

ARMED FORCES EPIDEMIOLOGICAL BOARD

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MEETING

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DALRYMPLE CONFERENCE ROOM
 THE U.S. ARMY MEDICAL RESEARCH
 OF INFECTIOUS DISEASES
 1425 PORTER STREET
 FORT DETRICK
 FREDERICK, MARYLAND

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WEDNESDAY

MAY 23, 2001

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PRESENT:BOARD MEMBERS:

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 AFEB Executive Secretary

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PRESENT: (CONT.)

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MAJ. BRIAN BALOUGH, USA, MC
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CDR. SHARON LUDWIG, USPHS
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FLAG STAFF OFFICERS:

RADM (Sel) STEVEN HART, MC, USN

COL. ROBERT DRISCOLL, USAR, MS
JAMES A. ZIMBLE, M.D.

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

(9:00 a.m.)

DR. LaFORCE: Let's reconvene if we could, please.

The next topic is LtCol. Schnelle, who will be presenting the Medical Risk Assessment of Biologic Warfare Agent Treat. This is a continuation of a request that the Board forwarded to Gen. Peak it would have been about a year ago, year and a half ago, and there are handouts that summarize Gen. Peak's response and also the document in terms of the Medical Risk Assessment of Biologic Treat. Col. Schnelle.

LtCOL. SCHNELLE: Good morning.

(Slide)

I'm Debra Schnelle, from the Office of the Army Surgeon General, and I had the pleasure of presenting my concept for how we would conduct this medical risk assessment last year on May 30, 31, and I'm pleased and proud to present to you the completed project for your review, in the great hope that you will accept it and forward it on through Health Affairs so that we could use this product both in terms of applying it to the acquisition community and acquisition decision, and also to pick up on the gentleman's earlier question so that CINC medical planners can use it in assessing their threat and in implementing appropriate operational guidelines. Next slide, please.

(Slide)

The methodology that we were going to use was we

1 were going to use the concept of risk management so that we would
2 have an integrated assessment of both the likelihood of the BW
3 threat, which we would acquire from the Intelligence community,
4 and the impact, the medical impact upon operations which the
5 Medical Risk assessment Project completed. Next slide, please.

6 (Slide)

7 And this is a notional unclassified example of
8 this integrated threat product. You can see that on the top how
9 this probability comes from the Joint Chiefs of Staff BW Threat
10 List and it's ranked in various categories by the Intel
11 community, and then the problems here on the left side are
12 essentially the medical impacts, and the integration of the
13 substance or the likelihood from the Intel community, and the
14 assessment of the impacts from the medical community produces
15 this horrible product. So, if your theater has a risk of ricin
16 and it has a very high Intel threat but a very low medical
17 threat, the overall assessment might be actually lesser than we
18 had originally envisioned just by using the Intelligence
19 community threat list.

20 And I should also honor and acknowledge some of
21 the people who worked in developing this product, who did not
22 flee the room fast enough. LtCol. Brian Scott was involved in
23 both the Military Panel and the Scientific Panel. LtCol. Bob
24 Borowski had the privilege of chairing the Military Panel, which
25 made herding cats seem like a pale comparison. And Cdr. Randy

1 Culpepper was also present. Next slide, please.

2 (Slide)

3 So, essentially what we did was we convened an
4 Oversight Committee because you expressed a concern that this
5 product not be too green, and that we also do it in appropriate
6 respect and acknowledgement of the other services and the
7 operational needs. And essentially what we decided to do, taking
8 into account your concerns, was to convene a Military Panel that
9 would consider the operational aspects of the impact and develop
10 a mechanism that the Scientific Panel would then use in
11 evaluating the agent. This also had the result that in
12 determining the operational impact or in ranking the agents, no
13 individual in any of these groups could then immediately war-game
14 an answer and then twist their judgment to move the answer to
15 where they wanted -- not that anyone would have done that, of
16 course -- but the process was sufficiently complicated that that
17 was simply removed off the table, so we felt it was a very honest
18 and integrated process. Next slide, please.

19 (Slide)

20 Essentially, the Military Operational Panel
21 devised a mechanism where they divided the operational impact,
22 defined the operational impact to be essentially that due to the
23 performance degradation upon the unit, and that due to the
24 logistics burden of the response of coping with a BW agent
25 impact.

1 Beneath each of those two criteria was a single
2 set of threat agent criteria, things such as morbidity, mortality,
3 lethality, infectivity, and so forth and so on. For each of
4 those threat agent criteria, they devised a ranking scale, and
5 then the Scientific community has essentially ranked all the
6 agents against that scale. Next slide, please.

7 (Slide)

8 The Oversight Committee, the Army Surgeon General
9 requested the Joint Services Integration Group to allow the
10 Medical Program SubPanel -- there will be a quiz on this later --
11 to serve as the Oversight Committee -- that's a multiservice
12 panel that's responsible for integrating the training and
13 doctrinal requirements for the Joint NBC Defense Program, so the
14 MPSP selected the members of the Military Panel and oversaw the
15 process to ensure both a multiservice flavor and an operational
16 focus. Next slide, please.

17 (Slide)

18 The Chem-Bio Information Analysis Center, a GOCO
19 operated by Battelle, conducted the study, did all the work,
20 produced the report, and did some outstanding quality work in
21 preparing for both panels. And, in fact, it was only due to the
22 presence on their corporation of Dr. Bailey, a member of
23 Battelle, that we were able to convene such a distinguished panel
24 of scientists to help us with this. Next slide, please.

25 (Slide)

1 In the end, we ended up using the expert software,
2 so we were not only able to define the operational impact
3 criteria, we were also able to weigh them so that we had a
4 numerical methodology. Remember, we talked about this last year,
5 and it would not be safe to say that this entire methodology is
6 quantitative and thus precise and accurate, it uses quantitative
7 methods as a way of expressing subjective judgment. So, I think
8 it's a good first step towards developing a quantitative analysis
9 method for determining medical impact. Next slide, please.

10 (Slide)

11 This was the list of operational criteria
12 developed by the Military Panel. The boxes in red were criteria
13 that were discussed quite hotly at the Military Panel meeting and
14 were later rejected by the Scientific Panel for a variety of
15 reasons. Essentially, the reasons had to do with the assumptions
16 of the study.

17 The first assumption was that we would suppose
18 that all service members were unprotected when entering the
19 environment. We would not put vaccination on the table as one of
20 the assumptions. and the thinking behind that was allied to the
21 cold injury threat assessment. When you assess the temperatures
22 or the weather in Alaska, you don't say, well, it's not that bad
23 because we give all our soldiers coats, you say it's very, very
24 bad and that's why we must make sure that all our soldiers have
25 coats. So, we didn't want to say, because we know we have a

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1 vaccine for anthrax, therefore, we don't care about it, see? So
2 we removed the aspect of the vaccination off the table.

3 The second one made the cats analogy look pale.
4 The second one has to do with the effectiveness, or the
5 infectivity, or the effective dose -- depending whether you're
6 talking toxins or others -- of the agents themselves. In the
7 room that we had, we did have some people who had experience with
8 medical intelligence, but we were not weaponeers. No one in that
9 room had expertise in actually designing the most effective BW
10 agent. Could ricin be weaponized to be effective against large
11 troops?

12 Not knowing the answer, we chose to simply ensure
13 that that also be moved off the table and, in fact, that whole
14 area needs to be looked at in greater depth by DoD in general.
15 And the MODSYM Oversight Group of the Joint NBC Defense Program
16 is indeed going forward and looking at the toxicity values that
17 are used in models and weaponization assessments.

18 So, one of the recommendations of our report is
19 that the Intelligence community proceed with examining effective
20 weaponization of BW agents in more depth, with the support from
21 the Medical community. So, those two criteria, for those
22 reasons, were removed off of the plate when the final ranking
23 occurred by the Scientific Panel.

24 Are there any questions at this point?

25 (No response.)

1 Next slide, please.

2 (Slide)

3 Here is a list of the Military Panel members. You
4 can see quite a multiservice representation. They gave us a room
5 about the size of this stage, so all these people plus 15
6 Battelle people were in this tiny, little room. I felt like I
7 was married to some of those people by the end of the week. Very
8 productive group, though. Next slide, please.

9 (Slide)

10 Great diversity and scientific expertise, as well.
11 Next slide, please.

12 (Slide)

13 The Scientific Panel essentially took this
14 operational criteria assessment, and then went through a very
15 detailed process to consistently rank the agents in accordance
16 with this criteria. I was not able to be present at that
17 meeting, but LtCol. Scott was present at that meeting, so if you
18 have any specific questions about that, he can answer those from
19 that meeting. Next slide, please.

20 (Slide)

21 And you see, indeed, a distinguished list of
22 scientists, including some of the ones we're keeping out of the
23 Russian hands. Next slide, please.

24 (Slide)

25 And this is essentially the chart I showed you

1 last year when I was briefing the concept. We would take, for
2 example, one criteria, morbidity -- and as it turned out, that
3 eventually ended up as a criteria, I believe -- and then we would
4 define it, we would weight it, then we would scale it, and then
5 it would be passed on to the Scientific Panel. Next slide,
6 please.

7 (Slide)

8 And then you'd end up with an overall score for
9 that particular agent, and then you would combine it with all the
10 other criteria scores, and then you'd have a ranking of that
11 agent compared to all the other agents. And in your book, you
12 have not only that final product that I showed you, but also some
13 of the intermediate tables. The Scientific Panel also looked at
14 other agents that were not on the BW Threat List partly as a way
15 of giving themselves a reality check, ensuring that their
16 judgments were being consistent, and also because why redo it in
17 two years?

18 The nice thing about this methodology is all that
19 would have to be redone if another agent entered the threat list
20 is that we would simply revisit the ranking and assign the agent
21 its appropriate ranking. We would not have to redo the entire
22 methodology. My real goal in trying to develop a semi-
23 quantitative methodology is that every time something changed in
24 the BW threat world, we would not have to gather a group of
25 assembled experts who would then, unfortunately, probably get

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1 engaged in discussions of what the previous panel of scientific
2 experts decided. So, this sort of sets a stable foundation for
3 these kinds of decisions. Next slide, please.

4 (Slide)

5 And this is just working through the operational
6 risk management process. Next slide, please.

7 (Slide)

8 And this is the preliminary unclassified look.
9 So, you do see some -- in this chart and in your book, you do see
10 some anomalies that are merging because of the weaponization
11 issues that we discussed earlier. Ricin is fairly high,
12 saxitoxin is fairly high, and I forget the other one that most
13 people look at and go "blaa", and that's because the question of
14 whether they can be effectively weaponized or not has not been
15 definitively resolved.

16 Now, when looking at this from a medical planning
17 perspective, clearly, this has some value from an acquisition
18 perspective. Just as a common layman, I would say, why are we
19 spending millions of dollars in vaccine development for an agent
20 that's in the green status, but I'm not an acquisition community,
21 so, fortunately, that's a totally uninformed opinion, but from
22 the medical planning perspective, if you are looking at a threat
23 in your theater and you have a red threat and a green threat, you
24 would orient your operational guidelines towards the red threat,
25 just as a matter of prioritization. Next slide, please.

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1 (Slide)

2 And this is, again, just capturing the integration
3 aspect. The larger context of this project is rather interesting
4 because up until now the Intelligence community has had the most
5 valid consistent methodology for evaluating BW threat. Now that
6 we've developed this methodology, really, the ball now goes back
7 over the wall to the Intel community with the question of "can
8 you tighten, refine, and update your methodology", because one of
9 the questions we asked is how do you rank, you know, from high to
10 low on your list, and I was kind of under the impression they had
11 this really advanced miracle assessment, you know, the number of
12 3s plus the number of 2s plus the number of 1s, and then you kind
13 of like throw it in a bucket and out comes this ranking. No,
14 they just kind of look at the chart and say, "Well, lots of 1s
15 here, so we'll move that agent down there, lots of 3s, this agent
16 only has one country who's supporting us so we'll move that one
17 down there", so it's a very subjective qualitative methodology.

18 So, my guess is now that we've thrown the ball
19 back into their court, they'll probably review their methodology
20 and tighten it. And, of course, the weaponization issue needs to
21 be looked at. Next slide, please.

22 (Slide)

23 And just to recapture. And since I don't think
24 the words actually show up in the back of the room, it is in your
25 manual. And that concludes my presentation. Do you have any

1 questions?

2 DR. LaFORCE: Questions for LtCol. Schnelle?

3 COL. DINIEGA: Are there definitions that go along
4 with the left-hand side?

5 LtCOL. SCHNELLE: Yes, sir, they're in the report.

6 All the operational criteria are carefully defined.

7 DR. LaFORCE: Adm. Hart?

8 RADM(Sel) HART: Would you explain again the --
9 what I understand is the missing piece, the weaponization threat,
10 why you don't have it in there, or what impact it may or may not
11 have with the validity of this scale?

12 LtCOL. SCHNELLE: The big question was over the
13 issue of is it even possible to weaponize the agent to be
14 effective in a mass casualty situation, which would then have a
15 major operational impact. And after lengthy discussion, it was
16 pretty obvious that none of us knew. And, in fact, it is not
17 necessarily known within DoD. It's not just the people in the
18 room didn't know, it's not necessarily a foregone conclusion that
19 we really know if you can effectively weaponize for mass
20 casualties ricin, for example. You know, the whole discussion of
21 can you effectively mass produce and deliver toxins is sort of
22 one of those open issues.

23 So, since there wasn't a firm knowledge on that
24 basis, we did not make the ability to weaponize one of the
25 criteria. We assumed the enemy could weaponize it to deliver it

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1 in a mass area mechanism. And if we get more information about
2 the weaponization, then that would change the criteria and
3 saxitoxin and ricin would change radically in its positioning on
4 the ranking.

5 RADM(Sel) HART: Well, initially I was troubled by
6 the fact that weaponization ability wasn't there, and then, on
7 reflection, maybe it shouldn't be because the pathology, the
8 infectivity of these agents is certainly relevant. What we know
9 from the intelligence is relevant. Weaponization is technology,
10 and that changes so fast that it may be better that that's not
11 part of this.

12 LtCOL. SCHNELLE: And our hope is that that will
13 become part of the Intelligence community's assessment of the
14 threat in a country and their ability to weaponize it.

15 COL. DINIEGA: Well, we just heard that they do --
16 whatever inspiration they do have, they were able to say which
17 agents were weaponized.

18 LtCOL. SCHNELLE: And I will defer to Col. Scott,
19 if he wants to handle this one.

20 LtCOL. SCOTT: Not to steal Mr. Birkner's thunder,
21 Dr. Birkner's thunder, but that weaponization assessment is not a
22 weaponeering assessment. In other words, if I say that, you
23 know, country Z has barrels of something, or country Z has
24 warheads full of something, that's not the same as saying country
25 Z can deliver 2 micrograms per cubic liter of air over a 10-mile

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1 front. So the weaponeering information is not directly related
2 to what Dr. Birkner presented, just how far did the program go,
3 and are there systems available, and are these systems that we
4 have acknowledged to be threats? It's not quite the same as how
5 many -- can I deliver an effective dose of Bot-Tox across a 10-
6 kilometer front, which is a very different question, and it is
7 currently only answered in modeling and simulation.

8 DR. LaFORCE: Questions?

9 COL. DANLEY: I would really appreciate it from
10 the acquisition standpoint, if you broke Bot-Tox down. They're
11 different and you've got seven of them, and when you say Bot-
12 Toxin, it really creates a misleading impression as to which ones
13 are serious threats and some of which are just absolutely not
14 threats at all.

15 LtCOL. SCHNELLE: Good point, sir.

16 DR. LaFORCE: Yes, Bill?

17 DR. BERG: On page 14, Table 7, and on Figure 4,
18 page 15, there's a variety of agents listed, and then it says
19 "worst case". Is that sort of a benchmark you derived of what
20 are the capabilities?

21 LtCOL. SCHNELLE: Given the scales and the
22 weighted criteria, they maxed out the weighted criteria on every
23 single scale just to see how it would benchmark against the
24 ranking of the agent, yes, sir.

25 DR. BERG: So, this hypothetical, in a sense,

1 Agent X would have a 33 percent morbidity, and so on?

2 LtCOL. SCHNELLE: The numbers don't quite equate
3 to percentages, sir. It's based on the analytical hierarchical
4 protocol software program, the AHP methodology. So, essentially,
5 in a previous chart --

6 DR. BERG: It's a weighting then?

7 LtCOL. SCHNELLE: It's a weighting, not a
8 percentage, yes, sir. I showed the slide showing the weights
9 assigned to the various criteria, it's on page 5.

10 DR. LaFORCE: I would say from the Board
11 standpoint, thank you very much. Have we got another question?
12 Yes?

13 LtCOL. BUNNING: You may have touched on it
14 already, but what were the criteria used to look at all the
15 different agents, and the agents that did not appear here did not
16 appear because the criteria wasn't high enough, or was this list
17 inclusive, or did you limit it when you started?

18 LtCOL. SCHNELLE: We started with a mandate of
19 addressing all the agents on the Chairman of the Joint Chiefs of
20 Staff BW Threat List, and the Scientific Panel then added
21 additional agents that their expertise felt would help them check
22 their consistency and their judgments. And the criteria are
23 presented on page 5 and then defined in the following pages.
24 Your first question? I think I answered your second question.

25 LtCOL. BUNNING: So, I guess I would assume that

1 it's not inclusive except for the list that was produced?

2 LtCOL. SCHNELLE: Right, yes, sir. Only the
3 agents presented in this report were classified and ranked.

4 DR. LaFORCE: Yes, Ben?

5 COL. DINIEGA: Just a couple more questions. The
6 recommendation, I guess, after page 16, from the Military Panel,
7 and Appendix E, the Scientific Panel concerns and
8 recommendations, are there any recommendations from your office
9 as to what should be done about those?

10 LtCOL. SCHNELLE: Our first priority was to ensure
11 that the Armed Forces Epidemiological Board was satisfied with
12 the methodology and with the product. If you felt these
13 recommendations had merit, we would certainly take the work on
14 and address them. I, along with most of the members of the
15 Military Panel, feel that we need to encourage and work with the
16 Intelligence community on the weaponization issue.

17 COL. DINIEGA: It states on -- I guess the
18 Military Panel feels that the weaponization issue, if there were
19 information on it, would make the process in the table, the
20 matrix, complete?

21 LtCOL. SCHNELLE: Yes, sir.

22 COL. DINIEGA: The Scientific Panel goes on to say
23 -- had concerns about not taking into consideration preventive
24 countermeasures. And I thought you had stated that it was a
25 decision to take that out on the Military Panel side, to not

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1 consider that, or to use an assumption that we all went in
2 unprotected.

3 LtCOL. SCHNELLE: The assumption we've used to
4 develop the criteria. Now that you understand the ranking of the
5 agents -- this is the logic of the Military Panel and, frankly,
6 of my office as well -- now that we understand the priority of
7 the agent, we then must prioritize our corrective action.

8 I personally -- this is a personal opinion --
9 would not devote huge sums of resources from my office to
10 addressing the threat of Q-Fever, for example, when I had not
11 adequately addressed the threat from anthrax. So, I feel that
12 although they're right in that we need to address the fact that
13 some of these agents don't have appropriate countermeasures --
14 that, of course, is a very important thing -- but the first use
15 of this ranking from my perspective is to use it in prioritizing
16 my limited resources to address those issues.

17 So, if we fed those issues into the ranking, it
18 would muddy up the waters of what is the most important thing we
19 need to do with limited resources.

20 COL. DINIEGA: So am I hearing that now that we
21 have the matrix, the combined matrix with some sort of a
22 prioritization scheme, the Scientific Panel is saying now that we
23 have that, then we can go ahead and consider the countermeasures
24 and reprioritize it either in medical planning or acquisitions or
25 whatever?

1 LtCOL. SCHNELLE: Yes, sir.

2 COL. DINIEGA: It's encouraging another
3 reprioritization using these specific factors.

4 LtCOL. SCHNELLE: Brian, do you have anything else
5 to add from the meeting with the Scientific Panel members?

6 LtCOL. SCOTT: Yes, one small item. Looking at
7 Appendix E, the Scientific Panel's concerns, I'd just add the
8 flavor of interpreting this, Col. Diniega, that the focus -- and
9 there is great concern here by Dr. Henderson, Dr. Franz
10 specifically focused on this -- just because they took pre-
11 exposure countermeasures out so that they could have a table upon
12 which to compare agents, they did not wish to derogate the
13 importance of those countermeasures, and that's the simple
14 interpretation of their first bullet.

15 And the second, the diagnostic part, we really
16 didn't get to, but that had great emphasis because it was the
17 speed and timeliness of diagnosis making the difference, that
18 they wanted to make a comment about emphasis. But, yes, you're
19 right, this is intended to generate application of this agent-to-
20 agent comparison to be potential use for another prioritization
21 and, of course, it does not say anything about prioritizing among
22 countermeasures for an agent, whether Saran Wrap versus vaccine
23 or whatever you have, but only if you were comparing one agent to
24 another was the only thrust.

25 COL. DINIEGA: I have one more question. You said

1 that one of the purposes in the process -- and I'm all for
2 developing a repetitive, repeatable process -- is that if the
3 list was changed, you would not have to go through having a
4 Military Panel and a Scientific Panel all over again, that you
5 could just plug it into a formula and it would come out with a
6 new matrix. Did I hear correctly?

7 LtCOL. SCHNELLE: Yes, sir. Let's say that agent
8 X joined the list. We could, in theory -- and this, I think, is
9 the business of the Board to address how you would want this
10 handled -- but we could, in theory, either send that agent to the
11 AFEB and say, "Given the rankings and the scales in this
12 methodology, would you please rank this agent", or we could send
13 it to send it as a task to RIID. I mean, whatever you thought
14 would be the most independent objective body, but we would
15 essentially take the formulas in the report and a board such as
16 AFEB or RIID could then evaluate the agent in that context, and
17 then it simply joins the rest of the agents appropriately.

18 COL. DINIEGA: Is there any way to validate this
19 process?

20 DR. LaFORCE: I think part of the validation is
21 this has now been tossed back to us to sort of review this and
22 see whether the criteria sort of makes sense, and whether the
23 document has actually met the charge that the AFEB had given in
24 terms of preparing this. And I think it would be a little
25 premature to say anything right now until this has been sort of

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1 read and digested, but my sense is, have you met the spirit of
2 the challenge, the answer is clearly yes. This is precisely what
3 the Board had in mind when we asked that this be prepared. Yes,
4 Pierce?

5 DR. GARDNER: One of the things that's not in the
6 criteria that I see is the immediacy of the effect. Ben
7 explained to me during the break that the concern -- my worry
8 about influenza is that while you've assigned the immediate
9 effect of a toxin or botulism on DoD issues is different than the
10 more community-based idea of seeding hoof-and-mouth or influenza
11 and having it spread in a less acute manner.

12 So, you have many things here. Smallpox, if you
13 seeded smallpox in a massive way, it would not take effect until
14 the incubation period had played out, you're talking about a week
15 or two, so would not have an immediate military effect as
16 compared to ricin or some of the other more direct things.

17 So, that, I would think, from this point of view,
18 might be something to factor in, how quickly once the weapon was
19 dispersed, the effect would take place.

20 LtCOL. SCHNELLE: And that range of discussion
21 fell immediately into what I call the "weaponization hole". Since
22 the immediacy of the effect is related to the dose received,
23 which is related to the ability of the enemy to deliver a massive
24 dose -- I mean, it's very hard to predict without the
25 weaponeering data.

1 DR. LaFORCE: The other thing is that when we
2 talked about countermeasures, if you'd just look again at Table
3 16, which I really find very useful in terms of looking at that
4 summary, in terms of critical greatest threat, if anthrax is
5 listed first, and if all the military forces are immunized
6 appropriately and are protected, you just take a black pen and
7 take that off. That no longer exists as a threat. It's
8 finished.

9 RADM(Sel) HART: I think one other thing needs to
10 be -- we need to be cognizant of. We're talking about biological
11 warfare threat here against our active duty troops as opposed to
12 bioterrorism which has some domestic implication for medical
13 treatment facilities and so forth. It helps clarify some of the
14 -- what's the value of knowing the immediacy. Well, if you've
15 got a division of forces advancing on you, that's very important.

16 If you're trying to create chaos in the country, then the
17 immediacy has less impact and your preparedness therefore is
18 accordingly.

19 DR. GARDNER: So smallpox would not be the thing
20 you would do if you needed an immediate effect, it would be
21 something with an incubation period before it took place. That's
22 missing from this analysis.

23 CDR. CULPEPPER: I just want to say that
24 lethality, criteria is broken down on our scales, not only case
25 fatality rate, but also speed with which it causes death. The

1 lethality does include the speed with which --

2 DR. ALEXANDER: So it's calibrated in that
3 variable?

4 CDR. CULPEPPER: Calibrated in that variable on
5 the scales by which the Scientific Panel then came out and rated
6 the different agents by.

7 DR. SHOPE: Along that line, when you say speed,
8 is it an advantage to have something that kills rapidly, or is it
9 an advantage to have something that kills slowly and would be a
10 real problem in filling up hospitals, et cetera? It's not clear
11 to me where you put the rating emphasis.

12 CDR. CULPEPPER: The question really boils down to
13 how does it affect troop readiness and how does it affect
14 logistics, and that's the two basic criteria that all these other
15 factors fed into. Col. Kortepeter was on the Scientific
16 Committee, he might be able to talk to that a little bit.

17 LtCOL. KORTEPETER: It's only been a couple of
18 months and I haven't seen the report, so it's hard for me to
19 comment.

20 COL. DINIEGA: I think there's been commitments
21 from the Board and also from Col. Schnelle's office that this is
22 a first cut, like a first generation like we talked yesterday,
23 and it needs to be reviewed. And as long as we're all committed
24 to refining the process to improve it, I think it's a good
25 starting ground.

1 DR. LaFORCE: But I think in terms of, again,
2 meeting the challenge of developing at least a process that is
3 much less ad hoc than was present before is a huge step forward
4 because at least you've set up a set of rules. We might argue
5 about the rules, but at least there's something that's there and
6 you're arguing about the rules and not somebody coming in and
7 yelling louder than somebody else. And that's a major step
8 forward. Yes?

9 DR. SHOPE: This is a question about semantics.
10 The agents that are listed as marginal, that's equivalent to --
11 it says here "operation stress to medium capacity". And to me,
12 if I were a battlefield commander and my stressed to a medium
13 capacity, I wouldn't call that marginal. And I'm wondering if
14 there's a better term.

15 DR. LaFORCE: Other comments?

16 (No response.)

