense or to replace the vaccine program. That is not
4 the intent of the use. There is a proper marriage of
5 all these capabilities as they fit together. I would
6 tell you that there's a feeling that maybe a vaccine
7 isn't required for all BW agents, as was discussed by
8 someone earlier, but there's a protective capability
9 that is required for all BW agents because they are on
10 a threat list. They do have some medical consequences
11 associated with them. So, getting that capability to
12 the commanders in the field or the decisionmakers that
13 are responsible for providing care in the DOD
14 environment as that program shifts is the goal to the
15 user community. Next slide.

16 (Slide)

17 I guess that's it. As I mentioned before,
18 I'm part of the Lint Service Integration Group. I
19 learned along with you that they're going away --
20 actually, I knew that before. The federal
21 requirements generation organizational process is
22 under review at the direction of DOD, and the new
23 requirement organization, currently called the Joint
24 Requirement Office, probably more aptly named, there
25 will still be an organization representing the DOD

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1 user community, as required by public law, and
2 establishing CBRN now defense requirements are
3 necessary, and the medical piece of that is going to
4 be a very important part. I'm a Battelle employee.
5 I'm a contractor, in contractor clothing, but -- I
6 don't say contractor very often -- but we are charged
7 to support the DOD in the development of these
8 requirements, and the facilitation of them through the
9 acquisition process, and there will be someone doing
10 that, myself included, potentially as we go through
11 the system in an effort not to throw the baby out with
12 the bathwater. We're kind of critical juncture. As
13 we indicated earlier, the requirements cross-
14 organizational community and the developmental
15 community is undergoing some changes to facilitate
16 trying to get the best things of all the organizations
17 moving forward to try to get things in the hands of
18 the users. Subject to your questions, that's the
19 information I have for you today.

20 DR. OSTROFF: Thank you. Any questions
21 from the Board?

22 (No response.)

23 I have one for Dr. Cirone, and that is, do
24 you have contingency INDs in place while this process
25 of changing the labeling is being pursued?

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1 DR. CIRONE: Well, sir, I inquired about
2 the possibility of an IND for these products, and
3 basically I was told we have to put a package together
4 and send it to the FDA. And we have to meet all the
5 requirements when we put together that package, and
6 that package has to include a certain amount of data.

7 And they said if we want data, we have to do some
8 studies and in order to do those studies again, you
9 know, to get into the queue, and that's what I'm
10 trying to do, see if I can get a joint requirements so
11 that that would support -- there's not really a
12 requirement in the S&T community for a joint
13 requirements document, it's more for the advanced.
14 But the bottom line is once you have a joint
15 requirements document that shows that the user wants
16 this, I think that gives you the argument that you
17 need to see if you can then get into the queue to get
18 the research -- the answer is, no, we haven't gone
19 down the line. We've gone down the line for INDs for
20 smallpox, anthrax and post-exposure with antibiotics,
21 the same basic ones that CDC is doing.

22 DR. OSTROFF: Well, I only ask the
23 question because we are pursuing INDs for all of
24 these.

25 DR. CIRONE: When you pursued your IND,

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1 did you exclude Department of Defense?

2 DR. OSTROFF: What's that?

3 DR. CIRONE: Did you exclude the
4 Department of Defense on the label in your IND, or can
5 we jump onboard?

6 DR. OSTROFF: It's an IND for use before
7 the labeling gets changed. The issue of having an IND
8 in place to give people these therapeutics on a
9 prophylactic basis for which they are not labeled is
10 distinct from getting the label to be changed. I
11 mean, that's not the purpose of the IND. The purpose
12 of the IND is so that we can give people the drug.

13 DR. CIRONE: I understand, but when you
14 submit the IND, sometimes the Health and Human
15 Services has put forth an IND that has excluded the
16 Department of Defense and sometimes they have. And so
17 if they haven't it specifically excluded us, then we
18 can jump on the bandwagon and use that same argument.

19 DR. OSTROFF: There's no reason not to,
20 it's just a matter of making modifications to the
21 consent forms for use in military settings.

22 DR. CIRONE: We need to talk and pursue
23 that because we've considered it, and I've talked to
24 FDA -- in fact, we're doing that and certainly we
25 might need get an IND, so at least we can use it as an

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1 IND. Of course, that would be with all the
2 requirements of VIG, we understand that. We're doing
3 that for all our other contingency protocols,
4 recognizing that we must meet the educational process,
5 the follow-up in management and, certainly, we want to
6 meet (inaudible).

7 DR. OSTROFF: Other comments?

8 (No response.)

9 Thank you. We have several other
10 presentations to go through. The next two
11 presentations are from Dr. Rick Stout and Mr. Kurt
12 Lyman from the Bioject Corporation. They are going to
13 provide an informational brief to the Board on needle-
14 free injection technology, and these presentations can
15 be found at Tab 7.

16 MR. LYMAN: Thank you very much. We
17 appreciate the opportunity to talk to the Board about
18 needle-free injection technology. I'll be joined by
19 Dr. Richard Stout, who is our company Vice President
20 for Clinical Affairs.

21 Before we get started with the text of our
22 presentation today, I'd just like to do a real quick
23 survey around the room. How many of you have
24 experience either as users or uses with needle-free
25 injection technology?

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1 (Show of hands.)

2 Looks like about 25 percent of the room.

3 Thank you. I thought it might be helpful before we
4 actually get started because we are going to be
5 talking about current and emerging technology, to do a
6 very quick demonstration of current state-of-the-art
7 needle-free technology, and I'm going to be assisted
8 here, if you can see, by my "patient who never
9 complains", and those of you who are physicians need
10 to get you one of these "patients".

11 The system consists of three main parts.
12 I have the actual injection device here. We have the
13 patient. And then we have the part of the device that
14 actually comes in contact with the patient, which is a
15 pre-filled -- I filled previous to this presentation,
16 needle-free syringe. It's made of medical grade
17 polycarbonate, and I'll walk through this several
18 times so you can see how the system works.

19 We take our syringe and insert it and lock
20 it into the device. The device won't work unless the
21 syringe is locked in place. That way we can't launch
22 a syringe at high velocity across the room. So we
23 lock our syringe in place. Pull off the safety cap.
24 Your site preparation would be exactly the same as for
25 any other sub-Q or IM injection. The injection

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1 technique calls for a 90-degree angle at the injection
2 site. You simply squeeze and release the blue button.

