

1 presented with today, as well as in the package within
2 the past few weeks, that make me want to put controls
3 on it.

4 Again, it has been poorly defined, and
5 actually what these things are, both the reagents, as
6 well as the methodologies, and there has been a
7 stunning lack of data.

8 CHAIRMAN WILSON: Dr. Thrupp.

9 DR. THRUPP: But by the same token, I
10 don't think there should be any implication that we
11 would not want adequate guidelines analogously, or any
12 newer likely technique that is going to be distributed
13 for market.

14 DR. GUTMAN: My hope was that a decision
15 on special controls being made when we bring
16 a particular entity to you, a particular device for
17 consideration, and with the data for that particular
18 device as it has been developed and used, and the
19 particular status of the reagent for that device, and
20 all the accessory details.

21 CHAIRMAN WILSON: Dr. Reller.

22 DR. RELER: I think Dr. Beavis brings up
23 an excellent point, and we are talking about those
24 three reagents presented to us before 1976, and if
25 someone later develops a reagent that you can take

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1 gram stain smear from a positive blood culture and do
2 in situ hybernization that says that this is bacillus
3 anthracis, and it possesses factors A and B.

4 And I think that is looked at in a new
5 context later, but w are talking specifically about
6 the current understanding and state of these reagents.

7 CHAIRMAN WILSON: I think those are good
8 points, and I think as a follow-up to that so that
9 members of the public understand, part of the
10 reasoning behind this is not to deal with these
11 reagent devices per se, but it is to establish
12 predicate devices so that future devices have
13 something to be compared against, because currently
14 there is nothing that is approved for this intended
15 use that we can use as a predicate device for a 510(k)
16 submission down the road.

17 And so I don't think it is the intent of
18 the panel to assume that this is state of the art
19 technology, and that we need to deal with this as a
20 stand alone item.

21 This is really part of a larger issue, and
22 that is establishing some sort of precedence early,
23 some of which actually exist.

24 It has been suggested, Barth, that we
25 actually move your motion to the subsequent question

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1 dealing with restrictions. If that is okay, then we
2 will go ahead and move it back there.

3 DR. RELLER: Sure.

4 CHAIRMAN WILSON: All right. Under Issue
5 3 then, there are a variety of options that we can do
6 for special controls. One is post-market
7 surveillance. We can require certain performance
8 standards, testing guidelines, and device tracking.

9 So I would like to know if the members of
10 the panel have any recommendations at this point for
11 that. Dr. Nachamkin.

12 DR. NACHAMKIN: Could you clarify for me
13 performance standards? How does that apply to this
14 class of device?

15 CHAIRMAN WILSON: Ms. Schulman.

16 MS. SCHULMAN: Performance standards, we
17 only have very few for very few devices. There would
18 be a performance standard written for rule making, and
19 I am trying to think of an example of one.

20 DR. GUTMAN: I would require that you know
21 enough about this device that you could say that it
22 would require certain sensitivity or specificity, and
23 to then meet that sensitivity or specificity in a
24 device.

25 So it is very rigorous and labor

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1 intensive, and not very well -- you know, actually,
2 the only standard that I am aware of are those
3 surrounding chemistry tests like cholesterol and the
4 glycosteral hemoglobin, which is a CDC-based standard.

5 DR. NACHAMKIN: The reason I asked, and
6 the thing that I am concerned about, is that we are
7 classifying this group of devices so it can be used
8 for comparison for the future.

9 And as Dr. Ng has mentioned, there is no
10 data on these tests, and we don't know their
11 performance characteristics. So how are we going to
12 judge in the future any 510(k)s that come through this
13 panel, in terms of their performance characteristics,
14 and what is actually acceptable.

15 Because if the criteria is that they have
16 to be equivalent to the predicate device, and we don't
17 know what the performance is, somebody could argue
18 that it is 70 percent sensitivity, and it is pretty
19 specific, and that is as good as the old test.

20 In my mind that is totally unacceptable
21 for this class, and so I am wondering whether or not
22 we should establish some performance criteria for this
23 class.

24 I don't know. I throw it out there.

25 DR. GUTMAN: Well, you are dealing with a

1 particularly challenging situation here, because the
2 comparison, any kind of comparison is likely to
3 require some kind of very clever manipulation if you
4 are using analytical data or at the best using bank
5 samples, unless we are fortunate enough to have an
6 outsider come in, and you could do a respective study.

7 The deal is that it would be -- well, I
8 agree with you -- and Marge might know if there is
9 some way to push us to make sure that each assay has
10 enough grounding that it stands on its own.

11 But to understand, it would be really
12 challenging for the division to try and figure out
13 exactly what performance standards to apply here. So
14 you can certainly do that, and we can at least respond
15 to that recommendation. But it would be quite an
16 interesting thought.

17 CHAIRMAN WILSON: Steve, do you think if
18 we established performance standards, do you think
19 there is any way that you could develop them and yet
20 still meet your least burdensome provision?

21 DR. GUTMAN: Well, there is a tension
22 there. I am less worried about least burdensome than
23 the scientific impossibility of knowing truth here.
24 So I am viewing this actually from a scientific pair
25 of eyes, and what we would want to do here, whether it

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1 is a new device, or whether it is an old device.