17 This is a lot of work, and it represents obviously
18 a lot of thought. You've got superb panelists who participated
19 in this analysis, and I think the ball is now in our court for us
20 to review and then respond in a reasonable length of comment in
21 terms of the effort that you all have put into this. I would
22 say, from my standpoint, congratulations. I honestly feel that
23 we're much further along now with again a much more stable floor
24 than we were before.

25 LtCOL. SCHNELLE: Thank you, sir. We will await

1 the AFEB's recommendation.

2 DR. LaFORCE: Thank you. Let's move on.

3 CAPT. YUND: Mr. Chairman, should you state at
4 this time, or do you anticipate stating a process review on this
5 report?

6 DR. LaFORCE: Yes. I think that's going to be one
7 of the topics that we're going to discuss a little bit after the
8 last of these formal presentations.

9 Dr. Linden, Research Area Director, from the
10 Medical Chemical and Biologic Defense Research Program. Dr.
11 Linden.

12 DR. LINDEN: Good morning.

13 (Slide)

14 I'm preaching to the choir here, but the first
15 slide outlines our rationale for investment in the Medical
16 Chemical and Biological Defense Research Program. And this
17 morning, even though some of my slides say Chemical Research
18 Program on them, I am going to focus on the Biological Defense
19 Research Program.

20 A couple of years ago, the QDR stated the threat,
21 and I think it's been reiterated in more recent documents through
22 the previous and even current Administration, so we all know that
23 there is a threat out there and why we are investing in these
24 research programs to address it.

25 (Slide)

1 These programs are joint programs, and they are
2 organized from OSD on down, as depicted here on this chart. The
3 oversight is exercised out of the Under Secretary of Defense for
4 Acquisition Technology and Logistics by a steering committee. I
5 think some of these titles are going to be modified in the very
6 near future with the new Administration, but functionally I think
7 it's going to remain pretty similar to what is depicted here with
8 Director, Defense Research and Engineering, and the Defense
9 Threat Reduction Agency with key players from those organizations
10 forming the basis of the Steering Committee, with input from the
11 Armed Services Biomedical Research Evaluation and Management
12 Committee, the ASBREM.

13 At the management level, there's Steering Group
14 here that maintains coordination with the Joint NBC Defense
15 Board, and that Board has two entities under it, the Joint
16 Service Integration Group and the Joint Service Materiel Group.

17 I want to just comment a minute because of Col.
18 Schnelle's presentation that we just heard and heard discussed,
19 that the JSIG -- this is the group that establishes the
20 requirements in the Chem-Bio Defense Program. There's Medical
21 Product Sub-Panel, the MPSP, under this that focuses strictly on
22 the medical issues and programs and products that reach all the
23 way from the Research Program through Procurement, and this
24 group, together with the CINCs, is now publishing a Joint
25 Integrated Priority List to get provided to the Joint Service

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1 These are the only weapons systems for which we can provide these
2 kinds of solutions. You can't immunize people against bullets,
3 you all know that. But it does mean that it's a unique set of
4 problems and a unique approach.

5 (Slide)

6 Our vision is to prevent casualties, provide
7 effective treatment for them and return them to duty, and also to
8 provide far-forward diagnostics for both chem and bio, as
9 appropriate.

10 (Slide)

11 We are but one piece of the pie, as you've heard
12 previously this morning. This is a big piece of the pie, the
13 intelligence, to tell us what the threats are, along with the
14 commanders, the CINCs, the requirements people, and so forth.

15 Medical countermeasures form one component of the
16 passive protection in chem-bio defense. The physical
17 countermeasures -- detection, protection, decon, and so forth --
18 is worked by the Soldier Biological/Chemical Command up at
19 Edgewood, at Aberdeen Proving Ground.

20 And there is an education and training component
21 here that's actually not funded by the research program, but
22 leverages the scientific and medical expertise found in the
23 research programs to provide education and training on management
24 of chemical or biological warfare casualties to both military and
25 civilian health care providers, and there are several folks in

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1 the room here who are very active in this program in the
2 Operational Medicine Division at USAMRIID here.

3 (Slide)

4 The locations of the principal laboratories are
5 depicted here. We're at Ft. Detrick, USAMRIID. My office is a
6 couple blocks down the street. At the Forest Glen Annex is the
7 Walter Reed Army Institute of Research and the Naval Medical
8 Research Center co-located with them. Also, the Armed Forces
9 Institute of Pathology, the Institute for Chemical Defense, and
10 the Institute for Environmental Medicine up at Natick, which
11 participates in the Medical Chemical Defense Research Program.

12 (Slide)

13 In both programs, our technical approach is pretty
14 similar. We need to identify the mechanisms involved in the
15 disease or injury process. Once we understand something about
16 those, develop and evaluate candidate products, candidate
17 countermeasures, whether they are drugs, vaccines or
18 pretreatment, to counter or mitigate or prevent the effects of
19 these things.

20 This bullet is one that's incredibly important and
21 occupies a lot of effort in both of our programs. When push-
22 comes-to-shove, we cannot test the effectiveness of our
23 countermeasures in clinical trials in humans. We can't give
24 somebody a vaccine and then expose them to biological warfare
25 agents to see if the vaccine works. Similarly, we can't give

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1 people pretreatment and expose them to a chemical warfare agent,
2 a nerve agent, or mustard.

3 So, we have to develop animal models that mimic
4 with some fidelity the human disease condition caused by these
5 agents. That's further complicated by the fact that the threat
6 that we're attempting to address is one where we believe it will
7 be delivered as an aerosol on the battlefield, and all of the
8 biological warfare threats are disease or toxins, disease agents
9 or toxins, that occur naturally somewhere in our environment, but
10 in the environment, in the naturally acquired cases of disease,
11 it's very rare -- I can only think of a couple of instances where
12 the transmission is actually by an aerosol route. Usually, for
13 example, plague is caused by getting bit by an infected flea that
14 picked up the bacteria from an infected rat.

15 On the battlefield, that's not going to be the
16 case. The battlefield threat for plague or for any of these
17 other agents is going to be an aerosol. So, we have to factor
18 that into development of these animal models, and so this is a
19 very challenging problem and one in which our folks have
20 developed a lot of expertise in our programs.

21 We develop diagnostic systems and reagents.
22 Again, here in the bio program -- and I think you're going to
23 hear a presentation from Col. Erik Henchal later this morning --
24 is that correct or not? Somebody tell me whether I've messed up.

25 DR. LaFORCE: Yes.

1 DR. LINDEN: So I'm not going to dwell on this, if
2 he's going to describe to you the approach here in the diagnostic
3 systems. We can't equipment medics with multiple diagnostic
4 systems just for the sake of addressing different categories of
5 threats, but in this case we -- you know, diseases are diseases.

6 A sick patient is a sick patient. You don't know when they walk
7 in, off the top of your head, whether they've been exposed to a
8 biological warfare threat agent, or whether they caught an
9 endemic from the area that they're deployed to. So we need to
10 focus on diagnostic systems that allow enough flexibility to
11 incorporate all the testing that those medical personnel are
12 going to need on a deployment or on a battlefield. And we've
13 already talked about the training piece a little bit.

14 (Slide)

15 The products that come out of our Tech Base
16 include not only those things that go into bottles hopefully,
17 eventually, as vaccines or therapeutics or pretreatment, but also
18 the diagnostic tests, the information, the education. As Col.
19 Schnelle mentioned, there's several folks from here and
20 elsewhere, subject matter experts on these agents and on the
21 threats, that were called upon to provide input and expertise in
22 developing the threat of medical risk effects under a threat
23 assessment.

24 Last, but not least, our Tech Base is our
25 readiness for the future. From the development standpoint, yes,

1 we need to focus on delivering things to the warfighter as soon
2 as we can now, people want things now, they don't like it when
3 you tell them, "Well, we'll get you something licensed in 12
4 years from now". Yes, we need to focus our energies on that, but
5 we also need to maintain an active investment in the Tech Base in
6 order to solve the future problems.

7 (Slide)

8 The Bio Defense Program is organized as depicted
9 here, the Research Program. We have Defense Technology
10 Objectives which represent those more mature research programs
11 for which we've been able to establish, we hope with some degree
12 of confidence, some target objectives and dates. Medical
13 countermeasures for encephalitis viruses would include a
14 genetically engineered vaccine that will protect against ideally
15 the three major groups of encephalitis viruses -- Venezuelan,
16 Eastern and Western Equine Encephalitis. For right now, we're
17 focusing on a vaccine that will protect against the multiple
18 different sero-types of Venezuelan Equine Encephalitis, a
19 challenging problem in and of itself.

20 Nobody likes the idea that we're going to have to
21 give one shot per agent, or one vaccine per agent, and we've
22 devoted some effort to focus on a multiagent vaccine where one
23 vaccine or one vaccine mixture would be able to provide
24 protection against multiple threat agents. You're going to hear
25 about the common diagnostic systems from Col. Henchal.

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1 We have a program that's still very much in the
2 Tech Base, but with some concrete objectives and medical
3 countermeasures for brucella. Again, that's focused on
4 development of a vaccine, and we're looking at two very different
5 approaches in that area. One is a basically live attenuated
6 organism and the other is in conjunction with our Canadian
7 colleagues, is for basically a polysaccharide-type vaccine.

8 We have a new Defense Technology Objective this
9 year to look at needleless delivery methods in combination with
10 the recombinant protein vaccines that we're developing. And,
11 again, this is to get away from -- this is looking a little bit
12 more toward the future. We're partnering with industry on this
13 where they are focusing both on patch technologies for delivery
14 of vaccines across the skin, as well as aerosol delivery systems
15 for immunization through the respiratory tract.

16 A subject near and dear to many people's hearts is
17 the next generation anthrax vaccine. We're working on the
18 recombinant protective antigen vaccine candidate, and that is the
19 subject and focus of intensive effort that's being managed
20 intensely and has a lot of oversight at a lot of levels.

21 Coming up right behind that similarly is a
22 recombinant plague vaccine candidate, and for both of these
23 actually the U.K. has some very similar candidate products, and
24 we're working under international agreements to try and develop
25 these into collaborative efforts.

1 The remainder of the Tech Base of the program is
2 organized broadly into the domains of vaccine, therapeutics and
3 diagnostics. Within each of those areas, or within the vaccine
4 and therapeutics, as you would expect logically, we do have those
5 broken out by categories of agents -- viruses, bacteria and
6 toxins -- as well as within each of those areas by the particular
7 organism or toxin that is the subject of the research. I can
8 talk more about that if anybody wants later on.

9 (Slide)

10 Some successes that we have had very recently and
11 we are planning to have this year include those that are shown
12 here, transitioning -- we transitioned the sero type A and B
13 components of a multivalent recombinant botulinum toxin vaccine
14 to the Joint Acquisition Vaccine Program, and Col. Danley will be
15 giving a talk on that I guess shortly. That had a transition, I
16 think, in FY00, and the recombinant plague vaccine candidate and
17 the recombinant Venezuelan Equine Encephalitis vaccine candidate,
18 that actually has had a limited milestone to advanced
19 development, but there is some work continuing in the Tech Base.

20 This advanced passed Milestone 0 of the older version of the DoD
21 5000 which describes the DoD acquisition system.

22 By the end of this fiscal year, we anticipate
23 having some kind of meeting, the title of which we are
24 continually debating actually, whether it's going to be called a
25 Decision Review or an In Process Review or some other variation

1 on that theme, under the new acquisition rules in the new DoD
2 5000. The effort here can be stated pretty straightforwardly,
3 and that is to get the decision and the head-nod up and down from
4 the people in charge of the dollars for both the 6-3 and the 6-4
5 dollars in the research program, research and development, to
6 jointly spend their money to focus on advancing these products to
7 an acquisition program, into fullfledged development. And so we
8 anticipate that by the end of this fiscal year for the next
9 generation anthrax vaccine, one of the candidates, the RPA, the
10 plague vaccine. And the Common Diagnostic System that I keep
11 mentioning you'll hear more about later from Col. Henchal is
12 anticipated to provide the candidates for consideration for
13 establishing the Acquisition Program for the Joint Biological
14 Agent Identification and Diagnosis System in FY02.

15 (Slide)

16 If I had realized that Col. Danley was going to be
17 giving a presentation at this, I would have taken this slide out,
18 but I'm going to let him address the products that are coming in
19 the future. Some of them are listed here, and I'm sure he'll
20 address those in his presentation.

21 (Slide)

22 Things that are coming down the pike that we're
23 focusing on in our program to get to the point in the Research
24 Program where we can have candidates that we can offer for
25 transition to development include the vaccines listed here. The

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1 multivalent Venezuelan Equine Encephalitis, which I already
2 mentioned; staph enterotoxin vaccine, again, a genetically
3 engineered recombinant protein; ricin vaccine -- several years
4 ago, a toxoid that actually transitioned to advanced development.

5 We obtained an IND on it. Then for some technical reasons, FDA
6 asked us to put that on hold. There were reversion issues with
7 the toxoid. WE went back, looked at a different approach to
8 chemical modification of the toxin as a vaccine candidate, did
9 some research on that, did some work on it, presented the data.
10 Again, there were some technical issues that were deemed to be
11 serious enough to send this effort back into the Tech Base for
12 review and for a renewed effort. This time, looking at, not
13 surprisingly, a genetically engineered approach to modification
14 of the ricin toxin, to make a nontoxic but immunogenic protein
15 that would be a good vaccine candidate, and that's where that is
16 right now. Again, the common Diagnostic System you'll hear about
17 from Col. Henschel.

18 We have a very promising candidate for Marburg
19 vaccine. Marburg and Ebola are both viruses. Interestingly,
20 what worked for Marburg in monkeys didn't work for Ebola. Both
21 of them worked quite well in guinea pigs, but then when they went
22 to do the critical testing in nonhuman primates -- and I found
23 out this is against an aerosol challenge with an agent that
24 requires Biosafety Level 4 containment, so these are nontrivial
25 research efforts to conduct -- the Marburg vaccine candidate

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1 worked quite well, but they were not able to achieve the same
2 success with the Ebola candidate which was constructed in the
3 same fashion.

4 (Slide)

5 What's coming down the pike? In the future, I
6 think as we all realize we've heard a lot actually, I think the
7 first time I read a paper, a DoD paper concerned about
8 genetically engineered threats was about 1984, and we are looking
9 at these things very seriously now. There's a large effort,
10 because of the funding that's been provided in the homeland
11 defense arena, the National Laboratories have a very large
12 investment, as does DARPA, in genomic sequencing of BW threat
13 agents, and we are working with those other organizations, those
14 other agencies, and the laboratories in order to do this, and not
15 only just to crank out sequences, but to understand the
16 significance and importance of what these sequences can tell us
17 about virulence factors for viruses and bacteria, about
18 mechanisms of action of the toxins, about drug resistance again
19 for both the bacterial agents and viruses.

20 We talk about focusing in the future on
21 immunomodulators and therapies. There is a strong desire,
22 especially on the part of some of the rapid deployment force
23 community, in having perhaps transiently acting nonspecific
24 medical product, drugs or whatever, that could be used to kind
25 of, you know, "pop your pill" or "use your inhaler" to provide

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1 you with some kind of short-term, generalized protection against
2 infectious agents or BW threats. This is going to be an
3 extremely challenging area of work, as you might imagine, and
4 we're keeping an eye on what's going on in academia and in the
5 scientific community in general, and I think we're really relying
6 at this particular point in time on some of the work that's being
7 supported in the DARPA programs which focus on the farther out
8 approaches to identify and kind of help focus on those approaches
9 that might be the most promising in this area. And there are
10 some that have been identified already, and we have some plans to
11 partner with them.

12 I already mentioned the multiagent vaccines, an
13 alternative to one vaccine per agent, and you realize one vaccine
14 may mean more than one dose of that vaccine, more than one shot,
15 depending on what the vaccine is and what the required
16 immunization schedule is.

17 (Slide)

18 Cooperation with DARPA. The Biological Warfare
19 Defense Programs at DARPA have enjoyed some significant funding
20 over the past couple of years. I think in toto their programs
21 are larger than ours actually.

22 The major programs which we have interfaced with
23 DARPA are listed here -- unconventional pathogen countermeasures,
24 advanced diagnostics, the genomic sequencing effort, and they
25 have a much smaller program now in sensors, but when that was a

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1 larger program we did work with some of their investigators. For
2 a long time, USAMRIID actually collaborated with the
3 investigators being supported under these DARPA programs because,
4 in general, these people are in biotech companies or in academia,
5 and they don't have the capability or expertise, in many cases,
6 to work with the biological threat agents, and so they would come
7 here and ask for support from the lab and, over the years, we
8 collectively evolved some sort of ground rules and guidelines for
9 interacting with people and supporting some of that research. In
10 many, if not all, cases in the DARPA program, not only are they
11 looking out far in the future, but especially in those cases
12 where it's a biotech company involved, they are really looking at
13 dual-use applications, which is great because it means eventually
14 hopefully down the pike, if any of these things pan out, that
15 we'll have corporate partnership in the development and not have
16 to bear the cost of that all by ourselves.

17 (Slide)

18 At some point a few years ago, after the DARPA
19 program was stood up and funded, folks realized that -- you know,
20 asked the question, where is this stuff going to go? Where are
21 the successes from the DARPA programs going to end up if we don't
22 provide a conduit for them into sort of the mainstream of the DoD
23 acquisition community and program, and thus was born the concept
24 of the DARPA Transition dollars in FY99. These dollars kicked
25 off this fiscal year with a modest amount of \$2 million, and in

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1 the medical line, medical funding line, this is the funding
2 profile for the so-called DARPA transition effort going out over
3 five fiscal years, and we're just coming up next month on Round 2
4 of basically reviewing the status of projects in the
5 Unconventional Pathogen Countermeasures and in the Advanced
6 Diagnostics Programs, and what we'll do is what we did last year,
7 which is to identify those projects that we think are either the
8 most promising in terms of technologies that are going to help us
9 solve our problems and address our threats and/or those things
10 that are close to the most mature, invite those people back, have
11 intensive discussions with them to help them focus on the
12 military problem, and then select some of those to submit
13 proposals and then we crank through our established procedures
14 for funding research contracts.

15 We're looking heavily at new vaccine-related
16 technologies, looking to the biotech folks to bring those in to
17 us and, as I just mentioned, we'll be selecting additional
18 projects shortly to bring into the program.

19 (Slide)

20 I'd like to shift focus to end this, on some of
21 the strategic challenges in our Chem/Bio Defense Research
22 Programs, our Medical Research Program, and the three areas I
23 wanted to just mention are listed here -- the Acquisition Model,
24 the FDA regulations, and the multiplicity of threats.

25 (Slide)

1 The Acquisition Model is pretty linear. You know,
2 you start at the beginning, you need a new piece of materiel for
3 whatever reason, and it proceeds in a stepwise fashion through
4 research and development and maturing things through engineering
5 refinements and so forth. The old DoD 5000, the new one which
6 was published this past year, which ideally and hopefully
7 provides us some more flexibility in that difficult area of
8 transition between the Tech Base and the development. And it's
9 not just us, it's not just DoD where this is a difficult piece of
10 terrain. If you talk to people in the pharmaceutical industry --
11 and I apologize for not knowing who all of you are individually,
12 and some of you may be from that industry -- but based on what
13 I've heard from those folks, that's also a very challenging area
14 for them to deal with.

15 We have things called Technology Readiness Levels
16 that have been incorporated into the acquisition paradigm, and
17 we're struggling with how to apply -- these were actually
18 developed by NASA, so you can imagine that we're having a little
19 struggle to apply those assessments of technology readiness,
20 translate them to the medical context.

21 And where do we focus on the risk reduction? Who
22 bears the responsibility for risk reduction, and where do we plug
23 that into the R&D spectrum for the medical product? And, as I
24 said, it's fairly linear.

25 In contrast, in scientific research and biomedical

1 research, and in the development of biologicals and
2 pharmaceuticals, things aren't linear. You know, you get to a
3 certain point, something doesn't work, you have to go back to
4 Square One, or you're pursuing a research path and you think
5 you're heading straight down a main highway, and all of a sudden,
6 for whatever reason, you find that it branches because the
7 results don't work the way you think things were going to work.
8 And so it's very difficult to sort of match up the way things are
9 in biomedical research with this acquisition model.

10 Again, we may have numerous candidates that look
11 promising, and more and more working in this area I've become
12 thoroughly convinced that -- you know, you want to kill products
13 early, there's a desire to down-select things in order to save
14 money. You know, we have limited dollars to invest in developing
15 a vaccine or limited dollars in our overall R&D programs. So,
16 there's a desire to kill things early, but what does that mean in
17 the context of developing a vaccine? I'm convinced that we don't
18 know the answers to any of these things until we can actually go
19 into people and see if something is safe and immunogenic. And so
20 there's kind of a real struggle here conceptually in how do you
21 manage the dollars, how do you down-select as early as you can,
22 to be as conservative as you can, realizing that you're really
23 not going to have definitive answers to some of these things
24 until you get farther down the pike in much more costly kinds of
25 efforts.

1 And another thing that I learned or became more
2 conscious of fairly recently is that vaccines and medical
3 products have a very finite lifetime. How many drugs or vaccines
4 are we taking today? How many of those are the same as the ones
5 that were used 20 or 30 years ago? Very few. There are some,
6 but the point is that our job is not done -- you know, we can't
7 just walk away from it when we develop a vaccine. Even when we
8 develop and hopefully get licensed the next generation anthrax
9 vaccine, we cannot walk away from that effort and say "Job's
10 done, thanks", you know, we have to actually maintain an effort
11 starting now on the vaccine or the medical countermeasure that's
12 going to come after that, and that's not going to be for another
13 20 years, but I really have become convinced that it's a mistake
14 to think that if we transition something and get the product
15 licensed, that we then walk away from it, and I'm sure that many
16 of you sitting on this Board can translate this very rapidly back
17 into the situation that we're facing right now with adenovirus,
18 or look at the bind we're in with tetanus-toxoid.

19 There are some folks developing a genetically
20 engineered tetanus-toxoid. It was great. They just decided it
21 wasn't -- the pharmaceutical industry decided it wasn't cost-
22 effective. Now look where we are with tetanus-toxoid, it's like,
23 what, one manufacturer, and there's not enough of it to go
24 around.

25 The next two or three of these charts or

1 eyecharts, and I apologize for that, but this is the old chart
2 where we tried to harmonize the DoD acquisition process with what
3 the FDA requires for getting an investigational new drug approval
4 and licensure of vaccine. And so what I wanted to -- my point is
5 that regardless of the Acquisition System -- and I'm going to
6 show you the new one on the next slide -- regardless of the
7 Acquisition System, all of these things still have to be done.
8 And one of the challenges in my office and in Col. Danley's is to
9 try and figure out how we align these things and marry them up
10 with the process, marry the science and the research up with the
11 process that we are forced to go through.

12 (Slide)

13 This new system doesn't have all the stuff lined
14 up down here and, in fact, the Tech Base is over here off the
15 edge of the chart on the left. But I mentioned earlier this
16 Decision Review or In Process Review for the vaccine candidates
17 that we're hoping to get into advanced development in the near
18 future, and that's where this falls on this chart. Milestone B
19 is commonly now interpreted to be the point at which you formally
20 establish the Acquisition Program.

21 (Slide)

22 Continuing with the strategic challenges, the FDA
23 regulatory requirements. I imagine many of you on this panel are
24 familiar with these. For licensing a product in the civilian
25 community, basically the company has to demonstrate that it's

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1 safe and effective. The FDA put that efficacy requirement into
2 their licensing process sometime when I was a kid, but I remember
3 when that happened, and about 30 percent of the over-the-counter
4 pharmaceuticals that we had on our shelves at the time
5 disappeared because efficacy had never been and couldn't be
6 demonstrated for a lot of these things. So, that was -- I
7 remember that. It was a pretty big deal at the time.

8 As I mentioned before, for our medical bio-defense
9 products and chem-defense products, we can demonstrate safety in
10 animals and in humans, and we can demonstrate efficacy in
11 animals, but we can only estimate the efficacy in humans, and we
12 have to rely on the best data that we can generate, and the best
13 models that we can develop in animals in order to do that.

14 (Slide)

15 The FDA published a proposed new rule which, to my
16 knowledge, is still in the proposed stage even though it was out
17 and commented upon and so forth. I don't know when, or if, it
18 will be finalized. And they developed this basically as a
19 consequence of intensive discussions with DoD and the fallout
20 from the Persian Gulf War over the use of investigational
21 products, and they recognized that we had this challenge of being
22 able to license products in the absence of being able to do large
23 field studies in human populations to demonstrate efficacy.

24 So this proposed new rule allows them to consider
25 animal efficacy data in support of a licensure request. However,

1 it doesn't just say, "Yeah, we'll take animal data instead of
2 human data", they lay out their expectations about the way those
3 studies would be conducted, which is to say not only a GLP, good
4 laboratory practices, studies, but essentially they want those
5 animal studies conducted according to the same guidelines that
6 you use to conduct a human clinical study, good clinical
7 practices, and in addition they've asked that we understand the
8 mechanism of action of the disease-causing agent. That's a big
9 challenge. We don't know the mechanism of action of many
10 disease-causing agents even today, and licensure of things for
11 public health purposes is really based on some fairly empirical
12 data. You know, you can do a large-scale field trial and show
13 that you protected 80 percent of one group with your vaccine or
14 drug versus the control group that didn't receive it, they're
15 going to license it, given all the rest of the supporting data,
16 without having to understand exactly the disease-causing process.

17 Do we know the basis of action of chicken pox? No, we really
18 don't, but they licensed the chicken pox vaccine and it worked.

19 Understand the basis of action of the vaccine or
20 drug. Again, most of the evidence that's used to support
21 licensure -- drugs, obviously -- you can do the pharmacokinetics
22 and study the mechanism of action, but for vaccines, the basis of
23 action of vaccine, unless it's very obviously antibodies,
24 circulating antibodies, it's not really well understood.

25 Demonstrate efficacy in two relevant animal

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1 models. I already mentioned earlier the challenge of developing
2 these animal models and selecting those or finding those that we
3 think accurately mimic or portray the human disease.

4 And last, but not least by any stretch of the
5 imagination, we have to identify surrogate markers of efficacy.
6 We're investing a huge amount of effort in that now for all of
7 the high-priority vaccine candidates that we're working on. This
8 is going to be the linchpin of the efficacy argument, being able
9 to show efficacy in animals, measure something in the animal, and
10 then go ahead and use the product, immunize or drug or whatever,
11 to people, measure the same parameter in the human, and then say
12 we can use this as a basis for predicting that the human is
13 protected. And that's a very large challenge and one that we're
14 focusing on intensively right now.