3 In the space of about half-a-second your IM or sub-Q
4 injection is given. If this poor, unfortunate patient
5 is like your average six-month-old, you're going to
6 require multiple injections, we can simply, as you
7 see, insert a new needle-free syringe into the device
8 for each injection, and we're off to the races. Also,
9 if we're giving mass immunizations like for an
10 influenza campaign or MMR or Hepatitis-B or something
11 like that, we can provide multiple injections fairly
12 quickly and really the level of expertise that's
13 required -- my wife tells me that I can be trained to
14 do this, probably just about anybody can -- but the
15 level of expertise that's required is perhaps less
16 than you'd expect to see with a needle and syringe.

17 So, I wanted to walk through the
18 technology so that you'll have an appreciation of how
19 the device works. Next slide, please.

20 (Slide)

21 These are the general points we'll cover
22 today. I'll briefly review the old technology. We'll
23 take a look at what's available today, and then Dr.
24 Stout will talk in significant detail about the
25 current and ongoing research that Bioject is

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1 participating as a member of industry that's working
2 with various governmental agencies on many of these
3 emerging vaccines that previous presenters have done a
4 real good job of discussing today. Next slide,
5 please.

6 (Slide)

7 A little bit about Bioject. We're quite a
8 small company, maybe 60 employees total. Our company
9 headquarters is in New Jersey, our Operations
10 Headquarters is in Portland, Oregon. Currently we
11 have six products that are FDA cleared to market. We
12 never say "approved" because we know that, at least in
13 medical devices, the FDA doesn't approve anything,
14 they simply agree that what the company is claiming
15 the device does, it in fact does. Pretty strong
16 patent position. And as you see in the first bullet
17 here, we are focusing on needle-free injection of
18 liquid medication. Next slide, please.

19 (Slide)

20 This is a little bit washed out, but what
21 the doctor is holding here is an inch-and-a-half 23
22 gauge needle, and I think most of us either as parents
23 or patients can identify with the patient here and
24 wonder if maybe there wasn't a better way, and that's
25 really what we're here to talk about today. Next

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1 slide.

2 (Slide)

3 Just a brief review. I've tried to depict
4 here two injections, one intramuscular, here on the
5 left, with a needle and syringe, and then
6 intramuscular with a needle-free device over here on
7 the right.

8 When we give an injection intramuscular
9 with needle and syringe, we're pushing the needle
10 through the skin, through the adipose, through the
11 muscle fascia, and then we're physically displacing
12 tissue within the muscle and establishing a bolus.
13 The patient's body can only utilize that medication
14 that's at the outside perimeter of the bolus, so you
15 have a real low surface-to-area ratio and pretty
16 limited tissue disruption, tissue exposure to the
17 medication.

18 When we give an IM injection to a lesser
19 extent sub-Q with a needle-free device, what we see is
20 that by forcing the medication at high velocity
21 through the skin -- in this case, the adipose and
22 muscle fascia -- by the time we get down into the
23 muscle tissue, medication follows the path of least
24 resistance and is dispersed over a much larger volume
25 inside the tissue, so you end up with greater tissue

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1 exposure and disruption to the medication, and perhaps
2 from the patient's point of view the advantage is that
3 the entire injection event lasts less than half a
4 second. Effectively, from the patient's sensation,
5 what that means is by the time they feel the
6 medication in their tissue, the event is already over.

7 Next slide, please.

8 (Slide)

9 Now, some of you may recognize the usual
10 suspects here. This is an example of some of the
11 older technology -- the gun-style injectors that were
12 widely used by the U.S. Military, World Health
13 Organization, even Public Health within the U.S.

14 Clinical efficacy was very well
15 established. They were literally used in the '50s,
16 '60s and '70s to give hundreds of millions of
17 injections as part of the World Health Organization's
18 disease eradication campaigns in the developing world.

19 Some of the devices, like these three on
20 the left here, were limited to subcutaneous delivery
21 because they were powered by springs, and there were
22 some other drawbacks with the large, high-volume
23 devices. They were pretty expensive, they tended to
24 be large and bulky and complex. They looked like
25 guns. The tip of the device was just a stainless

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1 steel nozzle here, and so the nozzle was not changed
2 in between injections. You had the risk of spreading
3 pathogens, which nowadays, of course, is pretty
4 damning and, in fact, that's why these devices aren't
5 being used in the U.S. or by the World Health
6 Organization overseas anymore. The devices were
7 painful. They would cause lacerations at the
8 injection site. So, from a clinical point of view,
9 although it was a great way to give a lot of
10 injections really fast to many patients, there were
11 some pretty significant drawbacks. Next slide,
12 please.

13 (Slide)

14 The body of data that's published about
15 needle-free injection is pretty well established.
16 Here you can see we've kind of broken it up in 20-year
17 periods. The different publications regarding
18 vaccines and other prophylactic drugs that have been
19 administered needle-free, so the body of evidence is
20 pretty significant. And as we get down here into more
21 modern times, look at some of the developmental drugs.
22 We see DNA-based vaccines, Hepatitis-A, Lidocaine,
23 Midazolam, Yellow Fever, MMR, Influenza. These are
24 all vaccines that we're all very familiar with. Next
25 slide, please.

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1 (Slide)

2 I apologize for the washed out
3 presentation here. What I was trying to show is three
4 different products, two of which are already cleared
5 to market here in the U.S. The B-2000 which is the
6 device I started off with a brief demonstration on,
7 the Vitajet 3, and the B-2000 are clinical devices
8 designed to be used on multiple patients for multiple
9 injections. A personal injector, which is called the
10 Vitajet 3, which is designed to be used with insulin,
11 and we are also developing -- or have developed two
12 different versions of that device for use with human
13 growth hormone for a Swiss-based company called
14 Cerono, and those products are now being used in the
15 U.S. And then emerging technology, which is the
16 disposable either clinical or self-injector called the
17 Iject, which will be a single-use pre-filled device
18 that will be designed to deliver the medication either
19 IM or sub-Q, and then the device itself will be
20 discarded. It will be just a little bit larger than
21 this laser pointer here. Next slide, please.