2 And that is exactly what Dr. Ticehurst was
3 saying, and characterizing and having full disclosure
4 on what is going on. And if we seek the truth here,
5 then we will never get these products on the market.

6 MS. SCHULMAN: Marjorie Schulman. We
7 would -- just for some clarification, we would most
8 likely develop a special control guidance document,
9 which could have any of the things that you were
10 talking about, and any sort of levels or anything like
11 that in it, and not a performance standard, which is
12 actually rule making that they all have to go through,
13 those that are monitored or the ones that are under
14 performance standards through rule making.

15 DR. GUTMAN: I think you understand, but
16 I wanted to just make sure that you understand that we
17 clearly as part of the deal here, we are trying to
18 the best that we could to characterize the
19 performance.

20 And where I am gun shy is that given the
21 state of information here, you know, that 70 percent
22 does sound too much, and 99 percent sounds just right,
23 and what I don't know what to do with is if it is
24 percent or 88 percent, and you are asking for a lot
25 you put that in.

1 So I am not suggesting that you can't do
2 that. You are the panel, and you get paid the big
3 bucks to come here and make these important decisions,
4 but you don't want to put something on the plate that
5 we can't deliver unless you want to turn around and
6 help, because we will just reconvene you, and you will
7 have to make the decision.

8 CHAIRMAN WILSON: Dr. Thrupp.

9 DR. THRUPP: Not only have we bundled the
10 three devices, but you would have to consider for a
11 true performance standard all different types of
12 populations, and the standards for low prevalence
13 population of samples is going to be completely
14 different for high prevalence and so on, and I would
15 agree that it actually seems to establish performance
16 standards would be extremely difficult.

17 I was going to suggest to move it along
18 that, number three, testing guidelines would be nice
19 to have I think, and maybe we all could agree on one
20 of these anyway. So I might make a motion that we
21 would like to have some testing guidelines suggested.

22 CHAIRMAN WILSON: Any specific testing
23 guidelines?

24 DR. THRUPP: Well, we are talking about
25 guidelines for these devices, these tests, and based

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1 on best available information, which has been
2 summarized from our experts, and by the FDA, and by
3 the literature.

4 I am not suggesting that we write out
5 exactly what they would be.

6 DR. ZABRANSKY: I think the guidelines
7 here would be more along the lines of whether anything
8 has been set up by the CDC for identification of the
9 organism. It is kind of already there, and if we
10 could develop those guidelines further.

11 CHAIRMAN WILSON: Dr. Gutman, are testing
12 guidelines something that you or the FDA could
13 develop?

14 DR. GUTMAN: Well, we could do it, or we
15 could piggy-back on CDC, or we could do it
16 collaboratively, and you could use it as the citation.
17 You could suggest that there be information about it,
18 and you interpret it in the package insert itself if
19 you felt that it was important enough.

20 If you wanted us to explore, and I don't
21 mean to be leading, but you could explore putting
22 certain information, such as a test report, that you
23 thought might be highly relevant. So you have got
24 lots of choices here, and you can --

25 DR. ZABRANSKY: Would this be done in

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1 guidance documents as well?

2 DR. GUTMAN: Yes.

3 CHAIRMAN WILSON: Dr. Nachamkin.

4 DR. NACHAMKIN: Now I'm confused again.

5 So if somebody could manufacture the gamma phage and
6 license and package it, and have a package insert that
7 says contains -- you know, 10 to the 12th particles of
8 gamma phage, with whatever stabilizer, and then sell
9 it, and not have a procedure to go along with that.

10 DR. GUTMAN: No, no, they would have to --
11 it would require a pre-market review, and we would
12 have to see what --

13 DR. NACHAMKIN: So there would have to be
14 a specific protocol.

15 DR. GUTMAN: Yes.

16 DR. NACHAMKIN: So maybe I am not -- so
17 the technical guidelines would be more for the
18 intended use, rather than the actual procedure?

19 DR. GUTMAN: Yes, that goes without
20 saying. I think there is a confusion here on testing
21 guidelines. I view that, and Marge, correct me if I
22 am wrong, but being something more akin to practice
23 parameters and use of information.

24 And it would be a requirement that
25 somebody actually outline that procedure, and have a

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1 complexity status to get through the FDA, but you have
2 to outline your procedure, and I doubt -- and again I
3 guess when we get the first one, we will be
4 challenged.

5 But I doubt that we would be satisfied
6 with just knowing how much it measured.

7 DR. NACHAMKIN: Well, I understand that,
8 but it seems like when you are talking about
9 guidelines, you are really talking about two different
10 things. And I certainly agree that we should include
11 something about what population should be tested in
12 the package inserts or whatever.

13 DR. THRUPP: I was interpreting this broad
14 category of testing guidelines as having several
15 components, all of which would be logically addressed.

16 The selection of specimens that would be
17 appropriate for testing, for example, and the
18 procedures to be used would be another category, and
19 the interpretation and how it should be reported, and
20 that could even include a fourth category, public
21 health notification.