15 (Slide)

16 Multiplicity of threats. Even though the chemical
17 warfare agents can be grouped into categories -- nerve, mustard
18 and the other agents -- even within those groups there are
19 variations amongst the agents and the effectiveness of
20 countermeasures and so forth.

21 For the biological agents, it's even more
22 challenging because we have a number of viruses, a number of
23 bacteria, a number of toxins, and they are all different. And
24 even one "toxin" -- and I use that in quotes -- "botulinum
25 toxin", as Col. Danley pointed out, has seven total sero-types.

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1 We don't believe that all seven are of concern to us, but we
2 essentially need to address each of those individually in order
3 to come up with an effective vaccine against them.

4 And the emerging threats are -- you know, include
5 those genetically engineered threats for which we're not going to
6 know exactly what the agent is, and we're going to have to
7 approach developing medical countermeasures based on more
8 fundamental principles, such as virulence factors or mechanisms
9 of action.

10 (Slide)

11 So, our programs present unique challenges. I
12 think we've discussed all of them here. We need the cutting edge
13 technologies, we're bringing them in by partnerships with
14 industry and the other defense agencies and national
15 laboratories, and we're also working very closely with industry
16 and the scientific community, using the tools that are available
17 to us in the form of cooperative research and development
18 agreements, and so forth.

19 I will just mention right here something that I
20 haven't put into the talk, and that is the work that we do on
21 therapeutics both for bacterial agents and antiviral drugs, and
22 those are done basically by the mechanism of cooperative
23 arrangements with the pharmaceutical industry whereby we get
24 promising compounds from them and test them in our systems. They
25 are not particularly interested in investing in an antiviral drug

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1 that's going to work against Ebola nor can they test it, but we
2 can and we're interested. Likewise, for the bacterial threat
3 agents, we are able to test not only the antibiotics that are on
4 the market right now and coming on the market, but the new things
5 that are emerging and being worked on in the industry so that
6 we're prepared to be able to make recommendations on those things
7 when they become available.

8 Subject to your questions, that concludes my talk.

9 Thank you.

10 DR. LaFORCE: Questions for Dr. Linden. I would
11 point out, Dr. Linden, that your assumption in terms of plague
12 largely and exclusively as an aerosol delivery may not be
13 entirely correct. During the Second World War, kilogram
14 quantities of fully infected plague fleas were produced and used
15 against Chinese forces, used successfully in Manchuria.

16 DR. LINDEN: True. Good point. Well, I think I
17 used that to illustrate the point, I kind of didn't give you the
18 other shoe on that one, which was you are aware that the old
19 plague vaccine is no longer available. In some tests that were
20 done here at USAMRIID, it appeared that that vaccine was pretty
21 effective against parenteral, against Bubonic Plague, essentially
22 that which would be acquired by flea-bite. But when they tested
23 it in animal models against an aerosol, it was not very effective
24 in preventing the aerosol exposure. I'm sorry, I didn't extend
25 that point. Not all vaccines that are protective against the

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1 natural route of infection can be expected to be effective
2 against the aerosol route, and that's really what our concern
3 was.

4 DR. LaFORCE: Questions, observations? Adm. Hart?

5 RADM(Sel) HART: Can we return to slide 6.

6 (Slide)

7 I guess what I want to do here is emphasize the
8 importance or the magnitude of what the Board has undertaken to
9 look at. By looking at this Medical Risk Assessment of a
10 Biological Threat, if such an assessment were to become a
11 recognized document and inserted into the process that is
12 depicted on Slide 3, the impact is considerable, and there are
13 some pet rocks that are going to be threatened by having this
14 kind of a process determining where the hundreds of millions of
15 dollars are going to go.

16 So, I think Dr. Linden's talk here emphasizes the
17 importance and the need for prioritization and what's at stake.
18 If we could put into this process a rational method of
19 prioritizing research efforts, I think we'd make a major step
20 forward in service to our troops. I don't know if that's
21 possible but, if it is, and if this is validated, and it's going
22 to need to get inserted into the scheme that you see on page 3,
23 if that happens it would have a worldwide impact on what we will
24 have done.

25 DR. LaFORCE: Steve?

1 DR. PATRICK: Carol, thank you for the wonderful
2 presentation. Every time that I hear you present, I just come
3 away in awe of the wonderful productivity of the research and
4 development infrastructure within DoD, and I once again -- I
5 mean, that the products that are coming down the pipeline look
6 just absolutely terrific.

7 I have a couple of questions for you. One of them
8 is, you only touched very lightly right at the very end about the
9 issue of therapeutics that might be of very high priority, and I
10 wonder if you could make some comments about what potential
11 therapeutic agents may be available in the not too distant
12 future, that would look good for some of the high threat agents?

13 And the second question I have is that while the
14 presentation is mostly concentrating on BW threat agents, is
15 there an equal push in terms of the production of vaccines of
16 military relevance that aren't necessarily from the BW threat
17 perspective, but are important to the warfighter?

18 DR. LINDEN: Okay. Let me answer your second one
19 first. My counterpart, Col. Charles Hoch, is the Director of the
20 Military Infectious Diseases Research Program, and in their
21 program they are focusing on development of vaccines for those
22 diseases believed to be high priority in terms of deployed
23 troops. And so they are focusing on things like malaria, dengue,
24 the gastrointestinal diseases, which are, I guess, the -- if you
25 look at the disease nonbattle injury profile, you know, they are

1 using some of that as their guideline for developing the
2 prioritization in their program. Otherwise, I can't really speak
3 to exactly the specifics of what they are working on, those are
4 just my general level awareness. So the answer is yes, and it's
5 an interesting challenge because, you know, the science is the
6 same. I mean, we're all trying -- you know, in the two programs,
7 we're trying to develop vaccines. We're using common
8 technologies. In some cases, we're sharing the same farmer or
9 biotech partners. So there's a lot of scientific crossover, but
10 programmatically and dollarwise, you know, our dollars come
11 through completely different stovepipes.

12 When I first started working for the Army over 20
13 years ago, I always sort of scratched my head about that and
14 thought it was sort of bizarre about how the programs didn't
15 match up with the science. And, unfortunately, that's still
16 true. So, we have to do our best within the Medical Research and
17 Materiel Command, for whom we both work, to leverage off of each
18 other's programs and maintain some communication.

19 Going to your second question about the
20 therapeutics, for the bacterial agent, as you're aware, we
21 achieved a success of sorts with the FDA last year, on changing
22 the package insert for ciprofloxacin to have that labeled for use
23 in post-exposure prophylaxis in treatment for anthrax.

24 My understanding is that doxycycline is -- the
25 labeling on that would allow that to be used not only for

1 anthrax, but also for some other threat agents -- for example, Q-
2 Fever. So, basically, we know what the existing antibiotic
3 recommendations are for the bacterial threat, that's been worked
4 through and sorted out in the laboratory, you know, doing
5 standard in vitro kinds of testing as well as focusing and
6 looking at the animal models and making sure that for a given
7 licensed drug, that when you give it to the animal and you have
8 the circulating levels that would be relevant pharmacologically
9 for what you would see in people given the drug, that that works
10 against that bacterial disease. So, we've looked at anthrax,
11 plague, brucella, Glanders, those things that we are planning to.

12 For the viral agents, in partnership with NIH, I
13 believe that there is an effort now to go forward with a
14 recommendation for use of Cytophvir for treatment of a pox
15 virus, specifically smallpox, and working with Gilliad, who is
16 the manufacturer of that drug, which is licensed already for the
17 indication of CVM retinitis, cytomegalovirus retinitis, which is
18 commonly found in immunosuppressed people. So, here, we're
19 starting off with a licensed drug. The challenge there is going
20 to be twofold. One is the existing drug is an IV formulation, so
21 we're working with the company on looking at oral formulations.
22 They're going to have to go to like a pro-drug formula for that
23 to get an oral formulation that will work, and then, as you know,
24 being at CDC, do the definitive testing there using smallpox with
25 that drug in order to see if we can arrive at a license

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1 indication for that.

2 There are some other drugs, as you know, that are
3 in testing -- I think they are down there right now -- both in
4 vitro and in other pox virus animal models, in an effort to
5 develop the smallpox animal model. The only natural host for
6 smallpox is human, so there is not a good animal model of
7 variola, smallpox. There are other pox viruses, pox viruses with
8 specific hosts that give us good models in general or
9 conceptually for pox viruses, but they are not smallpox. And
10 what they've discovered in the in vitro testing in cell cultures
11 is that when you -- you would like to be able to select another
12 pox virus that you could work with someplace other than the
13 maximum containment lab at CDC, to be able to use a sort of an
14 indicator of what would be effective against smallpox, but it
15 turns out that there isn't any one other virus that definitively
16 gives you that answer when you look at a spectrum of different
17 families of antiviral compounds. And so this is a very
18 challenging scientific problem.

19 DR. LaFORCE: We really should break for about 15
20 minutes, and then we'll try to wrap up the rest of this morning's
21 session. Thank you very much for your presentation. Let's break
22 for 15 minutes.

23 (Whereupon, a short recess was taken.)

24 DR. LaFORCE: We're in the homestretch. What I'd
25 like to do now is describe a little bit what's going to happen

1 from now until early this afternoon. We have two presentations
2 from Col. Henchal and Col. Danley, and that will finish the
3 formal presentations, and sort of looking forward to some
4 discussion time. And what I would propose to the Board members
5 is -- the lunch, I think, is going to be a box lunch, right?

6 LtCOL. RIDDLE: Yes, sir.

7 DR. LaFORCE: Okay. I forgot about the picture.
8 When we break then to pick up the box lunches, all the Board
9 members, if you please could come with Rick and I and also the
10 Preventive Medicine Officers, to get a picture out front. And
11 then if you pick up the box lunches -- and let's just work
12 through noontime, if we could. I really would like to finish
13 somewhere around, at the latest, 2:30. For those individuals --
14 and there are several people who are driving back to Washington -
15 - I've learned over the last couple of years of living here, that
16 it's a lot easier if you hit 270 somewhere around 3:00 o'clock
17 than 4:00 o'clock. That one hour is just -- makes all the
18 difference in the world. So, I, frankly, would like to see if we
19 could finish off somewhere around 2:30. If we go to 3:00, we go
20 to 3:00, but hopefully no later than that. And if we work
21 through lunch, then I think we should be able to finish on time.

22 There are several things that we are responsible
23 for. The list is actually getting reasonably long, and so we're
24 going to need some help in terms of trying to figure out who's
25 going to do what. And, also, Julian pointed out yesterday to me

1 during a conversation, that you're better off being right than
2 being quick, and that maybe some of these deliberations need to
3 be vetted through more than a single draft. And I think that
4 Julian's advice -- I reflected on it last night, I think he's
5 absolutely right, but we'll get to that a little bit later on.
6 Okay.

7 Let's move on to the formal part of the
8 presentations, Chem/Bio Diagnostics Research Program, and this is
9 Col. Henschal, Research Coordinator for Defense Technology
10 Objective on Common Diagnostic Systems. Col. Henshaw.

11 COL. HENCHAL: Good morning. I'm Col. Erik
12 Henschal. I'm Chief of Diagnostic Systems Division here at
13 USAMRIID, I'm also the Research Coordinator for Defense
14 Technology Objective called Common Diagnostic Systems.

15 (Slide)

16 Over 50 different infectious diseases and
17 biological agents threaten the health of our service members
18 worldwide. And when we started to improve the deployable medical
19 laboratories, we found that we were unable to sustain the support
20 of these laboratories with 50 different technologies and all the
21 reference laboratory capability that was required to support the
22 clinical diagnosis required in a theater. Next slide, please.

23 (Slide)

24 The objective that we have had is to assess the
25 technologies that could be used to broadly support the diagnosis

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1 of infectious disease and agents. One of the things, the lessons
2 learned that we found very early was that we'd be unable to use a
3 single technology, no single technology is sufficient to do that
4 job.

5 And so the concept that we've been developing is
6 one of using an integrated diagnostic system that combines
7 several different technologies along with the information that's
8 provided from the clinical diagnosis and medical intelligence,
9 backed up by classical microbiology in order to provide the
10 definitive diagnosis that's required especially in the first use,
11 or discovery of the first use of a biological threat on our
12 battlefield.

13 (Slide)

14 Here is the evolutionary strategy, and I want to
15 emphasize that this is a strategy based upon the need to stepwise
16 proceed to this comprehensive system. And so the first milestone
17 that we have is really to transition technology suitable for
18 rapid nucleic acid analysis. But we recognized that rapid
19 nucleic acid analysis is insufficient when we're dealing with
20 agents that don't -- that aren't replicating agents, such as many
21 of the toxins. It's insufficient if you can't discover -- if you
22 don't have medical specimens that contain the agent. A good
23 example of that is in the case of Bacillus Anthracis, it doesn't
24 appear in the blood until quite late in the disease. And so this
25 technology will be limited to the specimens where you can

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1 actually find the agent. And so we hope to be able to closely
2 follow these developments with an improved diagnostic system that
3 will identify both the antigens related to many of the agents,
4 especially the protein toxins, as well as the antibodies that
5 would be developed by a patient infected with one of our agents.

6 We hope to culminate this over the course of several years into
7 a single platform integrating many different kinds of
8 technologies in order to support the diagnosis of disease.

9 (Slide)

10 So the first objective, the first milestone that
11 we're dealing with is actually the development of that portable
12 system for rapid nucleic acid analysis.

13 (Slide)

14 We are not just talking about a device. If you
15 talk to many in the community, you think we're just talking about
16 an instrument or a device, but in fact we're really talking about
17 a system because the devices by themselves are insufficient, and
18 so without the protocols and the reagents that go with them, in
19 addition to the fact that when you talk about nucleic acid
20 analysis, there is always the requirement for some amount of
21 specimen processing to occur before we actually do gene
22 detection, and I'm going to talk about more of that later.

23 So, the research base has primarily been evolving
24 new protocols and new reagents and systems that can contribute to
25 the total architecture for portable nucleic acid analysis.

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1 (Slide)

2 I mentioned to you the challenge of specimen
3 processing in particular, and this is probably one of the most
4 single technical barriers really to be able to put this
5 technology in the field in that we really have to deal with a
6 large number of medical specimens in order to cover the broad
7 range of infectious diseases that we could be faced with.

8 In addition to that, we would have to add on
9 refining many of the environmental specimens that are also going
10 to come to our deployable medical laboratories as they service
11 the in-theater confirmatory resources for the biological detector
12 systems that are also being deployed.

13 Each one of these different matrixes may actually
14 require a unique processing protocol, so it's going to be very
15 difficult to make one module, one box that can do all of these
16 different kinds of matrices.

17 (Slide)

18 In the course of our research, we've actually
19 concentrated on developing many different kinds of tube-based and
20 paper-based methods, and we have protocols for all the different
21 matrices I showed you on the other slide, but we've also been
22 involving more easily fieldable devices through the program, and
23 this includes a manual cartridge system. This manual cartridge
24 system can process a specimen, a liquid specimen very quickly.
25 It can process up to 2 mls of blood and provide purified DNA.

1 The system is compatible with higher volume processing, or larger
2 number of specimens, automated process systems. In addition to
3 that, within the program we're also working towards what I
4 consider to be the "Holy Grail", which is this integrated
5 cartridge system. The role of the integrated cartridge system is
6 to really put specimen processing and gene amplification in a
7 single disposable cartridge. And one of the first prototypes
8 that does that is a deliverable to my program in October of this
9 year.

10 (Slide)

11 Here are many of the manual methods that we are
12 currently using. A lot of these are commercial off-the-shelf or
13 have been developed within our SBIR program or within the program
14 itself. There are many automated methods as well.

15 And our strategy has been to evaluate not only
16 evaluate these methods for each matrix for the efficiency of
17 extraction, quality of nucleic acid, how long it takes to do the
18 processing, the ease of use of each of the methods, and how well
19 we can support these in the context of our deployable
20 laboratories.

21 (Slide)

22 I just want to show you some example results.
23 These are three difference kinds of buffer systems or matrices
24 that are used in our laboratories, pretty common medical
25 specimens, represent medical specimens here. The swabs are also

1 an important medical specimen, but they can also be used
2 environmentally.

3 And here are the methods, these are pretty much
4 the gold standard methods that are currently used. They are very
5 effective. They are not very portable, as I'll show you in a
6 little while, but there are some methods, such as IsoCard
7 methods. It's a commercial method, I'm not endorsing it
8 necessarily, but it's a very sensitive way and very quick way to
9 process a sample, prepare DNA for gene amplification.

10 I want to point out that if you do no treatment,
11 you can see that there's a pretty big difference between what
12 happens when you don't treat, you essentially have an order of
13 magnitude less sensitive test.

14 (Slide)

15 This just shows you some other parameters we use
16 to evaluate methods, which includes how fast things can be done.

17 One to two hours is the standard for most of the current methods
18 that are used in the research laboratories. The focus has been
19 to pretty much shorted that time, and really our goal is to have
20 methods that can do specimen processing in less than 15 minutes.

21 Many of these are much more useful in the context of field
22 ability. And we do those assessments in the context of a Theater
23 Army Medical Laboratory which has a component here at component
24 here at USAMRIID.

25 (Slide)

1 This is the integrated cartridge that I've been
2 talking about. It's made by a contractor to the program that
3 started out as an SBIR program and was transitioned to the core
4 Acquisition Program that we have. This is a cartridge where the
5 reagents are onboard. The technician would load the sample and
6 through a microfluid environment, the sample would be processed,
7 and the purified DNA delivered to a gene amplification tube for
8 analysis.

9 (Slide)

10 Core technology for this cartridge is really based
11 on microsonication. We found that break open the spores or break
12 open the bug, your ability to amplify those targets is much
13 lower, and microsonication has been an effective way to break
14 open the spores. You can see the difference in the signal when
15 we have untreated spores and treated spores. As a matter of
16 fact, microsonication duplicates the same results if we germinate
17 spores, where we open it up, allow the spore itself to naturally
18 open up and allow extraction of the target DNA.

19 (Slide)

20 This is the proposed prototype that we have a sa
21 deliverable to the system. It's a four-cartridge system as the
22 first prototype, where we have the integrated specimen processing
23 and gene amplification in a disposable cartridge. We'll be
24 continuing to do those evaluations through the next year.

25 (Slide)

1 Very early on in the process, we pretty much chose
2 a common gene amplification technology. There's lots of ways to
3 do PCR. There's lots of ways to do gene amplification. But it
4 was this particular approach that led to the ability to do really
5 real-time analysis of specimens. This is called "Probe
6 Hydrolysis Method", sometimes called "Taqman". It's a commercial
7 off-the-shelf approach. And if you wanted a common gene
8 amplification chemistry, this is it because within the DoD
9 program -- and I'm not just talking about USAMRIID, I'm talking
10 about contributions that are made by both the Air Force, the
11 Navy, and Army scientists. Within the DoD program, we pretty
12 much have developed assays for 26 biological agents already using
13 this chemistry. And certainly over 50, and probably hundreds of
14 assays have now been developed within the program. This is an
15 effective way to do gene amplification in the presence of
16 fluorescence probe and the fluorescent reporter is released. And
17 the devices themselves depend upon the release of that reporter
18 and look for it as the signal for detecting the gene.

19 (Slide)

20 This is an example of the reagent development
21 that's gone on to-date. We have a large number of assays that
22 are developed for two leading platforms. The one platform is the
23 Roche LightCycler, or the Idaho Technology R.A.P.I.D.S., as you
24 can see, and the SmartCycler is an SBIR contractor to USAMRIID,
25 to the U.S. Army Medical Research and Development Command, and we

1 have those.

2 In the beginning, many of the assays that were
3 being developed were investigator-driven. So, it's very
4 difficult to make apple and orange comparisons between the assays
5 that are done here. And so what we've also done is we've
6 developed a set of model assays where they are directed against
7 the same sequences, using the same basic chemistry, and so that
8 we can now, using these model assays, essentially do head-to-head
9 comparisons of these two device options.

10 We have similar sets of assays that are also being
11 developed for the MDRP reagents, and there's a long list actually
12 of assays that have also been developed mostly using the
13 R.A.P.I.D.S./Lightcycler technology to identify diseases such as
14 malaria, dengue, Shigellosis and other enteric diseases.

15 (Slide)

16 The strategy that we're using we began really by
17 developing assays that were specific, that were recognizing the
18 specific virulence markers for these agents, and the strategy
19 that we used in our program is really to build depth and
20 diversity. And the purpose of that is really to avoid
21 technological surprise.

22 We recognize that we're dealing with a new
23 environment, an environment where genetically engineered threats
24 may threaten health of service members, and one of the problems
25 with PCR is that if you don't know what the agent is, you either

1 have to do a lot of testing or do de novo development of your
2 assays. And so the strategy is one of overlapping independently
3 derived bow markers in order to definitively recognize what agent
4 might be involved in a particular attack. This consists of
5 developing reassays against specific virulence markers, genus and
6 species markers, and common pathogenic markers. A new part of
7 the program also includes new assays against antibiotic
8 resistance. We're developing assays, for example, to identify
9 ciprofloxacin resistance or tetracycline resistance in these
10 organisms that we know may be critical towards identifying some
11 of the genetically engineered bacillus anthracis. We're also
12 including assays now against some common host-response markers.
13 These are also being included in the package so we can tell if
14 someone is infected at all with a particular agent early on
15 before any clinical symptoms may be obvious.

16 (Slide)

17 At the same time in the program, we recognize that
18 we have to be able to get these reagents out of the reference
19 laboratories, and one of the things that the Combat Developer has
20 told us is that these reagents must be stable, and they must be
21 in a form that doesn't require refrigeration. So we've been
22 working with a variety of contractors -- here are three separate
23 ones that we've been working with -- really to evaluate the
24 ability to make these pre-formulated, pre-dispensed, single-dose
25 assays. And if could look at this picture, you could see that

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1 there actually little beads that contain the reagents or
2 reassays. And actually this bead technology has been standard
3 for us for doing gene amplification in Theater Army Medical
4 Laboratory for over three years.

5 We continue to evaluate the ability to develop
6 these kits with these manufacturers in the program.

7 (Slide)

8 These are currently the leading instrument
9 options. We have really gone through in the program looking at a
10 number of different options of cartridges and
11 electrochemiluminescence and other things for detection of genes.

12 Really, when we get down to it, this is almost the fourth year
13 that we've been doing this work. Really, the two leading options
14 in order to meet the milestone in 2000 really has come down to
15 these two instruments, and they are both very rugged and portable
16 in their current framework. They are very rapid. They can do
17 agent identification in 25 to 40 minutes using that fluorescent
18 chemistry that I talked about. They are both very sensitive, and
19 really the sensitivity and specificity assays really depend upon
20 the chemistry that was developed by our scientists, but they do
21 have different engineering and operational concepts.

22 The R.A.P.I.D. thermocycler, based on LightCycler
23 technology, is a 32-well carousel. It essentially is inserted in
24 kind of a convection oven architecture. All of those assays in
25 that 32-carousel have to work exactly the same. And so what is

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1 done usually is we now have to standardize assays to one set, a
2 particular set, of amplification conditions.

3 The difference in the SmartCycler XC, which was
4 developed first in the SBIR program, these are 16 different,
5 independently operating thermocycler modules. Each of these can
6 be programmed to the optimum conditions for agent identification.

7 I'm not going to say which approach is better right now, but I
8 can tell you that from the broadest sense, either one of these
9 devices actually can be used to identify agents.

10 (Slide)

11 And, actually, I could go through a whole long
12 list of these kinds of profiles -- they are probably clearer in
13 your handout, I hope -- where you will see that if you use assays
14 to develop against the same gene targets -- and these are dose-
15 response curves, this is the changing amount of target in the
16 assays -- that the performance of these devices is comparable,
17 very comparable. And that makes sense because the core is that
18 assay chemistry that was originally developed.

19 (Slide)

20 This is one of the first parallel descriptions,
21 parallel comparisons of the performance of the two technological
22 device options, and within what we consider to be the most
23 important clinical range, which is 100 to 100,000 femtograms of
24 target DNA, this is equivalent to about 30 organisms to over
25 100,000 organisms. We consider this the most important range.

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1 You can see that the two options are virtually identical. Where
2 we start to see some diversions -- and I don't want to put too
3 much importance on this yet because we haven't gone to formal
4 trial -- but where you see the most divergence is at the lower
5 end of the range, and that's perfectly understandable.

6 (Slide)

7 These devices also differ in a variety of ways.
8 From the engineering aspects, SmartCycler takes a little bit
9 larger volume. We believed in the beginning that the larger
10 volume may actually be more robust in dealing with inhibitors.
11 The other option is that the R.A.P.I.D.S. device that was
12 originally proposed -- I should mention, by the Air Force -- has
13 to have a plug-in. It's AC powered. Other devices that are now
14 emerging operate on batteries. The SmartCycler can operate up to
15 18 hours with an external battery pack.

16 (Slide)

17 What is our strategy for doing our evaluations?
18 Really, what we're doing is we're organizing a variety of
19 different evaluation trials, and there's really four different
20 categories of trials. There are the laboratory trials, and the
21 laboratory trials are really to get to the heart of the standard
22 performance measures that we demand for diagnostics. We believe
23 that no diagnostic should be fielded unless we can define what
24 the sensitivity, specificity, and variance of that assay is in
25 the hands of the operator, and that's the purpose of these

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1 laboratory trials, as well as to establish standard measures of
2 limited detection. There are also some other characteristics
3 that are spelled out in the requirements documents that also
4 require, for example, the ability to detect eight agents
5 simultaneously.

6 The purpose of the animal models is really to help
7 support some of the FDA trial work that's necessary. The animal
8 trials tells us what are the most important medical specimens we
9 want to use, and when these technologies are most effective
10 during the course of disease.

11 Also, the FDA tells us that we can substitute
12 animal specimens with other data as a substitute for human
13 clinical trials. And so these animal studies are going to be
14 very important, using animal specimens are going to be very
15 important as we approach the FDA and ask for an investigational
16 device exemption for our diagnostic assays.

17 The field studies really are split into two parts.

18 The first kind of field study is where we actually take these
19 assays to our deployable laboratories. We work closely with the
20 Theater Army Medical Laboratory, but we also work with two other
21 deployable laboratories, two other laboratories in OCONUS
22 supporting major CINCs, and we can test our technologies there to
23 see if these technologies are compatible with the CONOPs, the
24 concept for operations for those units.

25 Field studies also allow us to demonstrate the

1 usefulness of these technologies in preventative medicine, and
2 we're developing field sites at different areas. In particular,
3 we're trying to work with the Canadians and look at a field site
4 in Western Canada where a number of endemic diseases related to
5 biological threats can be found.