22 (Slide)

23 And then a brief introduction to the
24 Biojector 2000. It is 100 percent needle-free. In a
25 time when we're looking at controlling the exposure of

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1 healthcare workers to blood-borne pathogens, it's a
2 technology that eliminates needle stick injuries. It's
3 pretty easy to use. In a lot of states today, we see
4 medical assistants or MedTechs who are giving
5 injections, and even people with fairly limited
6 training can pick up the use of this technology fairly
7 quickly.

8 I think you will agree that most patients
9 would certainly prefer to get their injections needle-
10 free, and there is an additional advantage in that by
11 using needle-free technology, you reduce the amount of
12 expensive and dangerous "sharps" waste that's
13 generated in the injection process. Next slide,
14 please.

15 (Slide)

16 As I mentioned in the demonstration, the
17 Biojector 2000 consists of three main components. You
18 have the actual device, which is a Class 2 medical
19 device. FDA market release initially in 1989 and then
20 in 1994. It's a pretty rugged, durable piece of
21 equipment, should last in excess of 120,000
22 injections.

23 What doesn't show up well here is the
24 power source, which is a small CO2 cartridge. Each
25 cartridge gives you enough power for between 10 and 15

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1 injections. And then for some of our larger clinical
2 customers, primarily the interest in this technology
3 has been in the military, we've developed a tank
4 adapter system that allows the Biojector to be hooked
5 into a large CO2 pressure tank, so that instead of
6 giving 10 to 15 injections per cartridge, you're
7 giving about 20,000 injections per pressure tank. And
8 for mass immunization campaigns, that's a very cost-
9 effective way to go.

10 And then the single-use, sterile,
11 disposable syringe is the part of the system that
12 actually contains the drug, comes in contact with the
13 patient and delivers the drug into the patient's body.

14 It's made of medical grade polycarbonate, it's latex-
15 free, and depending on the configuration you select,
16 you select the correct syringe and then you give
17 either a sub-Q or an IM injection. Next slide,
18 please.

19 (Slide)

20 Giving an injection with the Biojector is
21 pretty simple. It's a five-step process. you put the
22 injectate into the syringe, whether it has to be
23 reconstituted or it's already a liquid medication
24 makes no difference. You put the syringe into the
25 Biojector like I demonstrated, at a 90-degree angle at

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1 the injection site. You push the actuator, keep the
2 device up against the injection site to a count of
3 three, and then once you remove the device the patient
4 or the patient's parent can simply hold pressure at
5 the injection site, and the whole process is pretty
6 fast and easy. Next slide, please.

7 (Slide)

8 And Dr. Stout.

9 DR. STOUT: I'd like to explain how we do
10 this injection. This is our pressure profile. Within
11 the syringe, when you pull the actuator, reacts with
12 up to 4,000 pounds per square inch during what's
13 called the "penetration" phase. This is where it
14 penetrates the skin. Right after we penetrate the
15 skin, we drop the pressure down into what's called the
16 "delivery" phase. That's given about 2,000 pounds per
17 square inch. Then at the end of the injection, we
18 abruptly stop everything. And if you look, this total
19 injection time was about a quarter of a second. Very
20 important that we maintain this type of a pressure
21 profile to be able to give a very precise injection.
22 Next slide.

23 (Slide)

24 With this pressure profile, we're able to
25 do three types of injections. Some of the older

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1 technology wasn't able to do this. We're now able to
2 do an intramuscular injection, which basically is
3 putting all of the injectee into the muscle, leaving a
4 very small track behind where we actually cut the
5 hole. Remember, we are putting a hole in the skin.
6 This is waterjet technology. So we put a very tiny
7 hole in the skin. This hole is smaller than a human
8 hair. This is a subcutaneous injection where we're
9 able to put it at the level of the adipose tissue, and
10 this is an intradermal injection which we recently
11 have started to develop. Se have several ongoing
12 clinical trials now where we're taking a lot of the
13 vaccines and putting it intradermally because we're
14 seeing that we get a lot of enhanced efficacy if we
15 put it right underneath the dermis, and I'll talk a
16 little more about this later on. Next slide.

17 (Slide)

18 We have a number of collaborations. We
19 have about 45 to 46, 47, 48 collaborations that we do
20 clinical work with, and they divide into about 16
21 percent is with the government. About 45 percent of
22 these collaborations are academic, and about 39
23 percent of these are commercial or pharmaceutical
24 partners. Next slide.

25 (Slide)

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1 Of these collaborations -- I'll just break
2 down a little bit about the clinical work of what
3 we're doing and what areas we're working in. About 73
4 percent of these are in DNA vaccines -- no surprise --
5 about 6 percent are in traditional vaccines, about 6
6 percent are in proteins, and 9 percent small
7 molecules, and 6 percent in other things. Next slide.

8 (Slide)

9 This will break down a little bit about
10 our clinical programs and what areas of research we're
11 involved in. About 45 percent of our clinical
12 collaborations are in small animals right now, this is
13 where we start off in the mice and rodents rabbits and
14 that type of stuff. We then have about 21 percent in
15 large animals. We have several programs where we're
16 working with large animals to develop vaccines for the
17 production animals as well as domestic animals. We
18 have a group right here that you can't see, this is
19 our nonhuman primates, which runs about 15 percent,
20 and our humans is about at 20 percent right now,
21 somewhere from about 14 percent up to about 20
22 percent. Next slide.

23 (Slide)

24 We've published in a lot of journals. I
25 mentioned earlier, the publications date back to 1946.

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1 That has to do with jet injection or needle-free in
2 general. These publications which you have a copy of
3 are the journals that we've published in with the B-
4 2000, and these are the categories specifically in
5 which we've published, which has to do with DNA
6 vaccines, conventional vaccines, local anesthesia,
7 live virus -- a lot of questions are asked clinically
8 can you give live viruses, a lot of the vaccine
9 programs, the DNA right now, we're giving a prime
10 boost regimen. We're looking at giving live virus
11 vaccinia and pox and those types of things. We've
12 published on pretty much all of those now, so we are
13 able to deliver that kind of medicine. Next slide.