6 We also have established a study site in San
7 Antonio that uses both Army and Air Forces resources in order to
8 evaluate the insertion of these technologies into a clinical
9 base, a clean regulated environment -- very critical if we are
10 going to be using these investigational diagnostics in the future
11 for medical care.

12 (Slide)

13 One of the first things that we found, though,
14 when we approached these studies is that there were no
15 international standards for these agents. If I went to an
16 investigator at the Air Force, or if I went to an investigator at
17 the Navy, we'd find that very often they were using different
18 strains, and the pedigree of those bacterial strains was very
19 often unknown.

20 Also, we found that there were different measures
21 for preparing DNA, and all these can be variables and have an
22 impact on the performance of our evaluation trials. And so one
23 of the things that we did at USAMRIID is we established a
24 rational method, a rational reference, bacterial reference panel.

25 We comprehensively documented the pedigree, strain history, the

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1 virulence, and characterized these for their phenotype and their
2 genotype in a way. What we hope is that these can now be a
3 standard against which we can compare all future and emerging
4 diagnostic technologies.

5 We've done the same thing with the viruses. This
6 process is not complete, it's kind of an ongoing process. Right
7 now we have over 81 nucleic acid, purified nucleic acid DNAs
8 ready to go for trial, all derived from very highly characterized
9 organism.

10 (Slide)

11 We started this with a milestone where we needed
12 to be able to transition to advanced development R.A.P.I.D.
13 nucleic acid analysis devices, and I told you that those devices
14 are insufficient to address all of the bacterial and all the
15 biological agents that we may be faced with, so we must
16 supplement nucleic acid analysis with other technologies in order
17 to do definitive identification.

18 A big part of our basic research program is to
19 develop a new medical immunodiagnostic assays, reagents and
20 platforms that can supplement the future total integrated system.

21 A technology that I've been talking about for three years is
22 electrochemiluminescence. This was the first generation device.
23 We are currently working with the manufacturer to put this in a
24 deployable framework. As a matter of fact, you can see it.

25 (Slide)

1 You see here it's in a deployable hardened case in
2 order to do electrochemiluminescence. This is a technology that
3 is 100 to 1,000-fold more sensitive than our core enzyme-linked
4 immunoassay for the detection of agents. In a single-tube
5 format, it can do agent identification in just about 30 to 40
6 minutes.

7 (Slide)

8 It's very robust, and the reagents are stable, and
9 it has this long dynamic curve which is very attractive for
10 diagnostic assay. This is today the most sensitive way to detect
11 antigens, and here I'm showing you results based on the detection
12 of at least in the femtogram range where we really get down to
13 the lowest range of biological activity for some of the toxins.

14 Having high sensitivity in our assays is going to
15 be critical for the injection of some toxins -- for example,
16 botulinum toxin and ricin toxin -- that quickly degrade once they
17 are introduced into a body or into the environment. Other
18 toxins, like staph enterotoxins, are much more stable.

19 (Slide)

20 Another technology, this technology has been
21 adopted by the Centers for Disease Control. It's called Time
22 Resolved Fluorescence, and uses a variety of lanthanide kelates
23 (phonetic). The advantage of this technology is it can be
24 multiplexed. You can have different dye sets labeling your
25 antibodies. Generally, we found that this technology is about 10

1 to 100-fold more sensitive than ELISA. It has the advantage of
2 also being used -- you could use this for immunoassays or DNA/RNA
3 probe assays.

4 The problem that we found is that we had a very
5 difficult time in putting this into a deployable laboratory. It
6 required a high volume of wash-bumper that the laboratories
7 couldn't do.

8 (Slide)

9 These results were contributed by my Navy
10 colleagues, and generally they are showing a sensitivity for Bot-
11 neurotoxin in the range of .3 nanograms, or about 300 nanograms
12 at the lower end of the curve.

13 (Slide)

14 Exciting technology also in the program for about
15 -- this is new technology we just started evaluating this last
16 year, is the use of paramagnetically labeled antibodies. And the
17 device I'm showing you here is powered by a Palm-top. We hope
18 that this could be a replacement for the standard hand-held assay
19 that currently is being developed for the inventory. It has a
20 potential of picogram sensitivity. It depends upon the detection
21 of a perturbation of the magnetic field. You can have
22 magnetically labeled antibodies in the same way we have our hand-
23 held assays and, using a strip technology, then rapidly, within
24 minutes, 10 to 15 minutes, 10 minutes, be able to detect that
25 antigen on the strip.

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1 (Slide)

2 This is also results provided me by the Navy
3 Medical Research Center, where they do a comparison with the
4 standard gold hand-held assay. This assay has been -- and these
5 are not optimized results -- has been, though, about anywhere
6 from three- to fivefold more sensitive than the standard hand-
7 held assay that's part of the detection program right now. These
8 assays have not been approved or evaluated for medical use yet.

9 (Slide)

10 Technology that we're looking at also in this
11 program at USAMRIID is the use of a technology called Luminex.
12 It depends upon using a large number of different kinds of
13 colored microspheres. And, essentially, if you can imagine, the
14 company claims that you can have as many as 50 different assays
15 all going on in one tube just by changing the color of the
16 microsphere that you're using for labeling the antibody. I don't
17 have any results to show you on this. I hope to maybe in the
18 next year, but the assays that have been published have had high
19 sensitivity. This is another technology that could be used to
20 commonly detect antigen or antibody or DNA all in the context of
21 laser signal colormetric detection of microspheres.

22 (Slide)

23 This next chart just shows you a comparison of the
24 sensitivity or limited detection for representative toxins. This
25 is pretty standard what we do when we evaluate some new

1 technology, we'll take model systems such as what you see here
2 and evaluate them in parallel with currently available
3 technology. You can see that ECL pretty much -- which is still
4 my favorite -- is a very sensitive way and consistent way to
5 detect these toxins.

6 (Slide)

7 And in another part of the program, we're also
8 doing everything we can to actually improve the antibody
9 reagents, and the fact of the matter is there's a repertoire of
10 antibody reagents that we have for immunodiagnosics is actually
11 pretty small. There's a need to generally improve these
12 reagents. A lot of the reagents that are being used in some of
13 the detector systems are based on polyclonal antibody or
14 insufficiently characterized monoclonal antibodies. And so one
15 thing that we're doing is we're converting many of the original,
16 older murine mouse monoclonal antibodies to recombinant
17 antibodies which can be manipulated to improve the affinity and
18 the avidity of the antibody. We currently have a program to
19 select specifically BOT, anti-BOT antibodies by using this
20 technology.

21 (Slide)

22 Many people are familiar with PCR and the
23 different immunoassays such as ELISA or hand-held assays, but I
24 want to make you aware that there are other technologies that
25 could be incorporated in future diagnostic systems. This is an

1 example of technology that's based on gas chromatography, and
2 actually this technology has been around for quite a while. The
3 deployable laboratories actually use this technology to identify
4 many of the chemical agents, and we're looking towards maybe some
5 of this technology as having dual use for biological agent and
6 chemical agent detection.

7 In this case, there's already an established
8 database to identify 2,000 different biological agents and
9 species, and it's based upon the detection of a unique fatty acid
10 signature. This is not technology that's ready to directly
11 evaluate a medical specimen, but could be used in the context of
12 a post-culture analysis method for many of the bacterial agents,
13 and it's based on the detection of a unique fatty acid signature.

14 (Slide)

15 These results show a comparison of cellular fatty
16 acid profiles of bacillus with some other related strains. This
17 is essentially a pattern matching database where you look at the
18 technologies, and here what I have in bold are two essential
19 peaks that are required for the identification of bacillus
20 anthraces.

21 (Slide)

22 Some of this technology has already been approved
23 for use in clinical laboratories, so there's a real advantage to
24 be able to explore the use of this technology for identification
25 in many of the agents of our concern. And already we've

1 established a Bioterrorism Panel that includes this long list of
2 agents that are part of the database.

3 The advantage is that we don't have to have --
4 actually, I'm opposed to having diagnostic systems that only work
5 for biological warfare agents and not infectious diseases, and so
6 this is a subset of the database that contains over 2,000 entries
7 and hundreds of these specimens are already related to standard
8 clinical microbiology practices.

9 (Slide)

10 And I just want to give some acknowledgement to a
11 long list of principal investigators both here at USAMRIID, Navy,
12 at the AFIP, and our commercial contacts, WRAIR, that supplied
13 some of this data.

14 (Slide)

15 Today, what I've done is I've introduced your
16 concept of needing a comprehensive integrated system that really
17 integrates medical intelligence with a lot of different
18 technologies to do definitive identification. I've shown you
19 some of the emerging technologies that we're going to be able to
20 use in our laboratories in the near future. Do I have any
21 questions? Yes, sir?

22 DR. PATRICK: I always have questions. Very nice
23 presentation. I guess -- maybe it's a dirty word to bring up,
24 and I'm curious about cost, and the two questions I have, one,
25 who is going to be using these machines, and the second is, how

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1 much is it going to cost not only for the machine itself, but to
2 be able to run some of these assays? When I look at the
3 SmartCycler and I look at the R.A.P.I.D.S., et cetera? I mean, it
4 strikes me that that technology must be fairly expensive, and if
5 it was me that was out there in the field, I wouldn't have a clue
6 as to how that machine, so obviously you're going to have to
7 train somebody, and how many of these machines are you going to
8 have to have?

9 COL. HENCHAL: My job is to assess the technology
10 from the standpoint of the Tech Base, and I can tell you that no
11 marketing evaluation has been done yet. The machines currently
12 have a market price of anywhere from \$28,000 to \$65,000 per
13 instrument.

14 Each of the services is developing a strategy
15 where these will be fielded. I suspect that they will be
16 initially fielded at the first level of definitive medical care,
17 which in the case of the Army might be Combat Support Hospitals
18 would be our deployable Theater Army Medical Laboratory. It
19 could be fielded, some limited amount, on task-organized
20 preventative medicine teams.

21 With regard to training, we are now training kids
22 that are 19 to 26 years old with only six months of laboratory
23 experience to use these technologies. And so there is a little
24 bit of -- there is a training burden that these technologies
25 currently have, but as we improve the engineering of these

1 devices, I expect that training burden to go down. We currently
2 train the laboratory technicians in deployable laboratories in
3 about a six- to eight-week training course in order to use our
4 approaches.

5 With regard to the assay cost, I can only guess at
6 what that is. I know that in times past when we've been asked to
7 estimate the cost of doing gene amplification, that cost comes
8 out to anywhere from \$50 to \$100 an assay. That includes the
9 labor. The actual material costs are much less. I suspect the
10 material costs are going to be closer to \$10 to \$20 per assay.
11 And I think there will eventually be economy-of-scale. There's
12 no question that diagnostic technologies of this type are going
13 to be expensive, and it's going to be up to the warfighter and
14 the user community to decide the value of that when faced with
15 biological warfare threats.

16 LtCOL. RIDDLE: Maybe Col. Bradshaw can help me,
17 but hasn't R.A.P.I.D.S. been fielded? I mean, the Air Force has
18 been using that for some time now in Southwest Asia and those
19 units are out there?

20 COL. BRADSHAW: Yes, they've been used in a few
21 cases and, in fact, I guess the one success story was identifying
22 a salmonella outbreak in Southwest Asia early on, using
23 R.A.P.I.D.S., and then they've done some field testing elsewhere.

24 DR. OSTROFF: I was at a meeting a couple of weeks
25 where Roger Breeze from USDA was saying that he's been in contact

1 with the Air Force about potentially developing an assay for
2 foot-and-mouth disease, that they can take these briefcases out
3 into the field where they're going to be drawing specimens from
4 cattle, and just run it right through the machine and link it up
5 to some massive GIS system that will tell them every farm in a
6 50-mile radius, and they'll have all the information that they
7 need. I assume that there must be some thought about
8 deployability. I mean, I thought it was spectacular.

9 DR. LaFORCE: Ben?

10 COL. DINIEGA: Two questions, Erik. The issue of
11 the FDA approval or certification, is the FDA involved with
12 approving these as a medical -- do they need to approve these?

13 COL. HENCHAL: Anytime you use a medical device
14 that supports the diagnosis of human disease, it must be approved
15 by FDA. The Center for Devices is a separate center at the FDA.

16 COL. DINIEGA: So they all have to go through the
17 FDA.

18 COL. HENCHAL: For human use.

19 COL. DINIEGA: R.A.P.I.D.S. has been through the
20 FDA? The other question I have, though, is a funding question.
21 Is this under the Joint Program Office? Is it funded through the
22 centralized funding?

23 COL. HENCHAL: My funding all comes from the U.S.
24 Army Medical Research and Materiel Command.

25 DR. LINDEN: The funding comes from the Joint

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1 Chem/Bio Defense Program, and a couple things, the way forward
2 with this, everything that Erik described, the R.A.P.I.D.S. and
3 LifeCycler, most likely will be the competing candidates for
4 transition into advanced development of a Joint Biological Agent
5 Identification and Diagnosis System, and that system is meant to
6 do two functions. One is to be used as a diagnostic tool
7 clinically, and for that application the device, the reagents,
8 the assays themselves, that whole package, is going to have to go
9 to the FDA and be reviewed and approved as a medical diagnostic
10 device.

11 The other application which can be done without
12 going through the FDA is to use these technologies and devices
13 for agent identification from nonmedical samples or for
14 nonclinical diagnostic purposes. And I think they are envisioned
15 to be used as the confirmatory devices for the environmental
16 samples for agent identification for those samples coming out of
17 the detection system in the short-term.

18 COL. DINIEGA: Thanks. And I think because it's
19 going to go through JPOBD, eventually it will need a Joint ORD.
20 It will be a joint procurement.

21 DR. LINDEN: There is a draft Joint ORD that is in
22 circulation right now that has been, I think, signed off by all
23 the services except the Army.

24 COL. HENCHAL: It's still in draft.

25 DR. LaFORCE: Yes, Bill?

1 DR. BERG: Bill Berg, Hampton. What plans do you
2 have for determining the limitations of these devices, and then
3 making that known? What I have in the back of my mind is that
4 one of the problems with Persian Gulf Illness is the false-
5 positives from some of the early detection devices which is
6 contributing to the idea that, yes, soldiers were exposed. And in
7 particular, I'm thinking about the Fox vehicle which, as I
8 recall, had problems with false-positives because of the teflon
9 in one of its acquisition devices, and I think also -- and I'm
10 not sure I'm accurate on this -- the Fox vehicle was designed for
11 airborne testing and it was applied to soil and that gave false-
12 positives. Had these been known ahead of time, this might have
13 helped to deal with the perception that, yes, there was a lot of
14 chemical warfare going on there. So, do you have any plans for
15 addressing a similar potential problem with these devices?

16 COL. HENCHAL: Well, as I mentioned in my talk, we
17 actually are structuring a series of evaluation trials that are
18 both laboratory-based animal trials, hospital-based, and field-
19 based, and all those are test-specific scenarios, the use of the
20 technologies to address your concern. Before the -- when we go
21 to milestone, the kind of data that I'm going to present is that
22 related towards the essential critical data that every diagnostic
23 assay should have and no one should use this assay without this
24 information, which is the sensitivity, specificity, and variance
25 of the assay for the indication that it's being used for.

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1 DR. LaFORCE: Thank you, Col. Henschal.

2 The final presentation will be given by Col.
3 Danley, Program Manager, Joint Vaccine Acquisition Program.

4 COL. DANLEY: There's good news and bad news in
5 being the last speaker. The bad news is that you have to listen
6 to me. You're all sitting there saying "when's lunch, hope he
7 shuts up soon" --

8 DR. LaFORCE: Are you finished?

9 COL. DANLEY: The good news is --

10 DR. LaFORCE: Oh, I'm sorry.

11 COL. DANLEY: The good news is I've had a chance
12 to listen to everyone else's presentations and have had a chance
13 to think about some editorial comments I'd like to open with.

14 Ladies and gentlemen, first of all, let me thank
15 you for this opportunity to address you. Let me tell you that
16 ten years after the Gulf War, we are less prepared today to deal
17 with a biological threat than we were in 1990.

18 In 1990, I had a licensed anthrax vaccine. I
19 don't have that in the year 2001. In 1990, I had a licensed
20 plague vaccine. I don't have that in the year 2001. In 1990, I
21 thought I had at least a very large stockpile of R&D vaccines at
22 the Salk Institute. I do not have that in the year 2001.

23 So, what the hell have we been doing for the last
24 11 years with all the money that's gone into this program? And
25 let me tell you that people have been working their backsides off

1 intensely to try to solve this problem. But as the DoD and the
2 FDA has begun to look into the way we do business, it's become
3 clear that we've not been following the rules, the same rules
4 that industry has to follow, and that's what we're trying to fix.

5 An early comment was made we need a national
6 program for the development of orphan vaccines. Let me propose
7 to you that the JVAP is a model, if not the colonel for such a
8 national program. But let me say to you also that this is a very
9 expensive program, and I'm not sure that our nation is willing to
10 make the kind of investment that is needed to make orphan
11 vaccines, and that gets to the final point I want to make on the
12 importance of your process for prioritizing threat and the work
13 that Col. Schnelle has done for you.

14 Historically, we have been handed vaccines by the
15 Tech Base and told, "Go out and get this product licensed". And
16 so you're going to see vaccines that we're working on that seem
17 to not fit that priority list, but we got them from the Tech
18 Base. And it's very, very important that someone independent of
19 the Tech Base and the acquisition process stand up and say,
20 "Stop. This is our priority, and this is where the investment
21 needs to be made".

22 Let me give you an example. In 1969-1970, a
23 pentavalent BOT-Toxoid vaccine was made at Michigan, what is now
24 BioPort. That pentavalent vaccine was made as an IND product for
25 about \$125,000. It was a summer grant. That same vaccine made

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1 with modern technology and licensed today, \$750 million.

2 Now, people think back because we have those same
3 people that were around when that vaccine was made, they're
4 thinking \$125,000, not \$750 million. If I take a look at the
5 serotypes that were in there, there was a serotype for D. D is
6 not a threat to humans. We don't have receptors for D. And it's
7 very likely we may not have got receptors for C either. So, it's
8 not enough to say Bot-Toxins, I need to know which toxins, and I
9 need to put those toxins in priority along with all the other
10 threat agents that are out there.

11 And so let me emphasize finally, please pursue
12 this process for prioritization, and lift the burden from us from
13 having to try to guess where we're going to make our investments
14 because each vaccine, a single vaccine, \$60-80 million
15 investment, 10-12 years. Okay. Having said that, let's move on.

16 (Slide)

17 The Joint Vaccine Acquisition Program Project
18 Management Office is under the Joint Program Office for
19 Biological Defense. It was chartered after the Gulf War to
20 address the shortages that we had in medical products, and
21 products to identify the use of biological warfare agents in the
22 field. It didn't make the chemical community happy that they
23 lost the detection programs. It did not make the medical
24 community happy that they lost the vaccine program. Get over it.
25 This is the Program Office. It exists. It's going to exist.

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1 And it's working very well.

2 (Slide)

3 I'm in the business of making vaccines. I'm not
4 in the science. The science is part of the business, but I am in
5 the business. Our job is to go out and apply a process that is
6 used by the Department of Defense to fund under the DoD 5000 to
7 develop products, and we have to use that process. I'm going to
8 show you how we're using that process, and I think it makes a lot
9 of sense to use this process.

10 (Slide)

11 We sit, sort of, between the Tech Base, which
12 you've heard from this morning, we sit right here. This is the
13 business of licensing vaccines. And in that process, we will
14 make some initial products, but ultimately, once we get them
15 licensed, they are going to have to be produced, and what we're
16 finding is that if we don't address this piece out here, you end
17 up with the problem you had with adenovirus vaccine and plague
18 vaccine -- companies don't want to make it because there's no
19 incentive economically to do so.

20 (Slide)

21 And so we have what we call -- what we call
22 affectionately "VP GOGO", that is a vaccine production facility
23 which is currently under consideration in the Department of
24 Defense. When we lose the industrial base for making a vaccine,
25 we don't just lose the vaccine, we lose probably 5 to 10 years of

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1 effort that it takes to re-establish that production capability,
2 and our nation cannot afford that.

3 (Slide)

4 I want to emphasize the final point here. The way
5 we are doing business is through a prime contractor. A prime
6 contractor is a company that is going to be our manufacturer. It
7 is going to be the manufacturer that represents the DoD to the
8 FDA. We, the DoD, do not have that capability, nor do we want
9 that responsibility, to act as a license holder.

10 So our particular company, the company that won
11 the contract was DynPort Vaccine Company, DVC. They have an
12 office just offsite post here. They are a limited liability
13 company that is formed from DynCorp, a sizable defense contractor
14 and important manufacturer vaccine in the United Kingdom. They
15 have a staff right now of about 75 people. That staff is going
16 to get enlarged as we put more vaccines into the program.

17 (Slide)

18 They are a virtual company. That is to say that
19 they use subcontractors for all of those processes associated
20 with the licensing of a vaccine. What they are doing is not an
21 unusual process. Major manufacturers follow a similar process --
22 that is, they can go out and find companies to do clinical
23 trials. They can go out and find manufacturers, such as
24 BioReliance down here in Rockville, to do the actual
25 manufacturing process. But the important thing that they do is

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1 to collect the information and maintain a large staff of quality
2 assurance risk managers and regulatory affairs personnel to go
3 out and monitor those processes that are occurring at each of
4 those subcontractors.

5 The business of licensing a vaccines is not a
6 process of making then. I can make vaccines here at USAMRIID.
7 The business of making vaccines is keeping track of all of the
8 information in not only the licensing or manufacturing process,
9 but the testing process as well.

10 (Slide)

11 The point I want to make here is that when we look
12 at a little bottle of vaccine, people say what's the big deal,
13 but the big deal is that that little bottle of vaccine represents
14 as complex a system as any weapon system that certainly a soldier
15 carries and probably even drives -- that is to say that this
16 little piece up here is the piece that's discovered, the antigen.
17 We've got to consider formulation, manufacturing, testing.

18 A big piece down here, regulatory compliance, is
19 just the same kind of regulatory compliance that the Air Force
20 has to go through in making an F-18 or '16 or whatever the
21 number. Logistics -- how are we going to get this thing out to
22 the field if a scientist comes to me and says, "I've got a
23 vaccine, but I've got to store it at a minus-20 degrees C", how
24 many of you have got ultra-low freezers out there on the front
25 lines to take that vaccine".

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1 Delivery system is a major issue here. I believe
2 personally that we'd have no problems with anthrax vaccination if
3 it was one shot, none whatsoever if it was a piece of gum or I
4 could put it in an MRE. And if I'm going to make an investment
5 right now starting in the year 2001 for a vaccine that might be
6 licensed in 2011, do I want it to be a shot? I don't think so
7 because in 2011 industry is going to have nosedrops, inhalers,
8 patches, and we have to think down the line where we're going to
9 make our investment. It's not losing money that's important,
10 it's losing time.

11 (Slide)

12 These are our challenges. Again, I want to
13 emphasize this industrial base. You know, when I first started
14 in the JVAP about in 1993, we had hoped that major industry, big
15 pharma, would be interested in supporting the DoD, but I'll be
16 quite frank with you, we just don't pay enough profit on our
17 products to interest big pharma. Moreover, you only have to look
18 at the kind of problems that BioPort has had with anthrax vaccine
19 to realize that companies may not want their name associated with
20 biological defense vaccines, even though they are safe and
21 effective. Big problem.

22 (Slide)

23 Let's talk a little bit about the challenges that
24 we have at JVAP, and one of them right now is the integration of
25 DoD 5000, this process up here, with the process that is

1 required by the Food and Drug Administration for licensure.

2 I want to make two points from this slide. One,
3 we cannot -- we simply cannot short-circuit the FDA process, and
4 the FDA process takes a long time, takes 8 to 12 years.

5 I cannot short-circuit the DoD process, that 5000
6 process, and the reason for that is that's where I get my money.

7 If I don't POM for my money -- and when I say POM, I'm talking
8 about putting in a request for dollars three years ahead of when
9 I need those dollars -- I don't have the money when the time
10 comes to execute the process.

11 So, one of the major problems that we have in our
12 program right now is to develop that model that allows us to
13 project when we're going to need the money, and then to make sure
14 that the money is there to develop the product. Big pharma
15 doesn't have that problem.

16 I want to point out here something that Dr. Linden
17 brought out about the formulation process. We believe, and I
18 fully concur with her, that we cannot go into this process
19 without down-selecting products, and that down-selecting process
20 has got to involve some human testing. And where we are going to
21 do that is up front and early, and it will be through a process
22 of working with the Tech Base and advanced development to achieve
23 that. Yes, sir?

24 DR. BERG: What is down-selecting?

25 COL. DANLEY: Down-selecting means that you have

1 several vaccine candidates, and then look to see which one is the
2 most responsive, the safest. If you look at industry, they go
3 into vaccine trials perhaps with as many as 8 to 12 vaccines, and
4 down-select the one. Historically, what we've done is gone into
5 these trials with one vaccine. And so, recently, for instance,
6 we had to kill our Q-Fever vaccine program because we only had
7 one vaccine. Ricin got killed, we only had one vaccine. And you
8 don't know how these vaccines are going to respond until you get
9 them to human subjects.

10 DR. BERG: Thank you.

11 COL. DANLEY: Sir?

12 DR. LaFORCE: That's just the problem with the
13 English language. Samuel Johnson would have said "select".

14 COL. DANLEY: Well, normally we use terms like
15 "fly-off", an Air Force term, or "sink-off", that's a Navy term.

16 (Laughter.)

17 (Slide)

18 COL. DANLEY: Dr. Linden mentioned to you about
19 TRLs, or Technical Readiness Levels. This is, again, another
20 important concept that we're integrating into our program. This
21 is next generation anthrax vaccine, and what we have listed here
22 are the various TRL levels that we've adopted from the NASA
23 approach. And what we've applied are the kinds of information or
24 products that need to be accomplished before we move on to the
25 next step.

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1 So, that information that is in green is work
2 that's been done and data that's been collected. Those steps
3 that are in yellow -- and I apologize if they don't show up in
4 your black-and-white slides -- those are work that need to be
5 done, or are in process, and work in red is work that needs to be
6 done or hasn't started yet.

7 What's important here -- and to go back and
8 emphasize what Dr. Linden said -- surrogate markers. Surrogate
9 markers are extraordinarily important. We've got to be able to
10 say to the FDA that this vaccine is eliciting in humans something
11 that we have observed in animals to be protective, and we cannot
12 go out into some of the Phase 2a trials where we're looking at
13 the immune response, without knowing what those surrogate markers
14 are, so that the earlier we start that process in vaccine
15 development, the better chance we have of staying on-track with
16 respect to cost and schedule. A big part of the process here is
17 strictly risk management.

18 (Slide)

19 These are the vaccines that we are currently
20 working on. The ones in green are the ones that we have full
21 funding for -- smallpox tularemia and a Bot-bivalent A and B. We
22 certainly have more BOT serotypes that we could put in there, but
23 I simply don't have the money, and A and B we believe represent
24 the highest threat agents right now.

25 We have a little money on VEE, we have a little

1 money on plague, and we believe we're probably going to get some
2 money for next generation anthrax vaccine. But, again, what we
3 are competing with for funding are suits and masks, chemical
4 defense products, and the pie isn't simply big enough to meet all
5 the requirements.

6 (Slide)

7 Let me talk a little bit about our contingency
8 stockpile. These are vaccines that were manufactured at Salk,
9 some of them 30 years old. They represent a small amount of
10 vaccine against these agents. We are currently going through
11 that stockpile and assessing it to determine how much of it
12 really is useful and to take that useful material and get it
13 tested so that it could be used in case of a contingency
14 requirement under an IND process because, quite frankly, some of
15 these products, like Eastern and Western, may not be ready for
16 another 5 or 6 or 8 years, and we simply have to have something
17 there, if not just for our laboratory personnel, potentially for
18 use in protecting our forces as well.

19 (Slide)

20 This is the summary. Vaccine development and
21 licensure is a long and expensive process. We believe the Prime
22 System Contractor is a valid approach because we're not only
23 talking about the capability to manufacture the vaccine, but to
24 get it licensed, and all of the pieces and parts that are
25 involved with that, from data management to risk assessment to

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1 regulatory affairs.

2 And, most importantly, we have this manufacturer
3 to represent our products to the FDA, and that manufacturer is
4 indemnified. That means that when these vaccines either go into
5 subjects during its testing process, or into our soldiers once
6 they are licensed or even as an IND product, the manufacturer is
7 protected against liability.

8 And, of course, the presence of this Prime
9 Contractor does not preclude the development of a Government-
10 owned, contractor-operated vaccine production facility because it
11 is simply a production facility, it is not all the pieces and
12 parts that go into licensing that vaccine. That's it.
13 Questions?

14 DR. LaFORCE: Questions for Col. Danley? Yes,
15 Ben?

16 COL. DINIEGA: Dave, nice presentation, a couple
17 of questions. When you look at the timelines on the Schedule of
18 Production, it does not match up at all with the Chairman's list.

19 COL. DANLEY: Right.

20 COL. DINIEGA: And I think it's been mentioned in
21 the past that the reason it doesn't is because the technical
22 readiness of each of the items as they come out of the Tech Base.

23 COL. DANLEY: Correct.

24 COL. DINIEGA: Have any of the auditing agencies
25 brought that up with your program, and what would your response

1 be?

2 COL. DANLEY: Well, no one has brought that up,
3 and obviously the response is that for at least the high-threat
4 agents, let's talk about anthrax, for instance. We have an
5 anthrax vaccine. Now, I believe it's going to be licensed. I
6 know that Col. Borowsky over there feels confident that's going
7 to happen.

8 LtCOL. BOROWSKY: I've had those questions from
9 the GAO.

10 COL. DANLEY: Have you? What did you say?

11 LtCOL. BOROWSKY: I basically have answered them
12 that, yes, we have a threat list. On the position of
13 programmatic, you've got to develop what you have and, in a lot
14 of cases, the ones that you will get that Technology Readiness
15 Level concept are the ones closest to being ready to get into the
16 pipeline.

17 So, it's sort of a, you know, "you gotta do what
18 you gotta do with what you got". I mean, it's not exactly what
19 the GAO wanted to hear, but the question is, do you invest at
20 this time a significant amount of money on your No. 2 or No. 3
21 threat when it may not come to an answer for the next 8 years? I
22 didn't get beat up for that.

23 COL. DANLEY: I think the other thing is that we
24 are addressing the high-threat agents. I mean, we've got
25 smallpox. We're actually going to start manufacturing it, if we

1 haven't already started manufacturing it down at BioReliance. It
2 will be an IND product this summer.

3 We've got anthrax vaccine which, as I said, I
4 think is going to get licensed, it's still an IND product.
5 Plague vaccine I think is problematic because it hasn't come out
6 of Tech Base, but we have several candidates that we're looking
7 at, and we actually are manufacturing the fusion protein in
8 BioScience, in Baltimore, and we could have an IND product next
9 year for that particular product, although we're still -- there
10 are still some issues as to its effectiveness.

11 So, the question of licensing a product is one
12 thing, the question of having it available as an IND product is
13 another, and I'm very confident that we've got the high-threat
14 agents -- we're manufacturing A and B also at BioScience. Again,
15 they haven't been into humans, but that's -- I'm sorry -- that's
16 at CoVents (phonetic) that we're manufacturing. So I think we've
17 got the vaccines in the manufacturing process, and they will be
18 IND products. How long it's going to take to get them licensed
19 is another issue.

20 COL. DINIEGA: The second part of the question is
21 on many of these we don't see a product out until FY'10 and
22 beyond, and the question was alluded to earlier when Dr. Ostroff
23 asked Dr. Linden about therapeutics, but who is looking at
24 interim countermeasures and treatment of chemoprophylaxis
25 possibilities during this long period of waiting for a licensed

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1 product?

2 COL. DANLEY: That's a really good question.
3 Going back to the Q-Fever issue, we recently killed our Q-Fever
4 advanced development program because we were looking at a Q-
5 vaccine which is an Australian product, and it turned out that
6 when we looked at it in depth, it really would not fit our
7 requirements. And the Combat Developer came back and said,
8 "Look, this is a fairly low threat" -- Col. Schnelle's study said
9 the same thing -- "why don't you go out and get doxycycline
10 licensed to address that threat".

11 Now, the earlier comment about ciprofloxacin to
12 use against anthrax, it's my understanding that was successful
13 because the company that manufactured ciprofloxacin wanted to
14 extend its license and was willing to make the investment in
15 extending its use and made that investment. But doxycycline,
16 that's an old product now, so who's going to make that
17 investment? And the answer is going to have to be the DoD.
18 Who's got that responsibility remains to be determined, whether
19 it will fall with the Joint Program Office or with USAMMDA, which
20 has the stronger drug program over there than the JVAP has. Good
21 question.

22 DR. OSTROFF: Thank you for the presentation. I
23 don't envy you your job at all, it must be very difficult. Last
24 year when we had a presentation on JVAP, one of the things I was
25 struck by is that when they put up the list of partner companies,

1 I didn't recognize about 90 percent of the names.

2 And you must have a terribly -- I mean, if you're
3 talking about 10 or 12 years somewhere down the line, 90 percent
4 of them aren't going to exist anymore. I mean, the way that the
5 pharmaceutical industry is, what do you do with a situation where
6 they are subcontracting the companies that even three years from
7 now, if you're talking about getting money for some project three
8 years from now, the company may not be there?

9 COL. DANLEY: Well, I think that's where the value
10 of VP-GOCO comes in. Ultimately, you are absolutely right, some
11 of these smaller companies, particularly these manufacturers, are
12 going to go by-the-by. The good ones are going to stay in
13 business, companies like BioReliance and BioScience where they
14 have demonstrated usefulness to big pharma because of the quality
15 control that they have.

16 My biggest concern is that those high quality
17 companies will find themselves in a situation where they will
18 make more money producing polio vaccine for big pharma than they
19 will for making a couple hundred thousand doses of vaccine for
20 the DoD and will get pushed to the back of their schedule. So
21 that's where I think the value of a Government-Owned Contractor-
22 Operated or dedicated facility is going to have benefit, and
23 that's why we support that concept. However, a facility like
24 that will probably take 8 to 10 years to come online. In the
25 meantime, we go to DVC and we say to them, "Do whatever you can

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1 to keep these companies interested and involved in our program".

2 DR. OSTROFF: The other question I had, I was a
3 little disturbed by your statement saying that you were having
4 some difficulty getting funding for next generation anthrax
5 vaccine to go forward. I mean, I think that probably nothing
6 would come out of this Board that wouldn't say that that's the
7 highest priority. Even if you get over the GMP problems that you
8 have with the current vaccine, it's still a lousy vaccine, even
9 though it might be wonderfully effective after six doses. I
10 mean, we need a next generation anthrax, so anything the Board
11 can do to help support you getting the resources to move that
12 forward, I think we ought to do.

13 COL. DANLEY: Well, you know, we've got to be real
14 careful about next generation anthrax vaccine. If you look at
15 the scientific data and you put the current RPA up against AVA,
16 there's no difference. One shot of AVA protects as well as one
17 shot of RPA. So, the scientific data would suggest that RPA is
18 simply purified AVA.

19 But what is next generation anthrax vaccine? To
20 me, it could take on several guises. One would be to say, first
21 of all, let's make this a very passive kind of vaccine, one that
22 is not traumatic or doesn't, in fact, cause people to rebel
23 against the idea about getting shots. So, let's look at those
24 drops or pills or eyedrops or patches or whatever. I think
25 that's important.

1 The second concept is, particularly where you want
2 to talk about multiple vaccinations, how immune does an
3 individual have to be, if they're a secretary or staff officer
4 sitting in the Pentagon? You see, that six shots of AVA was
5 designed to protect people walking into the old anthrax building
6 down the road here. And I would proffer that the FDA, in
7 requiring our soldiers to get six shots, probably went a little
8 bit overboard because I don't work with anthrax every day. I've
9 never worked with anthrax, but I had to take six shots.

10 So, part of it may very well reside in our
11 ability, for instance, to look at the surrogate markers and ask
12 the question, can we give individuals a single or one or two
13 shots at some point in their career, to prime them, or maybe we
14 give them chewing gum to chew on, but before they go into a
15 potentially hot area, we boost them to bring that level of
16 immunity up to where it needs to be.

17 These are concepts that we certainly, I think,
18 need to be addressed to the FDA when we look at licensing these
19 products, and we need to consider whether or not we're putting
20 undue stress on our soldiers by giving them too many shots. I'm
21 concerned, for instance, let's say, with BOT, and we're going to
22 do a little study here to ask the question, if I immunize people
23 against BOT A and B, am I going to make them immune to the
24 therapeutic uses of BOT A and B sometime later in their life?

25 I think that's a serious question because about 1

1 percent of the population may require some sort of BOT therapy
2 sometime later in their lives when they're 50 or 60 or 70 years
3 old, and I would hate to think that a vaccine we gave someone
4 when they were 18 or 25, suddenly caused an untoward reaction
5 later on in their lives.

6 DR. LaFORCE: Okay. Last question.

7 DR. BERG: The VP-GOCO, we're talking about a
8 manufacturing facility here.

9 COL. DANLEY: That's correct.

10 DR. BERG: Do you anticipate the Government buying
11 one or building one from scratch? One of the problems for the
12 current manufacturing capabilities for vaccine is a lot of them
13 are getting old.

14 COL. DANLEY: Correct. That's a good question.
15 All we've done so far is to ask the question how much would it
16 cost to build a facility that had a certain capacity. I'm going
17 to have to assume that we would go out on the street with a
18 Request for Proposal that would include -- that would simply say
19 the Government desires to have the following. It desires to own
20 a facility to be operated by a contractor that will do the
21 following things, and give us a 20-year plan for building and
22 operating that facility.

23 Now, it's entirely possible that a company will
24 come in and say "I've got that facility, and it's going to cost
25 you this", but you let the marketplace determine that. There

1 would have to be, however, some sort of transfer of that property
2 to the Government, and that remains to be seen how that might
3 happen. But I think the Government at this point in time is open
4 to any or all alternatives.

5 I think that's a big problem, this modernization
6 business, and I think that's what's affected a lot of industry in
7 terms of their investment, and the problem with the tetanus
8 toxoid, as I understood, was this problem of we had an old
9 facility and if we built a new facility, all of a sudden you've
10 got new FDA rules imposed upon us and we're not going to return
11 our investment.

12 DR. BERG: Exactly. This played a role in the
13 influenza shortage last fall, and was a key factor in the
14 adenovirus.

15 COL. DANLEY: Yes.

16 DR. LaFORCE: Thank you, Col. Danley. That closes
17 this morning's session. I would ask that Preventive Medicine
18 Officers and Board members, let's get our pictures taken, pick up
19 the box lunch, and begin our discussions hopefully within 15 or
20 20 minutes. Thank you.

21 (Whereupon, a short recess was taken.)
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W-O-R-K-I-N-G L-U-N-C-H

(12:33 p.m.)

DR. LaFORCE: I'm going to start. There are several items that are really on the plate as far as either recommendations or work issues that the Board's been asked to look at. I'm going to start with the easiest, or at least what seems to be the easiest, most straightforward, first. And if we could spend a moment talking about this document, the Medical Risk Assessment of the Biologic Treat document, to historically go back -- and we covered a little bit of this during the course of the discussion. Some of you were members of the Board when

1 this was requested, and the request was linked with the
2 following:

3 In a series of presentations over the last three
4 to four years in terms of DoD vaccine development, some of the
5 Board members -- and I would say almost all the Board members
6 were concerned during the presentations about some of the almost
7 ad hoc nature of vaccine development within the process, where
8 there seemed to be biologic agents with low attack rates did not
9 seem to be -- what we would consider to be more major threats in
10 terms of biologic warfare, and yet were listed and were sort of
11 moving along. And this brought up the larger question about how
12 does this prioritization take place. And those of you remember a
13 very complex presentation by Col. Hoch -- that was the famous 75-
14 slide presentation, if you remember that. I think Charlie was
15 trying to crush us with data. And the end analysis was it wasn't
16 very clear, and this then led to more discussion, and then maybe
17 two meetings later -- and Ben may be able to help out in terms of
18 some of the history -- a request that a more systematic approach
19 to establishing medical risk of biologic threats be developed by
20 DoD, and this has now subsequently led to the document that was
21 presented this morning by Col. Schnelle. And so this now has
22 been given back, and this requires, I think, all Board members to
23 read this and to read this in light of what we heard this
24 morning, and also, I think, discussion that will go on a little
25 bit further.

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1 But I need to identify on the Board a point person
2 who will assume responsibility for being the point person for
3 comments as it comes back on this particular report because the
4 ball is essentially back in the AFEB's court. In other words, we
5 are to read, digest, and respond to this in terms of does it
6 meet, are there certain issues that still remain unclear.

7 It's clear that they went at this work very, very
8 seriously, and I have not fully read the document, but I think it
9 at least meets a lot of the challenges that we set forth. But I'm
10 going to need a point person who is going to be willing to read
11 this quite carefully and also integrate the comments of the rest
12 of the Board members, and then I would be more than happy to work
13 directly with that individual to help craft a response that will
14 then be circulated to all Board members and will then go through
15 the official channels.

16 DR. SHOPE: What do you see eventually happening,
17 this document going through official channels with an addendum?

18 DR. LaFORCE: Yes. What we will do is respond to
19 this, and this is -- from what I understand, and correct me if
20 I'm wrong -- this is potentially modifiable.

21 DR. SHOPE: By whom? By the Board or by --

22 DR. LaFORCE: Well, the Board is going to have to
23 respond to this particular document. If there are additions,
24 deletions, or whatever, those will then be taken into account by
25 DoD. So, I think they are asking for -- and this is important

1 because the -- again, what we are talking about is a system
2 that's going to establish a floor in a way to look at new threats
3 which I think over a period of time should be important to DoD in
4 terms of making prioritization decisions and funding decisions in
5 terms of a variety of the agents -- because you're never going to
6 have enough money to do everything.

7 So, I would hope that the document, when it's
8 finished, becomes part of the portfolio that DoD will use to make
9 funding decisions about certain products or certain scientific or
10 therapeutic directions or preventive directions that it wants to
11 follow. Yes, Julian?

12 DR. HAYWOOD: I would suggest that we formally
13 acknowledge receipt of the report, and state that official
14 commentary will be forthcoming.

15 DR. LaFORCE: Fine. Does anybody disagree with
16 that as a strategy, that as soon as we get back, I will work with
17 Rick and send an official letter back saying that we have
18 received it, this will be digested, and we will respond back.
19 Yes?

20 DR. BERG: I think it would help if Rick could dig
21 out the original paperwork that started this so we could go back
22 and say what was it that this group was supposed to be working
23 on.

24 DR. LaFORCE: Fine.

25 LtCOL. RIDDLE: Is it acceptable to everybody,

1 with those PDF files, that I scan in and send out by email?

2 DR. LaFORCE: Okay. Then that's task No. 1 is
3 that we will get the background information sent out to all Board
4 members. You have the report. Please, if you are flying back
5 somewhere today, read it carefully, if you would, and if you have
6 questions or issues that are unclear, either call me, Rick, but I
7 still need a point person. Volunteers?

8 DR. BERG: How quickly do you need him?

9 DR. LaFORCE: This response, this is -- to quote
10 Julian -- it's better to do this right than to do it quickly, and
11 I think this is a very important document, and I think a very
12 thoughtful analysis is likely to take a month or two, you know,
13 in terms of being able to look at comments and getting back.

14 DR. SHOPE: Do you just need a person who will
15 accept the comments and collate them?

16 DR. LaFORCE: Well, I need somebody who will
17 accept -- who, No. 1, will study this and own it. By own it,
18 will understand it and really know this document quite well, and
19 will be willing to take the comments and integrate them in terms
20 of the ownership that that individual has.

21 DR. BERG: I'm willing to take that on, but I
22 can't get to it for about three weeks because I'm going on
23 vacation.

24 DR. LaFORCE: Does anybody else --

25 DR. SHOPE: I could do it.

1 DR. LaFORCE: This would be a great way to start.

2 This is a very good project to actually sort of take on.

3 DR. SHOPE: I could get busy --

4 DR. LaFORCE: Everybody knows that one of Marc
5 LaForce's dogmas is one is never too busy.

6 DR. SHOPE: It would be interesting in this to
7 take a couple of agents that are not considered threat agents, or
8 not at least in the agents here, and see how they come out.
9 Somebody mentioned influenza, I think you did, and to take one of
10 the -- maybe the 1918 influenza, and see how it would fit in
11 there.

12 DR. LaFORCE: I would say fine, go with it.

13 DR. SHOPE: I would also suggest somebody take
14 aerosolized rabies and look at it and see --

15 DR. LaFORCE: Okay. If you could serve that
16 function in terms of reading this, owning it, and accepting the
17 comments from Board members, and then it may require one -- if we
18 could do everything by email, fine. If not, it may require one
19 trip, either mine going down or you coming up, and one day.

20 DR. SHOPE: We'd love to have you in Galveston,
21 but hopefully it can be done by email.

22 DR. LaFORCE: I think it would be important,
23 though, to try to turn this around in terms of getting it back,
24 certainly before the next AFEB meeting, and I would hope two or
25 three weeks before the next AFEB meeting, so there would be

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1 something that would be back that could at least go out to the
2 Preventive Medicine Officers or to whomever needs to see that.
3 Would that be okay, if we did that as sort of a working deadline?

4 So Bob will take care of that.

5 Could all AFEB members, though, please, I'd ask
6 you if you'd just take an hour off either on your way home, if
7 you could read it, annotate it, and either ask questions or say,
8 "Look, it makes sense to me", fine, but we do need everyone's
9 feedback on this.

10 DR. GARDNER: One of the things that wasn't in our
11 book was the list of who we are and our email addresses, and if
12 we're going to send emails to Bob, we need to get those --

13 DR. LaFORCE: Right, because I noticed at this
14 time, the roster -- Jean Ward's list wasn't in the document
15 itself.

16 COL. DINIEGA: Marc, remember that the report that
17 was handed to you is a contractor report, so the goal is not to
18 make changes to the contractor report, but to comment on the
19 report. So, don't look at wordsmithing the contractor report.

20 DR. BERG: Part of what we may end up doing is
21 saying the committee needs to go back and relook at this, you
22 know, one part of it, or redo the analysis, or something like
23 that.

24 DR. LaFORCE: Absolutely right. Absolutely right,
25 you know, because, for example, during the course of the

1 discussion, if you remember, there were a couple of things that
2 were taken off the table. One is the weaponization of these
3 particular items.

4 The expertise for what can be weaponized and what
5 can't be weaponized, I think, was developed here in the United
6 States and is in some file back here at Ft. Detrick --

7 DR. SHOPE: It's all retired.

8 DR. LaFORCE: Yeah, well, whatever, but it's not
9 that it hasn't been done. I think that kind of information, I
10 think, is probably available in DoD somewhere. Whether it's
11 classified or unclassified, I mean, that obviously I don't know,
12 but I'll bet that sort of stuff is already known.

13 The other issue that was taken off the table was -
14 - I've forgotten the exact term --

15 DR. BERG: Effective dose.

16 DR. LaFORCE: Pardon me?

17 DR. BERG: I think it was effective dose.

18 LtCOL. RIDDLE: Pre-exposure prophylaxis.

19 DR. LaFORCE: Yes, pre-exposure prophylaxis, which
20 was taken off. What we may want to do as the AFEB -- what I
21 would suggest is individual look at that. Does that need to get
22 put back on the table in terms of pre-exposure prophylaxis, in
23 terms of does that so modify the threat list that it actually
24 takes some items off there? In other words, if you have pre-
25 exposure prophylaxis that is so simple -- and I'm having trouble

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1 thinking of one --

2 DR. SHOPE: Yellow Fever is one. It's taken
3 Yellow Fever off this list. It would be on the list otherwise.

4 DR. LaFORCE: Okay. But if there was an example
5 of pre-exposure prophylaxis, would that so modify how we would
6 look at that table and, if not, then we sort of leave it alone
7 and say it's not an issue, or it is an issue.

8 And as I recall -- and I'll just finish -- I think
9 those were the only two items, Ben, that were taken off, because
10 you were on those committees.

11 DR. BERG: Bioregulatory peptide, psychological
12 impact were the other two that were taken off.

13 DR. LaFORCE: Fine, I don't have any problems with
14 that. Ben?

15 COL. DINIEGA: The dose, lethal dose was one of
16 the other things taken out.

17 DR. LaFORCE: Lethal dose?

18 DR. BERG: Effective dose.

19 COL. BRADSHAW: Effective dose.

20 DR. BERG: Because units of measurement differ.

21 DR. HAYWOOD: Effective dose is still in one of
22 the tables.

23 DR. LaFORCE: Pardon me?

24 DR. HAYWOOD: Effective dose is still in one of
25 the tables.

1 DR. SHOPE: Yeah, Table 2 -- although, coming back
2 to a point made this morning, the interval from exposure to
3 incapacitation seems to be -- I would have thought would have
4 been an important variable, but it's not addressed in this -- the
5 impact criteria, even though they said it was included in
6 lethality, but it isn't under this definition.

7 DR. LaFORCE: Okay. Let's get this stuff to Bob
8 and let's turn it back in terms of the comment on the
9 contractor's report, and see where that takes us. I'm sorry,
10 Ken?

11 CAPT. SCHOR: You know, it seems to me that the
12 contractor's report describes the process, the operations,
13 analysis, or whatever you want to characterize that as, which is
14 great and useful, but if this has value, enduring value, as a way
15 to modify the process in which money is invested and other
16 things, and doctrine is written and that sort of thing, then
17 somebody's going to -- it would be nice to have a list of
18 strengths and weaknesses, things that are set to the side and not
19 considered in the analysis, the limitations, those sorts of
20 things, and I don't have a sense of who can do that except
21 perhaps the Board here. I don't know of any other standing
22 organization that would necessarily provide that level of
23 objectivity that could then --

24 DR. LaFORCE: That's exactly what we're asking the
25 Board to do.

1 CAPT. SCHOR: -- that could then be sold back to
2 DoD to say, "Hey, you know, this makes sense to us, and these are
3 the various considerations".

4 DR. LaFORCE: I happen to think this is a very --
5 and I've said it before, but I think this is a very important
6 document, and this commentary is very important.

7 LtCOL. RIDDLE: It was my understanding from
8 talking to Col. Schnelle that that's exactly what they're going
9 to do, is they've delivered this to the AFEB as a deliverable.
10 Our comments will go back to Col. Schnelle who will then take
11 those and staff those through OTSG to the services as their
12 function as the Executive Agent for CBD. So that's what she
13 wanted to do.

14 COL. DINIEGA: And, you know, the product that
15 everybody is looking for is this matrix --

16 DR. LaFORCE: Page 16.

17 COL. DINIEGA: This is the key product.

18 DR. LaFORCE: That's it. And that's why I
19 couldn't have been happier, as we were going through the
20 discussions, if you look at those four agents on the upper left,
21 which are the most serious agents, they are being addressed. And
22 then if you moved over, the empty box was Marburg and Ebola, and
23 I was delighted to hear that there was activity in terms of
24 Marburg. And so I was really very pleased that the analysis
25 appears to be really reasonably tightly linked with what is being

1 proposed as far as R&D work for these particular agents.

2 DR. SHOPE: Some of the things they are doing in
3 R&D, though, are way down on the list.

4 DR. LaFORCE: Okay.

5 DR. SHOPE: The VEE vaccine.

6 DR. LaFORCE: Correct.

7 DR. SHOPE: I'm not sure it belongs way down, but
8 that's --

9 DR. LaFORCE: And that's why this is important.
10 Okay. Any other observations or comments? What's the matter,
11 Linda?

12 DR. ALEXANDER: It's just a thought, that in terms
13 of the utility of this document, right now it seems so obvious of
14 its blatant utility with DoD. I was thinking about the civilian
15 implications in terms of translating that into a civilian
16 response document or something that FEMA might be interested in.

17 I mean, that's not within our purview, but it seems to me
18 there's utility to transit beyond DoD, and maybe there would be
19 some opportunities for partnership and funding as an issue to
20 take this further for greater analysis that we might suggest DoD
21 consider.

22 DR. LaFORCE: That's an interesting idea. I mean,
23 the analysis itself, you're saying why is this strictly
24 restricted. Okay.

25 DR. SHOPE: I think that's a very good point,

1 however, the analysis is done for the warfighter, and I think
2 you'd need a different analysis. But what we might suggest is
3 that this matrix be looked at by a group. There's a lot of
4 bioterrorism money out there to do a similar exercise.