14 (Slide)

15 We have about -- this says 30 -- I'd say
16 we're up to about 45 collaborative research programs
17 right now. Some of them are public, and I can talk
18 about other ones that we haven't talked about yet. We
19 are involved in the NIH program with the HIV trial
20 that's going on there. We've done work and published
21 with NCI on lymphoma vaccine. We've currently
22 announced not long ago that we are part of the
23 Memorial Sloan Kettering melanoma trial that's going,
24 which is a DNA-based vaccine, and we're involved in
25 the malaria program with the Naval Medical Research

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1 Center, and a number of other ones that we haven't
2 talked about yet. Next slide.

3 (Slide)

4 Kurt?

5 MR. LYMAN: Thank you, Dr. Stout. One of
6 the questions that we encounter in the clinical
7 setting is, why would I consider needle-free? What
8 we're hearing in a lot of clinical centers is that
9 there are issues of patient compliance. There are
10 actually patients who avoid coming in for treatment
11 because there is a needle involved in the injection
12 process. Health care workers say this is a big issue
13 since President Clinton, in November of 2000, signed
14 into law the Health Care Worker Safety Act, and now
15 commercial, private practice, and federal facilities
16 do have to be getting themselves into compliance and
17 using safer technology for their health care workers.

18 We have seen anecdotal information in a
19 number of studies that indicated that the needle-free
20 injection delivery mechanism seemed to enhance the
21 immune response of selected vaccines, although
22 certainly we can't say that categorically, but there
23 was some real interesting information that came out of
24 the Hepatitis-A study in the State of Alaska, and also
25 a Yellow Fever study that was done in the mid-'90s.

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1 And then, finally, not only OSHA, but of course now
2 JCAHO has gotten involved in looking at health care
3 facility safety programs, and they'll be looking to
4 see what safer technology is being used by the health
5 care workers. Next slide, please.

6 (Slide)

7 As we look at the issue of safety, this is
8 a question that program managers need to ask, for
9 doctors, for nurses, for medical technicians, is this
10 an acceptable medical occupational risk. Needlestick
11 injuries are costly both from a dollar-and-cents point
12 of view, and also from a human cost point of view.
13 There's a lot of uncertainty involved in that. The
14 scary thing is that of the 600,000 needlesticks that
15 are reported in the U.S. each year, probably for each
16 needlestick that's reported, one goes unreported.
17 Next slide, please.

18 (Slide)

19 In the field currently there's a number of
20 different applications for this technology. Dr. Stout
21 has talked in detail about the research application,
22 and this is what I'm trying to get at here with the
23 first bullet that talks about biotech delivery
24 products. The biggest direct users in the U.S. of
25 this technology currently seem to be Public Health,

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1 military sector, and for-profit immunization sector
2 that's really targeting mass immunizations for
3 Influenza and for Hepatitis-B. We are seeing
4 increased interest among private practices, peds, and
5 outpatient clinics, and we've talked in detail about
6 the research end of it. Next slide, please.

7 (Slide)

8 Here is some contact information for Board
9 members or members of the audience who are interested.

10 At the end of this session, we'll have some
11 additional technical and clinical data available.

12 This concludes our presentation then, subject to your
13 questions.

14 DR. OSTROFF: Thank you. Are there any
15 questions from the Board?

16 DR. GRAY: I can see where this would be
17 very handy in the Department of Defense. This is Greg
18 Gray, from Iowa. But I'm wondering if we get into an
19 event situation where there is a bioterrorism act, is
20 this adjustable for different amounts of subcutaneous
21 fat such as with perhaps the elderly?

22 MR. LYMAN: That's an excellent question.

23 Bioject has conducted extensive research on the issue
24 you're getting at, which is really depth of
25 penetration. And what we've found is that with our

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1 No. 2 syringe -- that's the syringe that's designated
2 for sub-Q delivery -- is that it just doesn't make
3 enough penetration power to get through the muscle
4 fascia even on very, very thin patients with almost no
5 adipose. It requires a lot of energy to breach the
6 skin and to establish an injection pathway, and then
7 the adipose, if you will, sucks up further energy.

8 So, what we've seen in live patient models
9 using contrast media and then measuring depth of
10 penetration with an MRI, and also with extensive
11 cadaver work that's been done at Cambridge University
12 in the U.K., is that even in those very thin patients
13 where there's not much adipose at all under the skin,
14 if the injectate goes all the way through the adipose,
15 it will just lay down flat on top of the muscle
16 fascia, it won't achieve high end penetration.

17 So, from our observation and the clinical
18 reporting of maybe the 12 million or so needle-free
19 injections that have been done with this product since
20 about '95, we don't have any documented evidence of
21 injection that was intended to go sub-Q going high
22 end.

23 DR. BERG: Bill Berg. What sort of safety
24 device do you have in place so that while they are
25 holding the device with one hand, twisting the syringe

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1 with the other, so that they don't have their finger
2 on the trigger and blow it up into the air or their
3 face?

4 MR. LYMAN: That's a great question. Each
5 syringe comes packaged with this little safety cap.
6 For example, if I was going to fill my needle-free
7 syringe, I would attach it to the medication vial, use
8 this needle-free adaptor to suck the medication out of
9 the vial into the syringe, and then immediately after
10 I've filled I take my little safety cap and attach it
11 to the front of the syringe so that even if I were to
12 activate the device inadvertently, instead of
13 aerosolizing the medication, all I do is just spill it
14 out the end of the safety cap. And in our training
15 program for clinicians, we train them not to remove
16 the safety cap until they are actually ready to give
17 the injection to the patient.

18 DR. PIERCE GARDNER: In the hands of a
19 skilled operator such as yourself, what's the
20 throughput in a mass immunization, how quickly? And,
21 secondly, for vaccines that you would like not to have
22 much intradermal -- you want an IM -- you worry about
23 arthus reactions and frequent tetanus, for instance --
24 how do you avoid the deposition intradermal, and have
25 you had arthus reactions in patients with tetanus.

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1 MR. LYMAN: I'll talk about the throughput
2 question and then Dr. Stout can talk about the
3 deposition question. We've done cooperative programs
4 primarily with the military, but also with various
5 Public Health agencies around the country. In using
6 the Biojector on the tank-adapted system, various
7 customers have achieved a throughput rate of 8
8 injections per minute with one Biojector. So, really,
9 the problem of constraint there was getting the
10 patients to step forward in the line fast enough.
11 Obviously, that was a very carefully controlled trial.
12 The people who were using the equipment were
13 carefully trained by Bioject's clinicians, but
14 certainly 6, 7, 8 per minute per device is an
15 achievable rate.

16 DR. STOUT: Regarding the deposition, the
17 orifice or the hole, the hole that we make in the
18 skin, is smaller than a human hair, so this syringe is
19 equivalent to a 36-gauge needle, which they don't make
20 so small, so the track, if you will, or the deposition
21 in the dermis is literally less than a drop because
22 it's the equivalent of a 36-gauge needle going in.
23 So, we don't deposit all the vaccine as it spreads
24 out, it's a straight line through to the depth we're
25 going in, and then we disperse it at that depth. If

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1 you take a needle and syringe, if you give the
2 injection, you pull back to form a track coming back
3 out. So you get basically more with the needle and
4 syringe than you get with needle-free.

5 DR. NESS: Roberta Ness. You answered one
6 of my questions, which is you just told us that there
7 have been about 12 million injections given using the
8 B-2000 device, is that what you just told us?

9 MR. LYMAN: Yes, that's correct.

10 DR. NESS: And the second question was,
11 you told us a lot about the safety concerns using
12 older devices, but then you didn't comment on the data
13 that you have regarding these 12 million injections
14 with the newer device. Are there safety
15 considerations, at what rate? And the second part of
16 that is, is there any pain associated with the
17 injection? I presume there's some pain. How does
18 that compare to what you find with a needle injection?

19 DR. STOUT: Let me address the pain issue
20 first. Yes, there is a sensation, but in the studies
21 we do, we collect a lot of data on pain. The majority
22 of the time it's the same or less than a needle and
23 syringe because it's over so quickly. We certainly
24 don't tell anybody it's pain-free. You do feel it
25 because you do get an injection, but it's over very

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1 quickly and I think a lot of times you don't feel it
2 as fast because there's no needle, and that makes it
3 feel better.

4 And the other part of your question
5 related to safety. The old devices or basically on a
6 safety issue because of potentially cross-
7 contamination. That tip was used consecutively
8 between everybody, it didn't get changed out. So, if
9 it didn't get clean, there's the potential to spread a
10 lot more pathogens. There's no safety issue with this
11 because it's all thrown away, it's totally disposable.

12 So the safety issues with this are zero as far as
13 cross-contamination. Other safety issues related to
14 some bruising and those types of things, it's
15 equivalent at producing, at least in the reported
16 literature we have seen after 1946 in what we
17 published, we probably have less bruising, if you
18 will. Discomfort you get at site of reaction as when
19 you give any vaccine, but we've had no reported safety
20 issues at all.

21 DR. RUNYAN: You mentioned applying
22 pressure post-injection for a minute. That is to
23 prevent back-leakage, or what?

24 MR. LYMAN: Actually, it's not.
25 Application of pressure is really a cosmetic and a

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1 base comfort issue. Some patients, perhaps elderly
2 people, people with real frail skin, very frail
3 capillary structure, you could see a bruise at the
4 injection site. You will see some redness at the
5 injection site because of the dispersion of the
6 medication, particularly in Caucasian or oriental
7 patients. So, really, holding pressure at the
8 injection site is really just designed to minimize
9 bruise effects.

10 DR. OSTROFF: I think that we'll have to
11 cut it off because we're a little bit behind schedule,
12 but just one quick question. You didn't mention
13 anything about cost.

14 (Laughter and simultaneous discussion.)

15 MR. LYMAN: When Bioject has participated
16 in the past and currently with different research
17 organizations, the company doesn't make any money off
18 that. In fact, it's probably a loss. But if you want
19 to be involved in the vaccine development, you have to
20 be involved from the beginning of that product cycle,
21 and so that's why we do that kind of work. Currently,
22 Bioject's federal customers probably pay a maximum of
23 about 68 1/2 cents per injection, and if there's a
24 large volume center like the Navy at Great Lakes, or
25 the Naval Hospital at Pensacola, or Camp Pendleton, or

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1 somewhere like that, they achieve some volume
2 discount. So, I think realistically something in the
3 63-64 cent per injection range is very achievable.

4 DR. OSTROFF: Thanks. We have to move on
5 to our last presentation which, as you can see from
6 the title, involves a question that's before the Board
7 related to threat agents in the blood supply, and our
8 presenter is Dr. Ed Tabor, from FDA.

9 DR. TABOR: Good afternoon. I'd like to
10 thank Col. Fitzpatrick and Col. Riddle and the Board
11 for giving us this opportunity to discuss one facet of
12 our program for preparation for possible bioterrorist
13 attack, and to solicit your comments on that. An
14 important part of the Food and Drug Administration's
15 response to the increased risk of bioterrorist attack
16 on the United States and the impact that such an
17 attack might have on the blood supply is through the
18 creation of a list of potential agents and their
19 characteristics related to their potential impact on
20 the blood supply. This list can be used as a guide to
21 research and policy decisions to enhance our
22 preparedness should such an attack occur. The FDA
23 list, titled Infectious Agents Potentially Transmitted
24 by Transmission of Blood Products With Potential Use
25 in Bioterrorism, through out an earlier list of

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1 agents.

2 For the past four and a half years, U.S.
3 Public Health Service Committee on Emerging Effects of
4 Diseases, a working group co-chaired by Dr. Mary
5 Chamberlain of the CDC and myself, who reports to the
6 Interagency Working Group on Blood Safety and
7 Availability, has met regularly to evaluate new
8 developments in infectious diseases that might signal
9 the emergence of a new threat to the blood supply.

10 The committee maintains a database of
11 known emerging infectious agents with a potential to
12 enter the blood supply. Most agents on that list are
13 those whose pathogenicity was known and whose
14 transmissibility by blood was considered to be
15 possible. A copy of that list as well as the list of
16 bioterrorism agents has been provided to the Board.