5 DR. LaFORCE: If the template looks like it works,
6 this might be a very useful model. I agree.

7 DR. PATRICK: Well, in fact, that may where there
8 was a question of validating this. That may be a way to move
9 closer to the validation of this sort of an approach. Perhaps
10 something would happen --

11 DR. SHOPE: Well, I think you'd grant these
12 differently in a civilian --

13 DR. PATRICK: Clearly, but if the same approach in
14 terms of methodology was useful, that question was raised, how do
15 we know that this is, in fact, valid. So, some tests, some
16 natural experiments which one would not hope for, but --

17 DR. BERG: I think that was part of the message
18 that Col. Schnelle was making, that much of the effort of the
19 group was figuring out how to get their arms around it, and they
20 came up with this methodology. And she said the beauty of it is
21 if the intelligence shifts on what's available, we can just plug
22 that back in and run it through. We don't have to reinvent the
23 wheel.

24 DR. LaFORCE: Okay. We'll proceed along that
25 line. I do want to introduce one other thing I was talking to

1 Kent Schor and also Ben and Rick earlier. This has to do with an
2 issue that's been bothering me as the morning progressed, and it
3 had to do largely with the final presentation that was Col.
4 Danley's presentation.

5 Col. Danley's presentation had the time frame in
6 terms of the R&D and the development until you have final FDA
7 approval. And if you remember, almost all of it looks like it
8 kicks in as real products somewhere after 2010. It was like 2010
9 to 2014 is when it kicked in. Okay. That was point one. That
10 means that from the year 2001 to the year 2014 there needs to be
11 an alternative strategy because that doesn't change Table 16.
12 Those items in those boxes are still real in Table 16. We may
13 not have the antigens, but the threat is still there. And the
14 concern that I have is this window -- you know, because I've said
15 what about interim plans for this window that exists for perhaps
16 10 or 15 years in terms of before -- or the time frame before
17 these vaccines actually roll out. Now, that's one concern.

18 The second, it is also linked to a question that
19 the Board received and I believe the Board received this question
20 about -- was it a year and a half ago, Ben, about the antibodies
21 --

22 COL. DINIEGA: Last year.

23 DR. LaFORCE: Was it last year about this time --
24 because one of the questions that came to the Board is, could the
25 Board make recommendations on chemoprophylaxis for biologic

1 agents, and we developed a small subcommittee and we responded to
2 that particularly with, as I recall, doxycycline, ciprofloxacin -
3 - and I must admit my memory is not good enough, I don't remember
4 what the other agents that we actually put down -- but it was
5 strictly to answer a very narrow question, and that narrow
6 question was, what agents might DoD stockpile in terms of looking
7 at chemoprophylactic agents for these particular threats.

8 What seems to be missing is how you link now the
9 chemoprophylactic agents with some sort of interim strategy until
10 these vaccines come up. And when the question was posed to Col.
11 Danley by Col. Diniega about sort of who is in charge of this,
12 the response was, no one, at least that was the answer that I
13 got. And I would put this out to the Preventive Medicine
14 Officers, is there someone in charge, or am I missing something?

15 CAPT. SCHOR: Well, just to give you a very
16 present example, anthrax, the change of label to use it as a
17 post-exposure prophylaxis. And now that we essentially don't
18 have, or nearly will not have, any anthrax vaccine available,
19 period, is a very current concern of the CINCs over in Korea,
20 Southwest Asia, saying, "How do I then protect my soldiers,
21 sailors, airmen, and Marine?"

22 The Action Officers at Action Officer levels have
23 been trying to get five days of supply of cipro within a 12-24
24 dispersement window. Let's say there was a validated exposure.
25 We want to have five days' supply of cipro near troops or Marines

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1 or sailors or airmen to get it in their hands so they can take it
2 within 12 to 24 hours of validated exposure. And, oh, by the
3 way, there's extra money to buy some of this stuff because we
4 don't have any anthrax vaccine to buy right now. So, it's just
5 shifting pots around, and I'm using some terminology fairly
6 loosely, but that's how I understand it.

7 And I understand that as this has gone on, there
8 have been some concerns about how to do this, and there's a lot
9 of sort of ricebowl issues -- is this a medical issue? Is it a
10 BW defense issue? Do you pay for it out of Defense Health
11 Program dollars? do you pay for it out of shifting monies? And
12 I understand that recently some decisions have been made to nix
13 that idea. I don't know all the reasons for that, but I use this
14 not to get into that level of detail, but it's very hard to work
15 around these very current present highest threat issues when it's
16 hard to figure out who is making decisions on how to influence
17 the decisions when you care about the protection provided to DoD
18 members.

19 DR. LaFORCE: Yes?

20 LtCOL. BOROWSKY: Just to introduce myself to
21 those who haven't met me, I'm Bob Borowsky. I'm the Medical
22 Deputy at the Joint Program Office for Bio Defense, and next
23 month I go to work for Dr. Ann Johnson Winegar who, if you don't
24 know, is the Deputy Assistant to Secretary of Defense for
25 Chem/Bio.

1 Let me, sir, answer one of your questions. One of
2 the things that didn't come out clear in the chart was that in
3 the process of developing consistency lots for the vaccines much
4 earlier than 2010 or whatever, in the process of doing that, they
5 will have met, from an IND standpoint, the stated number of
6 vaccine doses. So, it's conceivable by 2005, 2006, that some of
7 these agents will have at least at the IND stage -- granted,
8 that's not license, and I know what our policy is -- but you'll
9 at least have material -- for example, small pox -- and enough
10 doses that if the balloon goes up and we get the right approval,
11 we can use as an IND.

12 Part of the problems with the antibiotics that
13 have come up in discussion is that, like with the anthrax usage,
14 a lot of these things require some policy FDA interactions
15 because they are off-label usage, particularly if you're going to
16 do prophylaxis with some of these antibiotics.

17 The problem we have is developers -- and it goes
18 back to the whole issue that product that was developed is the
19 developer will give you what you want, the customer, but we have
20 to know what the customer wants.

21 So, one of the biggest things -- I've been doing
22 this since I got back from Germany in '92 -- is wrestling with,
23 well, what is the soldier going to see on the battlefield? Just
24 because a monkey gets 1000 LD50s of something, what does that
25 relate to reality? And so as we struggle, we're really looking

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1 at the people who establish policy and requirements to tell us
2 exactly what is it they want. And once we know that, then we can
3 move forward. Now, I know that's a gray area. We can't go out
4 and expose people to agent, but we do know that in the archives -
5 - sir, you brought it up earlier -- places like the Institute of
6 Defense Analysis has buried somewhere in their vaults some of our
7 '50s, '60s, and '70s testing on some of these offensive weapons.
8 So, it's just a matter of coordinating and collating, and
9 hopefully in my new job next month I can have some influence
10 under that. But there are people who are looking at the interim
11 approach. I do put on the table that some of these things will
12 be available for IND usage in the next several years.

13 What is an issue, though, in some cases, exactly
14 what is the requirement. The Regular Army or the Regular
15 Department of Defense, when they build planes and ships and what
16 have you, will put on the table how many they need. What's
17 driving us right now is one program budget decision done about
18 three years ago that set \$300,000 for the lesser threats, 1.2 for
19 things like BOT, and obviously an immunization program for
20 anthrax. What that influences is the small companies that are
21 going to develop these vaccines, is whether they are a micro-
22 brewery or Budweiser. So, once they go down the road of meeting
23 a small requirement, they may not be able to make 40-to-100
24 million doses of smallpox vaccine like Health and Human Services
25 wants.

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1 So, for me, my hands a lot of times as a medic who
2 has also gone through acquisition training, is, how do I spend
3 the taxpayers money smartly, and what is the requirement, and
4 that can't come from the developer, that has to come from the
5 people who set the requirements because, like I said, once you go
6 down the road of saying "I'm going to build that" to produce, you
7 know, half a million doses, and it's going to sit on the shelf,
8 it's going to be awful hard to crank up to a million or a hundred
9 million, or whatever the magic number is. So that's a problem we
10 face trying to meet the requirement.

11 DR. LaFORCE: That still doesn't answer if, for
12 example, you say, well, look, we have IND lots that are going to
13 come in '05 or '06 -- okay? Assume that I'm a cynic --

14 (Laughter.)

15 DR. LaFORCE: I mean, you've told me that before,
16 is what I would say, and I'm going to say that my experience
17 tells me that you might say '06, but I'm going to be very happy
18 if it's '10.

19 LtCOL. BOROWSKY: I won't disagree.

20 DR. LaFORCE: Okay, fine. That still leaves me of
21 a question of somebody in Pusan, or somebody in North of Seoul,
22 with the question of an anthrax exposure and the need to have an
23 interim strategic plan with proper stockpiling to make sure that
24 that warfighter is taken care of if we can't get enough antigen
25 in him to make sure that he's taken care of.

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1 LtCOL. BOROWSKY: And the Captain brought up a
2 good point. Right now, we're in the midst of discussions for the
3 use of anthrax -- not anthrax -- cipro, and what we have to do is
4 come to grips with are we willing to pay for that because I think
5 we figured out it might be a total of I forget how many, \$60- to
6 -\$80 million to buy everything we want.

7 CAPT. SCHOR: \$96-, sir.

8 LtCOL. BOROWSKY: So, yes, there are discussions,
9 but it's all being driven by can we afford it.

10 LtCOL. RIDDLE: Brian, from the Joint Staff, would
11 you all generate out those requirements, let's say, based upon
12 this list that plague was a threat if doxy was your own
13 antibiotic because you had no vaccine in the inventory. The CINC
14 says, "I want a response, it's not labeled". Does the Joint
15 Staff generate the requirement to DoD to work with FDA to work
16 doxy labeled for use with plague?

17 MAJ. BALOUGH: Col. Diniega might be able to add
18 to this also, but my understanding is, if the CINC's comments say
19 they want to use, say, cipro for pre-exposure, we don't -- the
20 Joint Staff doesn't have the authority to grant them permission
21 to do that, that's a requirement, and we would turn around and
22 coordinate that with Health Affairs, and Health Affairs is the
23 one who would have to establish the policy to do that or not to
24 do that. And in this case, because cipro isn't licensed for pre-
25 exposure, it would have to be done in an IND, and we would go

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1 through the IND stuff. The Joint Staff is involved in -- right
2 now, we're trying to work with the CINCs and MRMC and Health
3 Affairs and OTSG to do the anthrax post-exposure IND, but we are
4 more in a coordination aspect of that because we can go out and
5 touch everybody.

6 DR. LaFORCE: So what is it that would have to be
7 nudged, Ben? Would it have to be Health Affairs, or --

8 COL. DINIEGA: There are a couple of issues here,
9 licensed product, labeled use. If you are going to be stockpile
10 or order is not a research issue and you don't have to do it
11 under IND, and I think the EA -- is Col. Schnelle here -- has
12 done work on stockpiling numbers, and it's a tri-service process.

13 They had a meeting, they do it with the junior CAV -- I remember
14 seeing a stockpile numbers list that was done up at the junior
15 CAV at one time, up here at Ft. Detrick. So, license, labeled
16 use, stockpiling is essentially just, you know, the Executive
17 Agency can do that.

18 IND use, that's a tough issue. IND, as we found
19 out, Brian, they are in the recent exercise. That is a tough
20 issue. FDA will not waiver, grant waivers on the IND. They need
21 the IND. The only thing that can be waived is getting people's
22 permission and signature to receive the IND. And so the CINCs
23 are being asked to be with full acknowledgement and acceptance by
24 the CINCs, and concurrence by the CINCs, and then it will be part
25 of their operational plan, their contingency plans for the

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1 theater. But they'll have to follow all the IND procedures down
2 the line.

3 That's the big problem we're having in IND, so the
4 fact that you'll get some IND products early, or the fact that
5 they're stockpiled, all those other IND products that Col. Danley
6 showed, really doesn't help us. We still have a lot of
7 administrative procedures to go through. But the aim should be
8 an FDA approved product.

9 DR. LaFORCE: And the approval that's currently
10 available now that has been negotiated has been the cipro
11 approval in terms of pre-exposure chemoprophylaxis --

12 COL. DINIEGA: For post-exposure.

13 DR. LaFORCE: Yes, post-exposure -- I'm sorry --
14 post-exposure chemoprophylaxis, cipro has now been approved,
15 right?

16 COL. DINIEGA: Right. Go ahead.

17 DR. LaFORCE: I was just going to ask a question.
18 In terms of plague, post-exposure chemoprophylaxis for
19 pasteurella pestis, is there a protocol for such an aerosol
20 exposure? In other words, what would you do if you have an
21 unvaccinated population --

22 COL. DINIEGA: They use doxy. It's an approved
23 use.

24 DR. LaFORCE: Okay. That's approved use. So
25 that's not an issue.

1 COL. DINIEGA: That's not an issue.

2 DR. LaFORCE: What about Q-Fever?

3 COL. DINIEGA: Is it on the label for use? I
4 don't know what's on the label for doxy.

5 DR. LaFORCE: Because it may turn out as you go
6 through this, it's a non-problem.

7 COL. DINIEGA: If it's a labeled use, it's not a
8 problem. If it's an unlabeled use, then it becomes a problem.
9 But on the JVAP -- and, Bob, you can correct me if I'm wrong --
10 but I recall that in the planning for the JVAP in the vaccines
11 they're working on, there are TEDs, troop equivalent doses,
12 already determined as to how many they have to manufacture.

13 LtCOL. BOROWSKY: That's true, but the issue
14 really comes up when you really get pressed by like the GAO or
15 whatever when they want to come in and ask where that number came
16 from. It's hard to go back to some very analytical thinking or
17 process that perhaps a group like this came to and said, you
18 know, "This is what we really think" -- if the balloon goes up,
19 we're not looking at just one, you know, major regional conflict,
20 which is one of the indications I got.

21 The other thing is on IND usage, the FDA has shown
22 a willingness with anthrax, for example, the new consistency lots
23 that are being manufactured at BioPort right now, a willingness
24 to sit down and work a list for IND usage under a contingency.
25 So, it's not that they're inflexible, they're just very cautious,

1 and we all appreciate that they're very cautious.

2 DR. MOORE: There is another aspect of this, of
3 course, it's life cycle cost. You're talking about \$90 million
4 one time to build a stockpile. When we started fielding DEPMEDs,
5 the dated and deteriorative items in the DEPMEDs kits were \$300
6 million. And I went to Sweden and Switzerland and studied how
7 they had extended the storage life, shelf life, of their items,
8 came back and talked with FDA. They said you get the
9 manufacturers to do it. I went to a number of manufacturers and
10 they said, "DoD is less than 5 percent of our business, we
11 aren't going to spend money studying how to extend the shelf life
12 of drugs and IV fluids. If the Army wants it done, let them pay
13 for it". And, of course, the answer to that was no. So we're
14 buying \$92 million worth of stockpile that's going to have to be
15 replaced three years from now with \$92 million worth of
16 stockpile, or at current drug rates, to \$120 million.

17 COL. BRADSHAW: I think the current answer to most
18 of that is stock rotation, do stock rotation agreements with the
19 manufacturers, and then you cycle it in and out, so you're not
20 going to have to do \$92 million every three years.

21 DR. MOORE: Well, we tried that with the
22 pharmaceutical industry, and we were able to get probably a
23 handful of things stockpiled with them, and our usage rates
24 within DoD would be, I think, difficult to maintain that and
25 stock rotate.

1 COL. BRADSHAW: Cipro and doxy are, I think, used
2 fairly often, although I'd have to look at the numbers to see.

3 DR. OSTROFF: Almost everything that we're doing
4 at CDC is -- I mean, it's referred to as "vendor managed
5 inventory" where basically you just pay for a chit in the system
6 where you pay for the bubble, and the availability of the bubble,
7 and then it just rotates in and out of the available inventory
8 and, you know, it works fine for items that are used on a fairly
9 common basis, it doesn't work for vaccines, you know, where
10 you're not using them constantly.

11 DR. LaFORCE: It should work for cipro and doxy.
12 By the way, the plague is off-label, Ben. That's off-label. So,
13 a significant progress could be made if you could have this
14 discussion and make sure that that was a labeled indication in
15 terms of post-exposure prophylaxis for plague.

16 DR. OSTROFF: The other one is the issue of
17 gentamicin, it would also make a major difference because that's
18 also not labeled for --

19 DR. LaFORCE: Yes, that's off-label, the
20 gentamicin one.

21 CAPT. SCHOR: I know within our service, there
22 would be great support to get some of these label changes to
23 support research to get the label changes. We're spending lots
24 of money to make vaccines, but we're not spending much money to
25 get basic labels. How about getting cipro as a pre-exposure

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1 prophylaxis?

2 LtCOL. BOROWSKY: One thing that I would offer --

3 CAPT. SCHOR: And I don't know what the parameters
4 of that are, but there doesn't seem to be even a hint of a
5 discussion that that can even begin to occur. There's no
6 interest. It's like it's not sexy enough to talk about.

7 LtCOL. BOROWSKY: One thing I could offer, and
8 this is on a personal level, is you look at the product that was
9 delivered today -- and, sir, I think you're hitting on this -- we
10 look at what is our short, mid and long-term solutions.
11 Antibiotics, antivirals may be one of them, but it's not for a
12 developer to decide. The people who have the need -- the
13 Marines, the soldiers, the airmen -- out there, and the CINCs,
14 have got to say, "Okay, these are the top five we think we're
15 going to get hit with in any theater, now what's the available
16 solutions?" And that is, I think, the first step, allocating
17 resources, and if we have to do an IND for a product or a label
18 change, then we better start doing it.

19 DR. BERG: I wonder if there's another solution.
20 I remember about a year ago reading in the paper about a study
21 that was done of the true shelf life of various pharmaceuticals,
22 and was actually done by some military pharmacist as part of a
23 tri-service effort, and the shelf life of many of the drugs was
24 just incredible. And what sticks in my mind, I think the
25 ciprofloxacin had not lost significant potency after something

1 like 17 years. And the point of the article was that drug
2 manufacturers have little incentive for documenting a long shelf
3 life.

4 LtCOL. BOROWSKY: Well, having worked for Baxter
5 myself, I know part of the shelf life issue is the investment and
6 stability studies over the years, and the submission to the FDA
7 that a product is got for 3, 5, 10 years.

8 DR. BERG: If this has been some sort of formal
9 research project that the military has been carrying on, that
10 might have generated some useful data that could be submitted to
11 the FDA to extend the shelf life of some of these things.

12 DR. LaFORCE: From what I understand, that's one
13 of the hardest things to do, is the shelf life thing, is what --
14 that's just been my understanding. In a prior life as a
15 clinician, I remember talking to a buying consortium in
16 Rochester, when we were buying a series of things, and then
17 looking at the issue of shelf life, and then having the
18 pharmacists sort of let us know that that was very difficult.

19 DR. BERG: The difficult was getting the extension
20 approved, or --

21 DR. LaFORCE: Yes, it was actually even
22 approaching that because the answer was almost invariably no.

23 COL. DINIEGA: Just to get back to the stockpile
24 issue, in my experience, stockpiling numbers have come from
25 several sources. One is the services, if it's licensed and it's

1 available, services can look at their own stockpiling issue. The
2 other one is, usually on any requirement in combat development
3 for BOT or whatever, when you ask for something to be developed,
4 a medical product, you have to estimate how many doses you need
5 and how are you going to use it. So the stockpiling numbers
6 would also depend on the strategy of use in the theater. At one
7 time, I know for some items it was only stockpiled for early
8 deployers, or for the people who flew in within 30 to 60 days and
9 the early deployers. So, the stock numbers can be obtained, and
10 some of the things are service-specific because of the laws and
11 the legal requirements, which is training, equipping and manning
12 the force. Other than initial procurement for developed items,
13 it becomes a service responsibility.

14 CAPT. SCHOR: That's a very good point because
15 this issue with cipro brings up where is the gray zone between
16 what the CINCs need that are expected to fight the wars with
17 forces supplied by the services, and the service responsibility
18 is to train, equip and supply, and sometimes those train, equip
19 and supply -- you know, we've seen that the POM cycles are --
20 you're planning three years ahead of when you ever actually get
21 the money in hand, yet here is a clear and present threat and a
22 need, and so how do you bridge that gap, and this really
23 crystallizes a structural problem within the Government that goes
24 well beyond a lot of these sorts of issues.

25 For instance, with the cipro, the planning issue,

1 most of the planners looked at personal supplies like point of
2 use -- aid station level distribution of five days of supply of
3 blister pack cipro. That was a reasonable risk determination to
4 make. If we could at least get them five days, we should be able
5 to get some more, somehow, somewhere, if we have some air
6 superiority in the theater.

7 Then they looked at perhaps 15 days of supply in-
8 theater, and then figuring that the additional 45 days to go out
9 to a full 60 days of therapy would come from strategic resupply.

10 So that's just to give you an example of how some of the
11 thinking very recently on this issue of post-exposure
12 availability of cipro has gone on.

13 DR. LaFORCE: That sounds very sensible.

14 DR. OSTROFF: I'll point out that DoD uses the
15 same vendor managed inventory that we do. It's the same exact
16 system, and part of the concern that we've had is that we're
17 double-paying for the same vendor managed inventory, and part of
18 the difficulty would be if we both asked for it at the same time,
19 who was going to get it first.

20 DR. BERG: Does the other guy get a refund?

21 (Laughter.)

22 DR. OSTROFF: And we've been assured that we're
23 paying for different vendor managed inventory at least by the
24 suppliers, but I'm not 100 percent convinced.

25 DR. LaFORCE: Okay. What I would propose to the

1 Board -- I think we've gone as far as we can with this issue.
2 What I'd like to do is work with Rick in terms of just exploring
3 this a little bit, and maybe with Ben, and without formally
4 coming back -- we may come back with just a short letter or short
5 note from the Board, but nothing will be sent out until it's
6 actually cleared or circulated, that would relate to this issue
7 about the interim sort of problem over the next ten years or 15
8 years.

9 DR. SHANAHAN: It strikes me we really don't have
10 enough information in that area, which makes it a good topic for
11 presentation before the Board, if we're interested in pursuing
12 that.

13 DR. LaFORCE: Actually, that's a great idea. Why
14 don't we actually just do that, rather than try to do something
15 precipitously, just move this on the agenda next time around, and
16 look at it as "the interim strategy" or "interim plans", or
17 whatever, for BW agents, and then this would give a chance for
18 people to really sort of think about it and see if there's
19 something that needs to be done and, if so, what makes the --

20 DR. SHANAHAN: And let's then identify specific
21 problems that we can better address, rather than try to push this
22 --

23 DR. LaFORCE: Off-label doxycycline for
24 chemoprophylaxis of plague.

25 DR. PATRICK: What I wonder is, are there other

1 strategies? I mean, Ken has just outlined a very interesting
2 strategy, and what other strategies are out there that have been
3 thought about and eventually proposed, it sounds like even
4 proposed, but yet --

5 DR. LaFORCE: But I would love to see the
6 presentation start at the furthest end -- in other words, from
7 your standpoint, from the warfighter standpoint in terms of what
8 would be those constraints. In other words, starting at the
9 distal end rather than at this end in terms of stock rotations or
10 stuff like that -- I mean, what actually would work if such a
11 threat did, in fact, occur.

12 DR. BERG: I think the analysis should include a
13 listing of what are off-label uses because the only post-exposure
14 prophylactic antibiotic use that I know of relevant to this
15 discussion is ciprofloxacin because we don't use antibiotics
16 post-exposure. So that means potentially all of the list, all of
17 the antibiotics need to be used, and gentamicin needs to be
18 looked at in terms of treatment.

19 DR. OSTROFF: We do use some antibiotics post-
20 exposure. I mean, you do for meningococcal disease and things
21 like that, so there are precedents for doing that. And we, in
22 fact, use cipro now.

23 DR. BERG: But there's a whole dichotomy between
24 what's on the label and what people use.

25 DR. OSTROFF: Right, and we were just talking

1 about this a little while ago. Off-label use, when it's between
2 a physician and a patient, it's physician discretion. A
3 physician can do anything that they want if they think it is
4 appropriate for the care of that individual patient.

5 The problem that you get into is when DoD or CDC
6 or a system makes a recommendation that this is the appropriate
7 thing to be used, you are not the actual treater, and so it falls
8 outside the usual off-label use discretion that a physician has,
9 and that's where we've all gotten caught up.

10 DR. BERG: Exactly. When you start to propose it
11 as the standard of care, you've taken it to a different level.

12 DR. PATRICK: An appropriate caveat is perhaps to
13 say these have been used for modeling purposes.

14 DR. LaFORCE: Okay. Other comments?

15 (No response.)

16 So, we have essentially one deliverable which Bob
17 is going to assume the sort of administrative leadership with,
18 which is this document and one of the items at the next AFEB
19 meeting will be this interim strategy which we will develop in
20 some detail over the next three months. Okay.

21 Other questions to the Board relate to the
22 formation of the Vaccine Health Center Work Group. This
23 discussion, I think we had a bit of it yesterday, and I sensed
24 that there was sort of unanimity that this was a good idea and
25 this was a good investment of AFEB time, and I have two

1 volunteers. Bill Berg and Linda Alexander wish to serve on that
2 committee, and they asked for two or three volunteers. I would
3 say that two are fine, and three is even better. Pierce, would
4 you like to participate as well?

5 DR. GARDNER: I'd be happy to.

6 DR. LaFORCE: Okay, that's great, because it
7 involves probably -- I don't think anymore meeting except maybe
8 stretching things over either a half-day and the work will be
9 done in collaboration with either the AFEB meeting or the ACIP.
10 Okay. That's good. Is there anymore discussion about that as an
11 issue?

12 (No response.)

13 Okay. Terrific. Now we'll get to the one that
14 I'm not ready for. Today, it reminds me of talking to my
15 daughter about doing her homework in high school. I'll do it
16 later, and I'll do it later, I'll do it at lunchtime. I kept
17 telling myself, I'll sit down and write my notes and sort of
18 never got to it.

19 The main -- or we owe a response in terms of the
20 questions that related to HIV, and what I want to do is finish
21 our formal deliberations by going back to that particular
22 question, and I would ask all of you if you would get to -- I
23 think it's Tab 7 of the document -- if we would go back to the
24 questions that were set forth by John Ball (phonetic) from --
25 that relate specifically to the HIV questions, and if you would

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1 just pardon me for one moment -- two of you gave me some written
2 material that, unfortunately, has gotten mislaid -- here it is --

3 DR. SHOPE: You gave mine back to me.

4 DR. LaFORCE: I gave yours back to you, that's
5 right. Thank you very much, Bob. What happened to Bill, because
6 Bill is going to have to read that. What I would propose in
7 terms of a general umbrella for responding to this is that we
8 continue some of the discussion that we started yesterday, and
9 that we've got some specific answers for some of the questions
10 that we probably should talk over this afternoon, but if you
11 would trust me to actually put a response together that I will
12 work over with Rick, and then send back to all AFEB members --
13 and hopefully this will get back to you within two weeks, if we
14 could sort of do it within two weeks or three weeks or something
15 like that -- and then I probably would like to send it to you by
16 email rather than just sort of send it any other way, and this
17 way you can just sort of read it as-is, and then just sort of
18 press Reply yes or no and send back what you want, but I really
19 would like -- this is an important question that's being asked,
20 and almost like the response to this document here, I really
21 would like to hear from everybody.