17 Now, in addition to Centers for Disease
18 Control, as you well know, maintains a publicly
19 available list of infectious and chemical agents that
20 could be used by terrorists. This list can be seen at
21 their Web site www.bt.cdc.gov. Using the CDC list as
22 a basis, we determined which of the agents could
23 present a risk for the safety of the blood supply. In
24 general, this meant identifying agents that have an
25 asymptomatic incubation period during which someone

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1 might inadvertently donate blood. In the event of a
2 bioterrorist attack, if infections caused by the
3 attack remain asymptomatic for days or weeks, blood
4 donations during that period could be infected, and
5 new infections transmitted by transfusions could be
6 unrecognized for a period of time.

7 Even after a bioterrorist attack has been
8 recognized, it might be difficult to maintain an
9 adequate blood supply if asymptomatic infected
10 potential donors could not easily be separated from an
11 uninfected healthy donors.

12 Our clinical data are sparse for many of
13 the agents on the FDA list, so we have had to rely on
14 expert advice rather than published studies in some
15 situations. Much of that advice is obtained from
16 various U.S. Government agencies, including the
17 Department of Defense, and we're very grateful to all
18 those who took the time to answer our questions about
19 these agents.

20 I want to emphasize that I am not an
21 expert on any of the agents on this list. I would be
22 grateful for any suggestions you could make to help us
23 improve the usefulness of the list.

24 I'd like to take a few moments to describe
25 some of the characteristics of the list and say a few

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1 words about the agents of greatest significance on the
2 list, using smallpox as an example, and some of our
3 concerns about agents that might enter the blood
4 supply after a bioterrorist attack. May I have the
5 next slide, please.

6 (Slide)

7 As I mentioned, the CDC maintains a list
8 of potential agents of bioterrorism. It's official
9 title is Strategic Plan for Biological and Chemical
10 Terrorism (CDC). The full Web site is shown on this
11 slide. The agents on that list are designated
12 Category A, B or C. Category A agents are those that
13 are easily disseminated or easily transmitted from
14 person-to-person. Their agents with a high mortality
15 rate and a great potential for causing panic in the
16 general population when word of their presence becomes
17 known.

18 Agents that are Category B are less easily
19 disseminated, have lower mortality, and less panic
20 potential.

21 Category C agents are those agents that
22 are emerging with potential to become Category A or
23 Category B agents. some situations, Category C
24 agents might be more serious than Category B agents.
25 Next slide, please.

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1 (Slide)

2 On the FDA list, we've assigned priorities
3 based essentially on the risk for the agents being
4 transmitted by individuals inadvertently donating
5 blood at a time when they were capable of transmitting
6 the agent in their blood.

7 We've designated those agents Priority 1
8 that have an asymptomatic viremic or bacteremic phase.

9 Priority 2 are those agents that might have
10 asymptomatic viremic or bacteremic phase, but the data
11 is either incomplete or not available. And Priority 3
12 are those agents with no known viremia or bacteremia
13 during an asymptomatic period, such as the incubation
14 period, but with transmissibility by donating blood.

15 Next slide, please.

16 (Slide)

17 I'd like to say a few words about smallpox
18 with regard to risk through blood transfusion. As you
19 all know, the last known case of smallpox was in the
20 late 1970s, and this fact has given us a sense of
21 security and, unfortunately, complacency, that's
22 illustrated by two quotes I'd like to read to you from
23 one of the latest editions of one of these leading
24 virology textbooks, Fields Virology. The first one
25 is, "Because smallpox is now extinct, we use the past

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1 tense in describing it". And the second quote from
2 Fields Virology is, "There is little point in
3 delineating the clinical features of this now-extinct
4 disease". Now, I think these illustrate the vanity of
5 human aspiration. Next slide, please.

6 (Slide)

7 Smallpox is an orthopoxvirus, and it's
8 primarily transmitted by oropharyngeal secretions. It
9 is, it's true, transmitted to a lesser extent by scabs
10 from the lesions, but the fact that it's transmitted
11 by oropharyngeal secretions means that a suicidal
12 bioterrorist can infect his or herself with smallpox
13 and take a three- or four-day walk on the subways of
14 one or more major cities, and infect tens of thousands
15 or more innocent susceptible individuals.

16 The incubation period of smallpox averages
17 about 12 days, and as far as we know it includes
18 between two to four days when the patients are viremic
19 despite the fact that there isn't lesions. And
20 smallpox progresses so rapidly that death can occur
21 even before a rash appears. Next slide.

22 (Slide)

23 Smallpox virus is resistant to drying at
24 room temperature for many months, and one other aspect
25 of its hardiness, so to speak, with regard to blood

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1 products, is that it consists of both envelope and
2 non-enveloped infectious forms. The fact that most of
3 the particles are non-enveloped means that it might
4 not be susceptible to the viral inactivation processes
5 that are applied to most classic derivatives that are
6 manufactured in the United States. Next slide.

7 (Slide)

8 As I mentioned, there is an asymptomatic
9 viremic phase during the incubation period in naive
10 individuals who are infected for the first time. It
11 appears that there might also be other situations in
12 which an individual can be asymptomatic and viremic
13 with the smallpox virus. It is believed that
14 previously vaccinated or previously infected
15 individuals whose immunity is incomplete or waning
16 might under go a viremic phase in the absence of
17 symptoms on re-exposure.

18 And, in addition, there is a 1971 report
19 of an outbreak of smallpox in which 27 percent of
20 post-contact of smallpox cases had inapparent
21 infections characterized by high antibody titers and
22 no symptoms. Although viremia was not studied, it's
23 very likely that some of those individuals were
24 viremic despite the fact they had no symptoms.

25 And, finally, there is a clinical syndrome

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1 that occurs in a small number of individuals infected
2 with the smallpox virus called variola sine eruptione,
3 in which pharyngitis and fever or in some individuals
4 just conjunctivitis can be present with no smallpox
5 rash. These individuals have been shown to shed virus
6 from throat or conjunctivae, respectively, and one can
7 assume that if you are shedding virus from throat or
8 conjunctivae, you could also possibly viremic. Next
9 slide, please.