22 The letter itself: I request the Armed Forces
23 Epidemiological Board to review available and provide a
24 recommendation concerning desired characteristics in use of the
25 subject proposed vaccine -- that is, the HIV vaccine.

1 I request the Board specifically to address the
2 following questions: (a) What level of effectiveness (for
3 example, induction of the desired primary immune or physiologic
4 response) of an HIV vaccine is acceptable for use by DoD?

5 During our discussions, we -- and correct me if
6 I'm wrong -- the AFEB felt uncomfortable with a specific number.

7 Who had discussed that? Was it Dennis? Yes, you had discussed
8 it.

9 DR. SHANAHAN: Yes, and I felt that to set
10 particularly specific limits like 90 percent was very
11 unrealistic, and I used the analogy of putting generation 3
12 requirements on a generation 1 product. I think we were all in
13 agreement that if it were, in fact, efficacious at some level,
14 that it probably had some degree of utility and that we wouldn't
15 want to eliminate from consideration a vaccine that, in fact,
16 say, had 60 percent efficacy, considering we have nothing right
17 now. So, if it were safe and met other requirements, 60 percent
18 -- the limits of the study are 50 percent -- so, there may be a
19 utility for something of that nature as long as it's safe and
20 also economical and can be handled through the logistic chain
21 such as it is today, or would be in the future. That was
22 generally my reasoning on it.

23 DR. LaFORCE: And my sense was pretty much
24 everybody was in agreement with that, and it also links to the
25 second, (b) What level of efficacy and protection from HIV

1 infection or HIV-caused disease is acceptable? I would lump both
2 (a) and (b) together and, if you want, I'll draft something along
3 those lines that we're sort of uncomfortable given the fact that
4 it's not like comparing a 60-percent efficacy vaccine versus what
5 could be 100 percent, it's really zero versus -- and from what we
6 understand, the power of the study itself is unlikely to pick up
7 any efficacy less than 50 percent because of the design of that
8 particular study. So, you immediately start off with a power
9 calculation that leaves the floor set at 50 percent.

10 DR. SHANAHAN: And there's one primary in the
11 pipeline. So, if you set too high a standard, that gets kicked
12 out.

13 DR. SHOPE: I think it's important in our
14 discussions we separate infection from AIDS or HIV disease. In
15 (b) they are asking two questions, efficacy and protection from
16 HIV infection and efficacy and protection from HIV-caused
17 disease. And I think our discussion was that we were talking
18 about infection.

19 DR. LaFORCE: That is correct. I think that was
20 pretty clear, wasn't it?

21 DR. OSTROFF: I wasn't here.

22 DR. OSTROFF: One thing that I just wanted to add
23 is that, in (a) -- response to what was just said -- it said what
24 level is acceptable for use by the DoD, and I think that that's a
25 very critical distinction because in terms of a 60-percent

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1 efficacious vaccine, I could think of a lot of circumstances in
2 which that would be a wonderful tool to have, but I'm not sure in
3 terms of routine use by the DoD I could think of a scenario where
4 they would wide-scale use that type of a vaccine. So, that's a
5 very important distinction, that they say specifically for use by
6 the DoD.

7 DR. LaFORCE: Unfortunately, you didn't
8 participate in the discussions we had yesterday, but one of the
9 things we ranged about would be the level of indication, and the
10 indication for a vaccine, particularly if the vaccine were, let's
11 say, not very effective in terms of contemporary vaccinology --
12 let's say it was 65 percent effective -- one may choose not to
13 make it a universal vaccine, but one may wish to use a vaccine
14 with 65 percent efficacy for deployed troops in South Africa. In
15 other words, the risk is so much greater, at least as a result of
16 that particular deployment, that the 65 percent may make imminent
17 sense in terms of the public health benefit.

18 So, the Board felt -- and I couldn't agree more
19 strongly -- I think the Board felt very uncomfortable in terms of
20 making a general recommendation about this being a universal
21 vaccine for all military forces for exactly the reasons that Dana
22 Bradshaw sort of put out -- you know, it may be X-number of
23 doses, it's not going to be well received, et cetera. I think
24 the research and the efficacy data from the Thailand studies are
25 really going to help set a framework for what are the levels of

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1 protection that you can expect, and prior to the completion of
2 those particular studies, I think anything that we're talking
3 about is "dreamsville" -- you know, it's all really pretty
4 theoretical.

5 DR. SHANAHAN: And I also felt -- and I don't know
6 how the rest of the Board feels -- but it's a question I don't
7 feel qualified to answer in terms of what is an absolute level
8 that the DoD should consider for use because, as Marc said, we
9 have all kinds of scenarios that we can see here where they may,
10 in fact, be useful. And I think, to put it farther than Marc,
11 say medical personnel deployed to an endemic area are at very
12 high risk of exposure, even with today's precautions. So, maybe
13 65 percent -- and if I were going over there, I'd say, hey, okay,
14 I'll take the 65 percent.

15 So what we felt was we didn't want to kick it out
16 of consideration when there were all these other issues that we
17 could consider. And, you know, in a way, maybe it does kick it
18 back to the DoD and say, hey, this is a tactical or economic or
19 strategic decision that the Board's not really willing to make
20 for you.

21 DR. LaFORCE: The other thing is, if you remember
22 Gen. Parker's both introductory and his closing comments, also
23 was asking the Board in terms of what the Board's feelings were
24 about an HIV vaccine being appropriate as a vaccine to be
25 developed by the military. In other words, what is the public

1 health benefit to the military?

2 And I want to make sure if it's all right with the
3 Board that the original draft will begin with a sentence or two
4 saying that yes, it is quite appropriate to consider this as a
5 vaccine that's appropriate for the military for either narrow or
6 broad considerations, but certainly for the risk of deployment in
7 countries or in areas that have high HIV rates. And as we talked
8 about yesterday, I frankly, in my own mind -- as I said, having
9 spent a fair amount of time in Africa over the last couple of
10 years -- I can't imagine that U.S. troops are not going to be
11 deployed somewhere from the Congo, south in areas that really --
12 or that the likelihood is going to be significant over the next
13 ten years, is probably the way I would phrase that.

14 COL. WITHERS: Dr. LaForce, the operative word he
15 used was military "relevance".

16 DR. LaFORCE: Is it military relevance? That's
17 the word I need to use?

18 COL. WITHERS: Yes, I think that's what you're
19 struggling for.

20 DR. LaFORCE: Okay, thank you. God love you, Ben.

21 COL. WITHERS: Just say it's a militarily relevant
22 vaccine in the eyes of the Board, if that's what you believe.

23 DR. LaFORCE: Okay. All right.

24 DR. SHANAHAN: Say "because" and use all of it.

25 DR. LaFORCE: You what?

1 DR. SHANAHAN: Say "Because" and use all of Gen.
2 Parker's arguments because they were excellent.

3 DR. LaFORCE: Is a vaccine that prevents AIDS or
4 other HIV-caused disease acceptable for use in DoD personnel if
5 it does not also prevent carriage and/or transmission of the
6 virus? How would use of the vaccine and other attendant
7 preventative measures vary depending upon the presence and
8 absence of prevention of transmission?

9 I had the world's worst time -- I read this last
10 night, and that's when I quit and decided to go to bed.

11 DR. SHOPE: I don't think transmission is the
12 issue, it's infection.

13 DR. PATRICK: And I think the sense there was the
14 transmission of the virus was too hard an endpoint to establish
15 through type of setup right now. That would require subsequent
16 analysis of other individuals, and so that was just an
17 unrealistic standard to include in the current --

18 DR. LaFORCE: You mean that was McNeil's point.

19 COL. BRADSHAW: I had a conversation with Col.
20 Scott and discussed this a little bit. I think part of what he
21 was getting at is, for instance -- I mean, you can look at other
22 populations, but if you have somebody who gets the vaccine and it
23 protects them maybe not from infection, but -- I mean, if we're
24 focusing on infection, we may be okay -- but if they could become
25 infected but never get AIDS, for instance, but then they could

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1 pass that along to other people -- in other words, you'd have the
2 situation of people with hepatitis-B carriage where you could
3 still be transmitting the virus to other people, but be protected
4 yourself against disease, and that was, I think, part of the
5 intent of that question, is would we really want a vaccine where
6 what was happening was people would never essentially be infected
7 themselves, but be able to pass it along to other people?

8 DR. LaFORCE: I would submit that that's an
9 unanswerable question because we really don't have an example of
10 this -- I really have a hard time answering that question. If
11 that's a theoretical possibility that you have enough cytotoxic
12 T-cells to actually keep the disease in abeyance, yet not enough
13 to eradicate the last retrovirus and you can then still spread
14 it, that's a whole series of presumptions.

15 In point of fact, if you've got the disease under
16 control, that means your viral load has got to be less than what,
17 10^3 ? It's got to be somewhere around 10^3 , if you've got it under
18 control. What is the transmission rates at viral loads less than
19 10^3 , it's quite low. It's almost nonexistent. You don't really
20 get good transmission amongst people until you get viral load
21 somewhere around 10^4 , 10^5 -- certainly 10^4 , 10^5 .

22 COL. WITHERS: Dr. LaForce, even if you don't like
23 the practicality of the question, that's what they asked.

24 DR. LaFORCE: We're going to have to answer it?

25 COL. WITHERS: My advice is to answer it and then

1 say that it's an unlikely scenario, but my strong advice is to
2 answer the questions that were asked.

3 COL. BRADSHAW: It may be obviated if we were
4 saying that we would prefer it to be prevent infection, and if
5 you say that, then I think we're okay. It answers the second
6 question.

7 COL. WITHERS: The info papers from the
8 investigators pointed out that two of the questions were probably
9 irrelevant or overcome by truth. There was another question, I
10 forget what it was, but two of the questions, the info paper that
11 RIID wrote up point out that two of the questions were really not
12 practical, but I would answer them anyway.

13 DR. LaFORCE: Got it.

14 DR. HERBOLD: Marc, I think this has been stated
15 already, but if this is what the Board means, it might be
16 appropriate to start off the answer to this particular question
17 with something like "The AFEB believes that the DoD vaccine
18 development effort should be focused primarily on a vaccine that
19 prevents infection", and then that sets the stage. And then if
20 you want to go on to talk about the rest of it, you can.

21 DR. LaFORCE: Got it.

22 DR. SHANAHAN: I think if it doesn't, also you get
23 back to the initial question, which is, what's the military
24 relevance if it doesn't prevent infection?

25 DR. LaFORCE: Bill, would you read your answer?

1 DR. BERG: Marc assigned me to draft an answer, so
2 here's what I wrote, and it's really two questions in (c).

3 The answer to the first one: "The Board strongly
4 recommends that the primary purpose of an HI vaccine should be to
5 prevent infection, i.e., to prevent transmission of HIV to the
6 vaccine recipient. A vaccine that prevents or reduces HIV
7 disease progression without also preventing infection at a
8 minimal or greater level should not be acceptable."

9 In other words, if it has an effect on AIDS but
10 doesn't prevent infection, we're not interested in it.

11 "No HI vaccine currently available or under
12 development will be 100 percent effective in preventing
13 infection. Individuals who become infected due to vaccine
14 failure will also become "carriers". This fact should not be a
15 deterrent in selecting a vaccine. It is likely, but not assured,
16 that even a vaccine failure will nevertheless reduce the amount
17 of HIV in an individual. This should reduce the probability that
18 the vaccinated but still infected individual will transmit HIV to
19 others."

20 And then the proposed answer to the second
21 question is: "The Board strongly recommends that an HIV vaccine
22 be administered to at-risk military personnel" -- and I'm not
23 defining "at risk" -- "even if the vaccine only reduces the
24 probability of becoming infected rather than eliminates it.
25 Because the vaccine will not be 100 percent effective in

1 preventing infection, all preventive measures currently in use
2 should continue to be used."

3 DR. LaFORCE: Yes, Jeff.

4 CAPT. YUND: That last sentence --

5 DR. LaFORCE: Love it.

6 CAPT. YUND: -- it is a good sentence, and it's
7 easy to say and it's easy to put -- it's easy to put in a
8 directive, but it depends on the compliance of the sailor,
9 soldier, Marine, and airman, and I think that there's at least
10 the theoretical possibility that a vaccine that does not have
11 very, very high efficacy could actually increase the number of
12 cases in your population, if people decide that, okay, I've got
13 this great vaccine now, I don't have to worry about catching HIV.

14 DR. ALEXANDER: They still have to worry about
15 STDs.

16 CAPT. YUND: Absolutely, but --

17 DR. BERG: The reason I put that sentence in,
18 because I didn't want people to say, oh, we've got a vaccine, we
19 don't need to promote condoms and so on. And this is a variant on
20 an argument that I get all the time as a Health Director -- if
21 you pass out condoms to teenagers, they'll just go out and screw.

22 So, you're right, we've got to do education, and I think a key
23 to it is saying the vaccine is not 100-percent guaranteed.

24 DR. LaFORCE: Well, fortunately, as Linda points
25 out, there's still chlamydia and there's still Neisseria

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1 gonorrhea, so that continued use of condoms is a pretty good
2 idea.

3 CAPT. YUND: Oh, absolutely, I agree with that.
4 I'm just saying that the young, invulnerable person on active
5 duty may not necessarily take all of the rational precautions,
6 and may make an irrational conclusion from this additional
7 special protection that he's just been given.

8 DR. LaFORCE: But that's why he needs to be
9 protected.

10 COL. BRADSHAW: Actually, there's already some
11 evidence of this. I think there was a report recently about
12 increasing or lack of compliance with condom use among certain
13 at-risk populations because -- which seems to be linked to the
14 availability of antiretroviral drugs, and that's been a recent
15 finding.

16 DR. LaFORCE: That's the San Francisco thing,
17 yeah. Okay. Keep going, you're on a role, Bill.

18 DR. BERG: That was it.

19 DR. LaFORCE: That's all?

20 DR. BERG: You gave me question (c).

21 (Simultaneous discussion.)

22 DR. LaFORCE: Geez, I made a bad decision
23 yesterday when I didn't give him more homework.

24 (Laughter)

25 DR. LaFORCE: The Chairman really acted

1 irrationally.

2 DR. SHANAHAN: You were tired.

3 DR. LaFORCE: It shows, I am getting tired right
4 now, too.

5 "How should DoD deal with the status of vaccinated
6 versus the effect of DoD deployability, assignment, and other
7 personnel actions?" I think we discussed that pretty clearly
8 yesterday, that the DoD already has its rules about deployment,
9 but that it was very important that whatever vaccine was used,
10 that there had to be a way of being able to sort out positivity
11 either on the basis of vaccine or disease.

12 COL. WITHERS: That was the other point that is of
13 impractical importance. I mean, it's not a practical problem,
14 but -- it's a good question, but it's not a practical one. It's
15 not a problematic one.

16 DR. LaFORCE: And then (e) "Is inability to
17 discern between vaccinated and infected prior to onset of
18 clinical illness an accepted outcome of vaccine use?" I think
19 all of us said no, it's not an acceptable outcome, and it had to
20 be one of -- apparently, when we looked at -- what did they call
21 those criteria?

22 DR. BERG: Key performance parameters.

23 DR. LaFORCE: Yes, the key performance parameters.
24 There were only two that really interested the Board. One was
25 this issue, the ability to discern serologic positivity on the

1 basis of vaccination versus infection with HIV, and the second
2 was FDA approval. We haven't changed that, have we?

3 DR. BERG: The first two were this one, and then
4 that it has to prevent infection.

5 DR. LaFORCE: No. We decided that that was too
6 sort of confusing because it subsumed some sort of definition of
7 efficacy. And so what we ended up was the key criteria was FDA
8 approval because the FDA is actually going to look at all of
9 those issues also and, two, the ability to discern being infected
10 versus being vaccinated.

11 "In what subpopulation of DoD would an HIV vaccine
12 be considered for use? How does this vary with the performance
13 characteristics of the vaccine -- effectiveness, sterilization,
14 markers of immunity?"

15 DR. SHOPE: I wrote a response to that.

16 DR. LaFORCE: Oh, you did, fine. Go to it. Oh,
17 yes, that's right, and I gave it back to you, didn't I?

18 DR. SHOPE: Yes. What I wrote -- this is three
19 sentences. "An HIV vaccine designed to prevent infection should
20 be used in military personnel who are at increased risk of HIV
21 infection and who volunteer to receive it. These personnel
22 include those exposed to blood and blood products, and those
23 deployed to high HIV prevalence areas of Asia, Africa, and South
24 and Central America. Assuming the vaccine prevents infection,
25 the subpopulation to be vaccinated will not vary with vaccine

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1 effectiveness or markers of immunity."

2 One issue that I'm not sure of is whether people
3 agreed about the volunteer aspect.

4 COL. DINIEGA: Take it out.

5 DR. LaFORCE: It needs to be discussed.

6 DR. SHOPE: Take it out?

7 COL. BRADSHAW: I'm not so sure. I mean, I'm
8 pretty much --

9 DR. LaFORCE: That's why it's open for discussion.

10 COL. BRADSHAW: I'm pretty much a believer in the
11 need for, in the military, particularly to protect the mission,
12 mandatory vaccination. It's like seat belt laws and a lot of
13 other things. But in this case, we're not talking about a
14 vaccine that in the acuity of the situation of somebody becoming
15 infected with HIV, that that's going to affect our mission. It
16 may affect our bill down the road for disability and, you know,
17 things that are linked, you know, to service in the military or
18 whatever, and maybe losing those people and having to replace
19 them, but -- and there may be other implications of that, and
20 perhaps maybe for certain personnel, maybe hospital personnel, we
21 may want to consider it as a condition of employment, but I don't
22 know if it should be a mandatory vaccine in the sense that we do
23 a lot of other things. I mean, this might be one of the few that
24 I would think that a voluntary vaccine might make sense.

25 -

1 DR. LaFORCE: I wonder if I could pose the
2 question back to you, Dana. Let's say that the studies are
3 highly successful and show a vaccine efficacy of 95 percent, for
4 the sake of argument. So, you have an HIV vaccine, 95 percent
5 efficacy, and let's say it takes two doses -- two doses of an
6 antigen, 95 percent protection for HIV. Boy, I would have a hard
7 time thinking of that as an antigen that you would volunteer --

8 COL. BRADSHAW: That's true, but that's not what's
9 on the table.

10 DR. LaFORCE: You have it now for hepatitis-B.

11 COL. BRADSHAW: Well, what I would also say in
12 that situation is that somebody who chooses to waive that would
13 also waive their rights to compensation for it. I mean, there
14 would be ways, I think, to address that.

15 DR. LaFORCE: How much do you want to bet that --

16 COL. BRADSHAW: I don't know. I mean, it's things
17 to consider.

18 DR. LaFORCE: But the idea of -- I really would
19 like to hear from either -- both Bens in terms of the idea of
20 volunteer.

21 COL. WITHERS: Well, let me say that the Army and
22 the Navy agree with Dana.

23 DR. LaFORCE: Pardon me?

24 COL. WITHERS: The Army and the Navy agree with
25 the Air Force.

1 DR. LaFORCE: Okay.

2 COL. ENGLER: I just want to reinforce the
3 clinical front lines that considering already the discussions
4 that have gone on about acceptability of HIV vaccine by numerous
5 people, this would be a very hard-sell, and we can't afford a lot
6 of things that drive people into the decision, I'm going to get
7 out of the Reserves because I don't want this vaccine, and that's
8 the risk you take. I mean, I'd like to know, and a lot of people
9 would ask us, "Well, what's the data about Peace Corps workers or
10 whoever, you know, working in Africa and those areas that they
11 actually, if they don't engage in high-risk activity, have
12 contracted HIV disease?"

13 DR. LaFORCE: There are hundreds of Europeans --
14 hundreds of Europeans -- you talk to any Belgian --

15 COL. ENGLER: And they opportunity to access post-
16 exposure prophylaxis? I mean, there's --

17 DR. LaFORCE: Oh, yeah. Well, post-exposure
18 prophylaxis, for what it's worth --

19 COL. ENGLER: -- they had a needle stick or
20 something.

21 DR. LaFORCE: Yeah. I mean, there are hundreds of
22 cases of Europeans that have unsafe sexual activity and --

23 COL. ENGLER: No, but that's what I'm saying. If
24 somebody says, "I'm going to go" -- I can tell you a lot of
25 medical people would say, "Well, I'm not going to engage in

1 unsafe sex, and I'm not going to do those things, so why are you
2 forcing me to get a vaccine?" That's what we're going to face at
3 the clinical front lines.

4 DR. OSTROFF: We screen all Peace Corps workers
5 when CDC does the testing, so we have all the data about
6 seroconversions in Peace Corps workers.

7 COL. ENGLER: I understand, but, again, you know,
8 data to say that they haven't engaged in high-risk activity --

9 DR. ATKINS: Oh, they have.

10 COL. ENGLER: Well, that's what I'm saying. So if
11 someone says, "Why should you force me to get a vaccine if I'm
12 not going to do that", that's what they're going to face.

13 DR. LaFORCE: Yes, Linda.

14 DR. ALEXANDER: Marc, actually two comments.
15 First, I think the volunteer concept is important, but I'm a
16 little concerned because of, frankly, the homophobia that exists
17 in the military environment. I'm afraid that if it's not
18 properly positioned, and we may inadvertently put people who
19 might want the vaccine by virtue of their lifestyle or whatever,
20 who don't do it because it may be perceived as an admission of a
21 particular lifestyle, so that concerns me. So, framing the
22 opportunity for volunteering within the context of all high-risk
23 exposure I think is imperative.

24 And just a reply to your comment about HIV endemic
25 areas, I think the period could go there as opposed to

1 identifying the areas because, for instance, if we limit it to
2 the areas you've defined -- for instance, if we suddenly have a
3 deployment to Haiti and Haiti's not on your list, then that might
4 create --

5 DR. SHOPE: Well, actually, I intended the
6 Caribbean to be on the list.

7 DR. ALEXANDER: But if we just say HIV endemic
8 areas, then we don't have to get into geographical
9 specifications.

10 DR. SHOPE: Is that satisfactory to everybody?

11 COL. BRADSHAW: Another thing I would add to the
12 list is those who have had a prior history of sexually-
13 transmitted disease, or you can have a list of things that would
14 be reasonable. I mean, the way we did this hepatitis-C was we
15 simply had a list of things for which you might be at-risk so
16 that if you -- and several of those were things like you had a
17 transfusion -- and you didn't have to pick which one of those you
18 were -- because the other things were like IV drug abusers -- so
19 all you had was this list of things and say "Would you like to
20 have this? Do you think you might be at-risk based on this
21 list?" And then people could say, "Yes, I'd like to have the
22 screening", or in this case the vaccine. So, if you are
23 volunteering, you wouldn't have to identify that you were
24 homosexual or that you had multiple sexual partners, but if those
25 things were on the list -- but in other cases, if you came in the

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1 clinic with an STV, then the provider should be offering you the
2 vaccine.

3 DR. LaFORCE: This is an important point. Yes.

4 DR. SHANAHAN: I'd just like to add, there is
5 another way of approaching this -- and I don't necessarily
6 advocate it -- but you can always stratify people by risk based
7 upon occupation as opposed to anything more social.

8 COL. BRADSHAW: And age.

9 DR. ALEXANDER: What did we find with the DoD data
10 about food service workers and medics and the Chaplain Assistant?

11 DR. MOORE: And male urology attendants, medics.

12 DR. ALEXANDER: There's the list, you have to be
13 really careful when we use it.

14 DR. LaFORCE: Would that be -- Ben?

15 COL. DINIEGA: Well, I have a little problem with
16 making it voluntary, and I speak as an individual. No. 1 is if
17 it's a militarily relevant disease and we're concerned about the
18 500-plus cases we have a year, and we're going through a military
19 development process, I don't understand how we can say that it's
20 only going to be offered on a voluntary basis, because there are
21 some instances where it shouldn't be voluntary. If they have
22 repeated sexual diseases, you know, it shouldn't be voluntary.
23 If they are going to go to a high-risk area and they have risky
24 sexual behaviors, it shouldn't be voluntary. That's one point.

25 The other point I want to make is that -- Andrew

1 is not here -- but the anthrax vaccination program, when it was
2 up and running in -- oh, he's here. You tell us what the
3 accepted -- it's voluntary.

4 COL. WARDE: The acceptance rate in the anthrax
5 vaccination program -- I don't think it's a fair comparison at
6 all because, I mean, the stigma surrounding anthrax vaccination
7 as a Gulf War illness and all these other things colored that
8 situation. But if you want the U.K. perspective is, in no way in
9 which a vaccine like this would ever be made mandatory in the
10 U.K. There's not the slightest hope of that.

11 DR. LaFORCE: What's the fraction that accept
12 anthrax vaccine?

13 COL. WARDE: The overall fraction of those offered
14 it when the vaccine program was running was just over 30 percent.

15 DR. LaFORCE: Thirty?

16 COL. WARDE: Thirty, and that was the overall. I
17 mean, there were units that were near 100 percent and there were
18 units with nearly zero. But that I think is a red herring as a
19 question because there's going to be different sets of
20 circumstances. There's a big difference between anthrax and HIV.

21 COL. BRADSHAW: I still think the critical issue
22 for me -- and we do religious waivers based on this -- is the
23 mission criticality of it. And with anthrax, clearly, if you had
24 your people exposed in the field, and you've got a case fatality
25 rate exceeding 90 percent, the effect on the mission of that, to

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1 me, is a clearcut case for making it mandatory, especially if you
2 only have 30 percent compliance with a voluntary vaccine.

3 DR. LaFORCE: Yes, John?

4 DR. HERBOLD: Not to speak to whether I'm in favor
5 or not in favor of a voluntary statement, but I would suggest
6 that it's not necessary to include that phrase at this point in
7 time in our response to the services. Whether it's going to be
8 used in a voluntary or nonvoluntary setting is not what we were
9 asked. So, to get back to the twin Bens point, answer the
10 question, we can answer the question without including that
11 phrase.

12 DR. LaFORCE: I won't do that, though, I think, as
13 President, without general agreement on the part of the Board
14 because this has really sort of come up as a -- I mean, how would
15 people -- you know, one way out of it is not mentioning it. Yes,
16 Ken?