10 (Slide)

11 I'd like to just briefly mention two other
12 aspects of the smallpox infection and the potential
13 for smallpox outbreak that have an impact on the blood
14 supply. In the event of a smallpox attack, there
15 would presumably be widespread vaccination, but we
16 don't know at the present time how long individuals
17 who receive vaccinia virus in the vaccine will be
18 viremic through this virus, and how long they should
19 be deferred from donating blood. So, in the presence
20 of widespread vaccination, we might have great
21 difficulty in maintaining an adequate blood supply in
22 certain regions. And almost as a corollary to that,
23 if we were to try to identify donors who might not be
24 viremic because of past immunizations before the early
25 1970s, we don't really have enough knowledge at the

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1 present time to do that. We don't really know how
2 fully or partially immune potential donors who were
3 vaccinated before 1971 are, or if, in fact, they have
4 any resistance at all in many cases.

5 So, we would like to ask the Board the
6 following questions. First, that the Board agree that
7 the agents on the FDA list, these agents that might be
8 used by bioterrorist, in fact, are agents that might
9 be used by bioterrorists and that might create a
10 threat to the safety of the blood supply.

11 The second question, does the Board
12 recommend the inclusion of any additional agents that
13 could be a risk to the blood supply?

14 And, third, does the Board feel that
15 prioritization of agents with regard to risk to the
16 blood supply is valid? Does a focus on asymptomatic
17 viremia or bacteremia appear to be valid? Are the
18 agents reflected correctly designated? Thank you.

19 DR. OSTROFF: Thank you. Questions from
20 the Board?

21 (No response.)

22 I have one, which is what are the
23 consequences of having an agent on your list in terms
24 of the blood supply if there was an incident?

25 DR. TABOR: I'm not sure I understand the

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1 question.

2 DR. OSTROFF: I'm trying to understand
3 what the purpose of the list is.

4 DR. TABOR: The purpose of the list, at
5 least at the present time, is to help us prioritize
6 our efforts with regard to both regulatory and
7 research activities that are related to the
8 possibility of a bioterrorist attack. The Center for
9 Biologics has many activities both regulatory and
10 research activities. Just to give you sort of a very
11 brief summary, we have products such as Varisole
12 Immune Globulin where energies are being focused with
13 regard to supply and regulation. If that's an
14 important issue, then that's where regulatory research
15 would have to be put. We have research activities
16 related to detection of potential agents in the blood
17 supply. If the individual agents are a high priority
18 for blood safety, then that's where we need to put our
19 resources.

20 DR. OSTROFF: But I guess the question
21 that I have is that if there was an incident involving
22 an agent that's on your list, what would you do in
23 terms of protecting the blood supply in, say, the city
24 in which the incident occurred?

25 DR. TABOR: That's difficult to answer.

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1 We have been in the process of setting up a crisis
2 response system with a situation room and teams of
3 individuals with appropriate expertise to deal with
4 situations like this. As an example, at the time of
5 the anthrax letters, there were issues that we had to
6 deal with in the center related to whether individuals
7 potentially exposed to anthrax could be accepted as
8 blood donors, or what about individuals who were on
9 antibiotics because of exposure to anthrax. And if
10 that could be used as an example, I think that's
11 probably the type of situation -- we are set up to
12 respond to the blood collection community and the
13 plasma and blood manufacturing communities to deal
14 with regulatory issues that arise.

15 DR. OSTROFF: I guess the question is, are
16 you in the process of developing policy that x-
17 individuals can't be blood donors if there was a
18 smallpox incident in community X?

19 DR. TABOR: I'm going to take this --
20 since I've answered -- let me take the opportunity to
21 ask Dr. Jay Epstein --

22 DR. OSTROFF: Jay, I didn't see you back
23 there.

24 DR. EPSTEIN: I think you're asking the
25 right questions, but we're not there yet. What we're

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1 trying to do is figure out where to prioritize our
2 efforts so that we can be prepared. And the idea to
3 figure out which are the agents of concern, what's the
4 relative threat, and then develop interventions, be
5 that donor deferral, be that donor containment
6 policies, or detection methodologies. We want to be
7 in the position that if the attacks occur, we already
8 know what to do, but that's not where we are.

9 DR. BERG: Bill Berg. I'm having a little
10 trouble getting my arms around what the issue is here.

11 Given the furor over blood-borne transmission of HIV,
12 Hepatitis-B and now Hepatitis-C, it's hard for me to
13 think of how there could be any policy in an acute
14 attack other than no blood donation.

15 You gave the example of anthrax, but
16 that's different. There are living organisms, or
17 spores rather, that can persist for up to 100 days in
18 animal models, and then blood donations have always
19 been excluded in people who were taking certain kinds
20 of medications. So, I don't think there is a directly
21 relevant lesson from anthrax.

22 DR. TABOR: No, I didn't mean anthrax as a
23 lesson, I gave that as an example of how we are trying
24 to prepare our response system to deal with these
25 crises as they arise. And it's true that HIV,

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1 Hepatitis-B and Hepatitis-C are important blood-
2 transmitted viruses, but they are basically almost
3 totally controlled by screening blood donors and
4 testing for the viruses.

5 What we are dealing with here are agents
6 that have not previously been threats to the blood
7 supply, and we need to prioritize our efforts to
8 respond to each of them individually. Now, as I said,
9 there is very little clinical data in the literature
10 about the aspects of these agents that are relevant to
11 the blood community. It's very difficult to find out
12 about the asymptomatic periods of some of these
13 agents.

14 And what we would like to get from the
15 Board is not so much a little wealth of your input on
16 policy, we don't really have a policy yet, so we're
17 not really asking that. We're asking whether this
18 list appears to be scientifically accurate in the
19 context of the bioterrorist threat, so that we can use
20 it to prioritize our efforts. I mean, if you go to a
21 textbook on infectious diseases, you cannot find out
22 really which agents are important to blood safety from
23 a terrorist attack.

24 DR. BERG: So what you seem to be saying
25 is we can't check out, test, evaluate all of the

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1 agents, AFEB, could you please tell us which ones
2 you're most concerned about so we can start working on
3 those first.

4 DR. TABOR: That's close. We can't
5 develop tests for all the agents at once, and
6 obviously we have only a limited research effort, just
7 as the DOD scientists were describing an hour or so
8 ago, but what we're asking now is for you to tell us
9 which ones, tell us if you see anything we're missing
10 from this list, whether you feel that the
11 prioritization is correct.

12 DR. PIERCE GARDNER: Pierce Gardner. We
13 demand an extraordinary level of safety in the blood
14 supply. I understand they're discussing seriously
15 testing all blood for Shiga's (phonetic) Disease
16 because there have been a couple of cases, and we
17 exclude people who have lived in England for a while
18 even though there's never been, I believe, a
19 documented case of Mad Cow Disease from a transfusion.

20 So, the possibility of even a theoretical risk seems
21 to drive our recommendations at least regarding
22 donors. So, I can't imagine, in a smallpox setting,
23 that someone who was exposed would be accepted as a
24 donor. Certainly, there would be -- and one could
25 even, if we lived through a smallpox bioterrorism

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1 event, one might even require vaccination of potential
2 donors at some point so they wouldn't be in that
3 situation.

4 I think the theoretical risk of almost any
5 agent is with us. So, the question you're asking is
6 not to prioritize, but just to give a plausibility
7 list, you would have to have pretty much everything on
8 it. If we're going to include BSS as a consideration,
9 even though there's never been a case, and exclude
10 people who lived in England for six months, we could
11 make this list enormous for you.

12 DR. TABOR: Well, I don't think BSS is a
13 potential bioterrorist agent yet. And I'd just make
14 one comment on the concept of zero-risk blood supply,
15 which is really not what we're talking about here.
16 There is a concept of zero-risk blood supply in the
17 United States, and it's driven largely by Congress in
18 response to consumer concerns about blood safety. The
19 American public does want a blood supply that has a
20 zero risk. That's not what we're talking about here.

21 What we're talking about here is being
22 prepared for a situation where the blood supply could
23 be contaminated by a new agent before we realize the
24 agent is here. If the list of question is too
25 detailed or seems inappropriate, I guess I would just

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1 like to ask you, is there anything about this list
2 that seems to be lacking, are there agents that should
3 be on this list?

4 DR. PATRICK: I can actually see this as
5 being somewhat relevant, and there may be a mixed
6 event of some sort -- you know, a bombing event and an
7 event that would involve smallpox or one of these
8 entities, that would require very rapid kind of coming
9 up to speed about, well, who can qualify as a blood
10 donor, who can't, in this particular geographic area.

11 So, one could imagine scenarios where, my guess is,
12 you would at least need to be able to explain to
13 others why you made a judgment based upon who you
14 triage in to becoming a blood donor and who not. So,
15 in my mind, it is relevant.

16 DR. OSTROFF: And it's worth pointing out
17 that just because someone has previously been
18 vaccinated for smallpox doesn't mean that they are
19 100-percent protected and, in point of fact, may
20 develop an asymptomatic viremia from having been
21 previously vaccinated and can still potentially
22 transmit through a blood supply.

23 DR. PATRICK: Part of this is relevant to
24 the modeling exercise that we saw this morning with
25 respect to endonicity (phonetic) and likelihood of

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1 infection and likelihood of agent. Again, more
2 information about this strikes me as being --

3 DR. OSTROFF: It's not an insignificant
4 issue because we know if there's a large-scale
5 incident with some of these agents, that there is a
6 great deal of need for blood. Even with the small
7 number of anthrax patients that we had last fall, many
8 of them ended up getting transfused, and where do you
9 get that blood from. And if you can tell the
10 potential issues related to this, it's not
11 inconsequential, if you have to end up excluding large
12 numbers of individuals and you can't get adequate
13 materials from elsewhere.

14 The difficulty, of course, is that all of
15 these agents potentially have viremias or bacteremias
16 at some point, so I don't see how you could permit
17 them to be donors, and the issue is theoretically
18 screening the supply to see whether or not the agent
19 is actually there, and that's not an easy thing to do.

20 I don't know, Dr. Cline, if you have any thoughts
21 about that, the issue of screening material.

22 DR. CLINE: One of the approaches in
23 disaster response is to bring your resources from
24 outside of the region affected. So, if you're going
25 to bring in rescue workers, you wouldn't necessarily

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1 mobilize them from there, where the hurricane hit or
2 the tornado hit. So, an approach for providing an
3 adequate blood supply would be to bring in blood
4 supplies from outside the region that's affected.

5 I know when we talk about vaccination for
6 smallpox or those types of anthrax exposure, then you
7 wouldn't go into the Washington, D.C. area postal
8 worker population to ask for your blood donations, you
9 would get your blood donations from outside of that
10 population. So, I think there are other noninfectious
11 ID laboratory-based viremia approaches to this problem
12 that might be generic. So, you plan to bring in
13 adequate blood supplies from outside of the affected
14 area, would be a simple approach.

15 DR. OSTROFF: It seems to me that the one
16 you really have to worry about is the one that we've
17 been worrying about with everything else, which is
18 smallpox, because of the long incubation period and
19 the communicability, in that you could have people far
20 away from the impact zone who potentially are
21 bacteremic and they are donating blood. But I think
22 the Board would be happy to take a look at the list
23 and give you some feedback about whether or not your
24 thinking on this issue is consistent with --

25 DR. TABOR: Thank you very much, we really

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1 appreciate your input.

2 DR. OSTROFF: I think based on the time,
3 we're probably going to have to bring this session to
4 a close. So, thank you very much.

5 We had some time reserved for general
6 discussion. We're considerably beyond the time period
7 when we were supposed to finish with today's session.

8 I might suggest that since we do have subcommittee
9 breakout sessions tomorrow in the afternoon, that the
10 Disease Control Committee can probably discuss at that
11 time the issues that were raised over the course of
12 the day.

13 Let me just ask the members whether they
14 have any specific comments about the presentations
15 that were given today, particularly those members who
16 aren't part of the Disease Control Subcommittee, so
17 that we can take them into consideration as we have
18 the discussion tomorrow afternoon.

19 People look like they need to get to
20 "happy hour".

21 (Laughter.)

22 DR. OSTROFF: So, with that, why don't we
23 come to a close for this evening.

24 (Whereupon, at 5:20 p.m., the session was
25 concluded.)

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