17 CAPT. SCHOR: You know, in the same light, I would
18 caution against just feeling that when you say that yes, HIV is a
19 militarily relevant disease, that you've really answered a
20 question. How does it rack-and-stack against all of the other
21 militarily relevant diseases when you're making purchasing
22 decisions?

23 DR. HERBOLD: That's a different question, and
24 Bill Berg and I discussed that a little bit offline here because
25 we probably have different opinions as to where HIV would end up

1 in the rack-and-stack, but I think we both agree that HIV should
2 be in the discussion, that it is not -- I can use a double-
3 negative -- it is not a not-militarily-relevant question. HIV,
4 as a disease potential, has a military relevance, and then we
5 also know that the use of that term has considerable -- bears
6 considerable weight as to whether that particular agent is
7 involved in military medical R&D. So, if we don't think -- if
8 we, as a Board, don't think it's a militarily relevant agent,
9 then we ought to argue about that.

10 CAPT. SCHOR: See, that's used as a defensive
11 shield to protect in other settings and probably some other
12 diseases to protect ricebowls where there are more critical --

13 DR. HERBOLD: Well, Charlie Hoch probably doesn't
14 believe it is, I don't know.

15 DR. BERG: I think we're trying to have our cake
16 and eat it, too, here, you know. On the one hand, we're arguing
17 for the vaccine because we're going to send troops into Africa,
18 they're going to be highly at risk, and then we turn around and
19 say it's voluntary. And the question is going to come up from
20 some poor, confused line officer or battalion surgeon, "Okay, if
21 it's voluntary and they choose not to get it, does that mean they
22 are not deployable?" So, I think if we say it's voluntary, we
23 ought to consider putting in a statement to the effect that
24 "failure to accept the vaccine does not mean an individual is not
25 deployable".

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1 DR. HERBOLD: The other statement I would make is
2 that including that phrase is going to open up more discussions
3 than just answering the HIV question. You know, that is a
4 significant issue that I think needs to be discussed because,
5 from a herd health perspective, I would argue that somebody could
6 probably do a study and show that you might be able to use
7 vaccinations in an informed, voluntary consent setting and reach
8 your herd health objectives, but that's a different question.
9 So, I'm not so sure the voluntary-nonvoluntary military thing is
10 all that clearcut, and that just by insisting on including that
11 draft phrase in there might have more impact that we understand
12 at this point in time.

13 COL. DINIEGA: Normally, DoD will follow all ACIP
14 recommendations, and Academy of Pediatrics. If there is a unique
15 military application, then the question comes usually to the
16 Board, like Lime Disease. You know, Lime vaccine was a nonissue
17 until somebody said, "Hey, should we be using it in a special way
18 for active duty troops", so the question came to the Board. The
19 decision of the Board was, there's no unique military
20 application, we'll follow CDC's and ACIP's recommendations.

21 But what we're saying here is, if you're going to
22 go voluntary -- I was telling Linda -- we may as well just say
23 we'll wait and see what ACIP recommends.

24 DR. SHANAHAN: Well, you know, also, the question
25 of specifically what subpopulations of the DoD would we

1 recommend receive that, most of the discussion seems to be
2 couched around the assumption that all or all deployed. Maybe we
3 should look at subpopulation, too, and see how we're going to
4 answer that question specifically.

5 DR. LaFORCE: Yes?

6 MAJ. BALOUGH: Knowing the problems that we've had
7 with the anthrax, any vaccine that we develop is going to go
8 under a lot of scrutiny, and if we're making a -- you know, on
9 one hand we're recommending that a 65-percent effectiveness is
10 okay and we're going to make it mandatory, that goes in front of
11 Congress. I think we're going to be shooting ourselves in the
12 foot -- in both feet -- and we've got to look at the entire
13 package. If you want to make something mandatory, then I think
14 it's going to have to pass more than a 65-percent reasonable
15 effectiveness, and I think we've got to kind of look at that.

16 And the other thing that -- I know this wasn't
17 asked, but based on some of the other discussions I've had with
18 other vaccines -- does the Board want to take the initiative and
19 make recommendations that when they go ahead an license the
20 vaccine -- say, it would be licensed for pre-exposure -- but what
21 about precluding the requirement for a post-exposure? Do you
22 want to go out and say, "Hey, also license it for after somebody
23 has been exposed to be able to get the shots before the disease
24 shows up". I just throw that out as something to consider.

25 DR. LaFORCE: Yes?

1 DR. PATRICK: Could I ask a point of
2 clarification? I lost a little bit of track of the statement
3 because we've been talking a lot about the voluntary, but I
4 thought we were talking about mandatory to those going to these
5 high-risk areas.

6 DR. SHOPE: No. That was not --

7 DR. PATRICK: Could you read that sentence again?

8 DR. SHOPE: "An HIV vaccine designed to prevent
9 infection should be used in military personnel who are at
10 increased risk of HIV infection and who volunteer to receive it."
11 That's the first sentence.

12 "These personnel include those exposed to blood
13 and blood products, those with STDS, and those deployed to high
14 HIV prevalence areas."

15 COL. DINIEGA: Can I suggest that instead of
16 putting the voluntary stuff, just don't put anything in, and
17 don't put anything about mandatory. "A vaccine should be
18 considered for use in" --blah, blah, blah -- and final decision
19 is going to be made when we know what the vaccine can do.

20 DR. SHOPE: We need concurrence by the whole
21 group.

22 DR. MOORE: That's what I meant by having a two-
23 level decision on this because I think what you would recommend
24 would depend on the effectiveness of the vaccine at the time it
25 was available to be utilized.

1 DR. ALEXANDER: And the military requirements at
2 that time. I mean, we have a large presence in endemic areas,
3 that's going to influence the decisionmaking. So, just don't go
4 there now.

5 COL. DINIEGA: Don't put in "voluntary" and don't
6 put in "mandatory".

7 CAPT. YUND: Specific wording of the question
8 doesn't refer to voluntary versus mandatory, does it?

9 DR. LaFORCE: No, it doesn't, Jeff.

10 CAPT. YUND: This refers to subgroups of the
11 population.

12 DR. LaFORCE: This is why this is so important.

13 DR. SHOPE: Unless you consider that a
14 subpopulation. I'm willing to leave it out.

15 DR. LaFORCE: Yes. Why don't we leave it out.
16 We'll circulate it and, if there's anymore feedback, we could
17 certainly circulate two versions, if you wish, but I think the
18 idea of leaving it unsaid doesn't preclude it from happening.
19 We're not precluding anything.

20 DR. ALEXANDER: It's just premature.

21 DR. LaFORCE: We're just simply not stating
22 anything, that's all.

23 DR. SHOPE: Is San Francisco considered an endemic
24 area?

25 (Laughter)

1 DR. LaFORCE: Oh, gee, I'm not going there.

2 COL. DINIEGA: I thought Hampton was.

3 DR. ALEXANDER: We've heard about Hampton.

4 (Simultaneous discussion.)

5 COL. BRADSHAW: Actually, the military HIV rates
6 are higher in areas where it is "endemic", so D.C. and San
7 Francisco areas, they're higher. I mean, they're not still lower
8 than most of the population, but --

9 DR. SHOPE: Personnel there are not under
10 deployment, are they?

11 COL. BRADSHAW: I'm sorry?

12 DR. SHOPE: Personnel in San Francisco are not
13 being deployed.

14 COL. BRADSHAW: No. I was just saying that if you
15 look at military HIV rates, they tend to reflect the local rates
16 where people are assigned.

17 DR. LaFORCE: See, this is why my argument
18 yesterday, if they reflect the local rates and there's any
19 deployment that's in these areas where carrier rates or HIV
20 prevalence rates are in the 20-30 percent range, that's a real
21 risk. That's a real risk. Okay.

22 DR. MOORE: Another issue, Marc. As I read (e)
23 last night, one of the things that occurred to me is if this
24 turns out to be a successful vaccine and it is used in other than
25 Department of Defense, then our screen recruits to come on active

1 duty might be impacted if we can't tell between natural infection
2 and vaccine-induced immunity.

3 DR. LaFORCE: Okay. And that's why one of the
4 criteria is to be able to do that. Good point. Okay.

5 Our final task apparently is to -- oh, yeah,
6 Vaccines to Protect Against BW Warfare Threats. This is a
7 summary of this morning's presentations, right? I actually
8 didn't see very much change over last year. Has there been any
9 change in terms of the vaccine development?

10 COL. DINIEGA: I think the -- what was added --
11 the new generation anthrax was added --

12 LtCOL. BOROWSKY: Loss of a Q-Fever.

13 COL. DINIEGA: You know, just on first look, the
14 smallpox seems to have been accelerated, am I right or wrong?

15 LtCOL. BOROWSKY: It's moving pretty nicely.

16 COL. DINIEGA: I know -- Steve's gone. Is Steve
17 gone?

18 DR. LaFORCE: Yes, Steve got an early flight.

19 COL. DINIEGA: I know the CDC is moving on their
20 smallpox initiatives.

21 Lt.COL. BOROWSKY: I was at CDC a month or so ago.
22 Yes, they are --

23 COL. DINIEGA: It just seemed to me it was
24 accelerated, but I wasn't too sure if they had moved up the --

25 LtCOL. BOROWSKY: But there's also interest in

1 antivirals for pox viruses, too. That came out at a CDC meeting.

2 So, there's two parallel --

3 DR. LaFORCE: One chemoprophylactic and then one
4 vaccine-related. My take on it is that it was pretty much a
5 revisit of last year. It seemed as though things were on track.

6 The smallpox vaccine, if it's accelerated, that's good news.

7 DR. BERG: I have a question, but there may not be
8 anyone here to answer it because this is a question about Col.
9 Danley's presentation.

10 LtCOL. BOROWSKY: I'll try.

11 DR. BERG: The JVAP schedule that he has here,
12 what does BLS stand for?

13 LtCOL. BOROWSKY: Biologic License Application.

14 DR. BERG: Okay. And FDA approval is the far
15 right diamond?

16 COL. DINIEGA: If that's the key. I mean, the key
17 is on the bottom.

18 DR. BERG: It doesn't say when --

19 COL. DINIEGA: I mean, it says BLA is when they
20 apply for the license.

21 LtCOL. BOROWSKY: Yes, BLA submission, and then
22 whatever the last one would be is when they would expect FDA --
23 which is usually a year.

24 DR. BERG: So that's a year after. So that far
25 right diamond is when they anticipate FDA approval.

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1 LtCOL. BOROWSKY: Right. So they submit it, and
2 normally without an accelerated process, it's about a year.

3 DR. LaFORCE: The question before the Board is
4 essentially endorsing the JVAP program, and whether there are any
5 changes. One of the issues that concerned the Board a year ago
6 had to do with staphylococcal enterotoxin B vaccine development
7 because I remember there was a concern from the Board standpoint
8 when we looked at vaccine development, this was an area that had
9 made the list in terms of an important biologic warfare threat,
10 and it didn't seem as though there was very much activity along
11 the lines of staphylococcal enterotoxin B, and I didn't hear
12 anything today. Did I miss it?

13 COL. DINIEGA: No. Carol Linden said it's in Tech
14 Base and it's a very active program. And it's on the JVAP
15 products, page 12, and I thought it was on the milestone --

16 LtCOL. BOROWSKY: Part of the controversy with SEB
17 has been that in the Tech Base there has been some who just waive
18 it off as just an incapacitant, but there are others who come by
19 and say, wait a minute, it's just as lethal as anything else.
20 So, some of the efforts in research have fizzled a little bit
21 because people didn't think it was as important in terms of
22 lethality, and there are others who disagree with that.

23 DR. MOORE: Well, in aerosol form, it is important
24 in lethality.

25 DR. BERG: I would like to suggest that the Board

1 may want to consider putting a statement in just sort of
2 reminding people that the Board considers this an important
3 agent, and that production on this vaccine should continue
4 because it tends to sort of keep getting shoved to the back
5 burner, and then somebody asks and, oh, yeah, we're working on
6 it, and then a year later it's "we're working on it", and a year
7 later it's "we're working on it". So, I don't think it would
8 hurt to just remind people that the Board considers this a very
9 important vaccine.

10 DR. LaFORCE: What we may do -- one way of really
11 stimulating it is to make a request that there be a presentation
12 on status of that particular antigen. I mean, the Board always
13 can do that, and if you wish -- I mean, that's one way of really
14 getting buffed up and getting a presentation that sort of looks
15 at it. I don't think that's such a bad idea, honestly.

16 I know that this concerned Dennis Perrotta
17 (phonetic), and I'm not as sort of up-to-date on this as perhaps
18 I should be, but Dennis was concerned about it, that it had
19 slipped in terms of, you know, a little bit off the radar screen,
20 and that was of concern to him because I remember when we
21 transferred, he had that on one of his lists, he said, to sort of
22 pay attention to that.

23 COL. DINIEGA: On the JVAP schedule, page 13, it's
24 on the timeline chart.

25 DR. LaFORCE: Did I miss it? Yes. Okay, fine.

1 We'll include general relief on the part of AFEB in terms of --

2 COL. DINIEGA: On the page before that, Marc, on
3 page 12, it says it's in the Tech Base, but they have it on the
4 milestone to be developed and coming out of the Tech Base.

5 DR. LaFORCE: And has that milestone been reached?

6 COL. DINIEGA: Well, it's FY02 is when they hope
7 to get it out of the Tech Base.

8 DR. BERG: What does being in the Tech Base mean?

9
10 COL. DINIEGA: Not ready to transition, that's
11 what they're saying.

12 DR. BERG: I think it wouldn't hurt to ask them to
13 do a presentation on it.

14 DR. LaFORCE: We'll discuss with Col. Riddle and
15 we'll get that done. Okay. I will prepare a response and will
16 circulate it to Board members, Rick and I, in terms of -- and
17 that's the last sort of official task as far as the Board is
18 concerned.

19 (Whereupon, the proceedings went into Executive
20 Session.)

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E-X-E-C-U-T-I-V-E S-E-S-S-I-O-N

(2:20 p.m.)

DR. LaFORCE: I need some feedback from Board members in terms of the subcommittees. I realize that this meeting that we usually have here is almost exclusively vaccine-related because it's the update in terms of the biologic threats, et cetera, and we've got to make sure that we sort of look at committee structure on the basis of the other tasks that we've got as far as the committee is concerned. Who is actually on the Vaccine Committee that we have right now? It's Pierce --

COL. DINIEGA: You mean the Disease Control Subcommittee?

DR. LaFORCE: Yes, the Disease Control Committee is -- Steve is the Chair of that, Pierce -- do we have a list -- Bill Berg, Bill Moore, and Bob Shope, and that's it, right?

DR. SHOPE: What committee is that?

DR. LaFORCE: This is Disease Control Committee.

DR. BERG: Three of us on it?

DR. LaFORCE: Then for Health Promotion, we have Linda Alexander and David Atkins. Elizabeth Barrett-Connor is going off the committee -- next meeting will be her last meeting. Who is rotating off? Julian, this is your last meeting? It's not. You can't, Julian, you have to stay.

All right. Elizabeth Barrett-Connor, Julian and Rosie Sokas. So, actually, that's going to be a fundamental

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1 hemorrhage of that group.

2 COL. DINIEGA: Was that Health Promotion?

3 DR. LaFORCE: I think that's Health Promotion.

4 COL. DINIEGA: I thought Rosie was on Occupational
5 and Environmental Health.

6 DR. LaFORCE: Julian, what group were you part of?

7 DR. HAYWOOD: The same with Barrett-Connor and
8 Atkins.

9 DR. LaFORCE: Okay, so you were Health Promotion.

10 LtCOL. RIDDLE: So we need one nomination on
11 Environmental and Occupational Health, and two nominations for
12 Health Maintenance and Promotion.

13 DR. LaFORCE: Okay. Two nominations for Health
14 Maintenance and Promotion, and one nomination for Environmental
15 and Occupational Health. Do we have those nominations now?

16 LtCOL. RIDDLE: I did get one nomination from Dr.
17 Sokas as a replacement for her in NIOSH. And it was that PM
18 Officers submit some nominations of Board members, and then we'll
19 probably go to the Schools of Medicine and Public Health to build
20 the nomination pool.

21 DR. LaFORCE: Okay. So how many are transitioning
22 off? We have three members that are transitioning off, and those
23 three members -- and of those three members, we have one name
24 that we're actually going through the process right now?

25 LtCOL. RIDDLE: No, that's just been nominated.

1 DR. LaFORCE: Oh, that's just been nominated. So,
2 the Board actually is in need of several nominees.

3 LtCOL. RIDDLE: Yes.

4 DR. ALEXANDER: I plead ignorance on this. Could
5 we just clarify for our discussion purposes what the term of
6 commitment is, whether or not there is eligibility for renewal,
7 and how the decisions are made about accepting members?

8 LtCOL. RIDDLE: For a Federal Advisory Committee,
9 you are appointed for a two-year term, and you can have a
10 reappointment for another consecutive two-year term. You can
11 only serve four years, and then you must have a two-year break in
12 service before you can be renominated. Any individual can only
13 serve on one Federal Advisory Committee at a time.

14 For the selection process, individuals are
15 nominated to be members of the Board, those nominations are
16 reviewed by the representatives of the Surgeons General and
17 Health Affairs from a pool of nominees, and they are then
18 endorsed by each of the three Surgeons General to the ASDHA, and
19 from the ASDHA, they are endorsed to Army Committee Management in
20 which they undergo the ethics review, the financial disclosure,
21 conflict of interest, and as long as they pass that hurdle then
22 they receive appointment by Army Committee Management.

23 DR. ALEXANDER: So the Board itself really does
24 not make decisions about new Board members.

25 LtCOL. RIDDLE: No, the Board itself makes

1 decisions about subcommittee chairs and president.

2 DR. LaFORCE: But the Board Committee can
3 influence these things in terms of saying, look, if you've got a
4 candidate that you feel is particularly -- I mean, we don't have
5 any problems just sort of calling around and actually saying, gee
6 -- I would say one thing.

7 Greg Poland, who has been a very strong supporter
8 of AFEB and was on AFEB, rotated off a couple of years ago, and I
9 believe is eligible for reappointment, as I recall, this
10 September, and so he would be an individual that I think would be
11 an excellent investment on the part of the Board. I mean, he
12 worked very, very well and actually authored the big vaccine
13 documents. And so he -- I talked to Greg and he's very
14 interested in being invited to sort of look back at Board
15 membership. But we need some help from all of you in terms of
16 other candidates.

17 DR. ALEXANDER: One thought that I think we've
18 expressed before is that the diversity on the Board is an
19 important consideration, and to be perfectly blunt, this is very
20 white, very male, and particularly when one considers the outside
21 skirt being sort of the public domain that we represent, that
22 probably is an image that we could improve.

23 LtCOL. RIDDLE: Yes, that's actually looked at.
24 We have to report on an annual basis the Board diversity. Not
25 only does the Board need to be diverse, as far as gender and

1 ethnic, but also if you look at independence of the Board from
2 the Institution itself, I think we currently have on the Board
3 six retired military individuals, and we had, with Dr. Sokas,
4 three Federal employees, which is a little bit unusual.

5 I don't think very many of the Federal Advisory
6 Committees within DoD have very many Federal employees. They do
7 have a mix of retired military or nonmilitary. There are no
8 restrictions. You can have an active duty military officer, you
9 can have a Federal employee, or you can have any civilian as
10 appointment to the Committee. We become even more white male
11 with Dr. Sokas' departure. You will be the only female on the
12 Board, and then all of the new appointees that we have are a mix
13 --

14 DR. LaFORCE: That's right, Barrett-Connor is
15 going, too.

16 LtCOL. RIDDLE: -- are white male.

17 COL. DINIEGA: There's one female.

18 LtCOL. RIDDLE: On the new ones coming in?

19 COL. DINIEGA: On the new ones coming in.

20 DR. LaFORCE: Who's coming in?

21 COL. DINIEGA: The last go-round there was Carol -
22 - University of Minnesota -- and Carol Runyan.

23 LtCOL. RIDDLE: We haven't sent those up yet.

24 DR. LaFORCE: Well, let me sort of encourage the
25 Board members that we're looking for two X-chromosomes -- I'm

1 sorry, I shouldn't have said that -- that if there are
2 candidates, that it really would be nice if --

3 LtCOL. RIDDLE: But if the Board members would, if
4 you would talk to an individual, and then if they would just
5 submit their CV, and they can email that to me, and then I can
6 give them an overview of what's required because it's -- I mean,
7 it's a fairly laborious process to go through the financial
8 disclosure, they have to understand that I don't think they are
9 able to have grants or stockholdings in companies that the Board
10 would make recommendations on.

11 It looks like they're going to make the ethics
12 review and the financial disclosure an annual requirement for us.

13 The individuals have to undergo a security investigation, you
14 know, all the paperwork that's involved with an appointment to a
15 Federal Advisory Committee, plus the without compensation and the
16 travel.

17 DR. LaFORCE: I'm not sure I'd describe that to a
18 potential person --

19 DR. ALEXANDER: A lot of hard work for nothing,
20 but you'll have a great time.

21 DR. LaFORCE: And the Preventive Medicine officers
22 usually have been a very good source of candidates, right? No?

23 LtCOL. RIDDLE: Recently, yes. They have been
24 good sources. There are several sitting here that came through
25 military recommendations.

1 LtCOL. RIDDLE: And we have Brad Dubling
2 (phonetic) who has expressed some interest in joining the Board,
3 Greg Gray who is retiring from the military has expressed some
4 interest. So, we've got a few, but if we have a nice pool of
5 nominees, then we can select from that pool based upon the
6 requirements of the Board.

7 DR. BERG: Is there a requirement or an informal
8 requirement that you have to have been retired from the military
9 so many years before you are considered for the Board?

10 LtCOL. RIDDLE: You could have an active duty
11 officer appointed to a Federal Advisory Committee.

12 DR. LaFORCE: So if you could get -- or think
13 about individuals to serve on the Board, but one thing I will
14 say, from my standpoint, it's really important that people come
15 to the meetings, though. The biggest frustration that I have is
16 that all of a sudden people don't show up, then it's really hard
17 to do the work because the subcommittees are relatively small to
18 begin with, and if all of a sudden you have a couple of people
19 and then by chance it's two people on one subcommittee, then you
20 end up with just a couple of people on a subcommittee, then the
21 people on the subcommittee are unhappy and then they complain to
22 me, and I can't do anything about that except really, in the
23 phone calls about individuals who are interested in joining the
24 Board, I think it's really important if people want to give --
25 even if they say "I'm only going to give two years", but two

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1 years, you come to all the meetings and you're really serious
2 about doing the work --

3 DR. ALEXANDER: Along that line, earlier this year
4 you all solicited dates when were available, which was fine. What
5 puts me in a difficult position now, I didn't learn until this
6 meeting -- as in yesterday -- that the fall dates you've
7 selected, so if you select the dates well in advance, we can
8 block them off and save them, or you can ask later and then we
9 can get a group consensus on what's more available, but to ask
10 far in advance and then not advise until late is problematic for
11 those of us who have busy travel schedules.

12 LtCOL. RIDDLE: I selected that date based upon
13 the calendars that were turned in.

14 DR. ALEXANDER: We turned them in, I believe,
15 early in the year, a long time ago. So, January my year looked
16 really wide open.

17 LtCOL. RIDDLE: So if there's any conflicts with
18 that date, let me know.

19 DR. PATRICK: And, actually, the farther out we
20 can go, the better. I mean, my study section goes out a year
21 now. And I think that's fine.

22 DR. LaFORCE: Do you want to block it out a year?
23 Fine, why don't we do that.

24 DR. ALEXANDER: Then you'll get better compliance
25 with the --

1 (Simultaneous discussion.)

2 DR. LaFORCE: Okay. What else do we have?

3 LtCOL. RIDDLE: Well, also, for me, is there any
4 feedback from the Board on how we can better organize the
5 meetings, or provide support? We tried to do the beforehand with
6 the notebooks, the read-aheads. Some members wanted them early.
7 We mailed them out.

8 For most members, we just had them here available
9 to pick up when you checked in. We can do virtually anything, it
10 depends upon getting the information in from those who are going
11 to present. And like the risk document, I would have had the
12 background, but they surprised me with that this morning, that
13 that was being presented to the Board. I had no idea.

14 But anything along those lines, I would
15 appreciate. And I visited with Committee Management, we visited
16 with the lawyers, we're looking at the appointment process,
17 trying to take into account what the requirements are, and
18 streamline that the best we can because it has been very arduous.

19 There's been a big turnover of personnel in that office, so I
20 give a little bit of apologies for them, but we're going to try
21 and stay on top of that and make that easier. It should be two
22 or three months, it shouldn't be nine to 12 months.

23 DR. LaFORCE: The security clearance issue, too.

24 LtCOL. RIDDLE: Well, the security clearance, if
25 you look at the actual directive for Federal Advisory Committees,

1 we should have that before we even nominate you as a member, but
2 we can initiate that as long as I have the paperwork and
3 everything is good to go, as quick as I can submit it, I can
4 request an interim clearance on a Board member. So, once they
5 have been appointed, I have the security paperwork completed, I'm
6 able to garner an interim clearance. Our problem this time was
7 some members I didn't have the paperwork, for six of our members
8 we didn't have the appointments back. So I'm really focusing on
9 that to try to work those issues.

10 DR. LaFORCE: I will say, from my standpoint, that
11 this was an extremely interesting meeting because of all the
12 questions we had and real issues to debate and discuss.

13 And from my standpoint, I've tried to lean on Rick
14 and also in terms of visiting the Surgeons General in terms of
15 saying please ask us specific questions that are sort of rotating
16 through, not to be shy, that we're really anxious to get
17 involved, and I think the meeting over the last couple of days
18 was really pretty exciting and pretty interesting based on the
19 fact that we had lots of specific questions to get into.

20 So, I think that's sort of moving along reasonably
21 well, but it doesn't work without the Preventive Medicine
22 Officers and the interest from your standpoint as well.

23 LtCOL. RIDDLE: A couple of changes. We also have
24 brought a contractor on to help support us, ACS and Lisa. This is
25 the first time that they've been engaged, and they are doing many

1 of the things for us. They are handling the refreshments for us,
2 doing some of our awards and those kinds of things. So that gives
3 us much more flexibility from the running of the Board to do some
4 things. So, any ideas that you have to help -- to improve the
5 Board, let me know.

6 DR. LaFORCE: Other comments or -- okay.
7 Finished.

8 (Whereupon, at 2:35 p.m., the meeting was
9 concluded.)

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