22 So several of these things could be
23 included under testing guidelines that it seems to me
24 would be reasonable to come up with, even on the old
25 devices now, without addressing performance standards.

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1 CHAIRMAN WILSON: Okay. We have a motion
2 that we recommend testing guidelines for this group of
3 products. Do we have a second?

4 DR. ZABRANSKY: I would second.

5 CHAIRMAN WILSON: All right. We have a
6 motion and a second. Do we have any further
7 discussion? All in favor, raise your hand, please.

8 (A show of hands.)

9 CHAIRMAN WILSON: Okay. It is unanimous
10 to vote yes. Are there any further motions for any of
11 the other special controls under Item 3(b)?

12 DR. ZABRANSKY: I would ask whether or not
13 the current arrangements that are already promulgated
14 through CDC for reporting the organism, and reporting
15 diseases and so forth, would not satisfy the issue of
16 tracking and/or even the post-market surveillance.

17 In other words, if CDC is going to get a
18 report of a positive and so forth, are they going to
19 be asking how was this identified and so forth, and
20 how was this confirmed.

21 MR. REYNOLDS: Well, if the State lab is
22 already established with other Level A labs to --

23 DR. ZABRANSKY: Well, Level A labs are
24 required to B labs.

25 MR. REYNOLDS: Well, what is required does

1 not always happen.

2 DR. ZABRANSKY: Well, I think the
3 sensitivity of this issue with the general public and
4 the general laboratories right now, I think it is
5 fairly safe that it is going to go through.

6 I mean, it took a while for HIV to wake up
7 that they had to do it, but there was also other
8 things attached to it; the stigma of the disease and
9 so forth.

10 But now a lot of those hurdles have been
11 broached. I think reporting in this country has
12 definitely improved. Again, it is the sensitivity of
13 the laboratory directors to follow the rules, and the
14 infection control personnel, and the ID people.

15 DR. ZABRANSKY: It is not just the lab.

16 CHAIRMAN WILSON: Then are you making a
17 recommendation that we --

18 DR. ZABRANSKY: No, I am asking whether or
19 not the panel thinks as I do that the issue of post-
20 market surveillance and tracking would not be handled
21 through the normal channels that we know is going to
22 occur because of the reportable nature of the disease.
23 And I guess you feel not particularly safe with that.

24 MR. REYNOLDS: It is my experience -- and
25 I am going to say that there is some level A

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1 facilities that are wonderful, and there are others
2 whose competence level is not the greatest in the
3 land.

4 You know, things will happen.

5 CHAIRMAN WILSON: Dr. Nachamkin.

6 DR. NACHAMKIN: The only thing that the
7 package insert could say is that this disease may be
8 reportable as per your State and Federal guidelines.
9 You can't say in the package insert we must report
10 this to your State laboratory. That is legislative,
11 and we are not responsible for that.

12 DR. THRUPP: Why can't you say it as a
13 reminder that this is something that has great public
14 health consequences and must be reported.

15 DR. ZABRANSKY: The question is are you
16 putting the responsibility on the FDA to do the
17 surveillance and the tracking, and this is what this
18 is going to do, correct?

19 CHAIRMAN WILSON: Ms. Schulman.

20 MS. SCHULMAN: Exactly. I was just going
21 to clarify again that this could be also be under
22 other and maybe labeling these recommendations, and
23 not necessarily market surveillance or tracking.

24 CHAIRMAN WILSON: Dr. Ng.

25 DR. NG: I guess my question, since we

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1 already report these all the way up the chain, is that
2 the report that we report this to, do they have the
3 wherewithal to track the performance of these things
4 that we are approving, and to then tell us how it is
5 performing in real time in the real world?

6 CHAIRMAN WILSON: Dr. Gutman.

7 DR. GUTMAN: Post-market reporting for the
8 agency has been challenging, and is challenging
9 towards the subject of scrutiny now as some of you
10 from the Post and those of you from the Baltimore News
11 saw the problem at Hopkins.

12 But we are trying to improve that area,
13 but we are also trying for leverage. So the
14 suggestion on the table to use the CDC and the State
15 as reporting mechanisms sounds to me like a better
16 idea than for FDA to try and do a duplicate
17 surveillance.

18 And that doesn't answer your question
19 about the specific performance, and you could
20 certainly put -- and we are certainly thinking out of
21 the box, and I can't think of a more interesting thing
22 to follow, and a more interesting packaging to follow.

23 And I don't know whether there will be
24 enough experience to ever find out the truth, but you
25 can certainly put on the table, and we could explore

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1 ways of linking with either CDC or other people in the
2 public health network, and if you try to restrict it
3 to the public health network, that does seem to me to
4 be a captive audience for information, if nothing
5 else, about how the quality control works and
6 examples.

7 So do you think that recommendation would
8 be made a part of the special control or some
9 recommendation and we tried to explore that, that is
10 your call. But we are interested in stuff like that.

11 CHAIRMAN WILSON: Dr. Beavis, did you have
12 a comment?

13 DR. BEAVIS: No, just a follow-up about
14 the reporting. I mean, that is a local and State
15 issue, and each statement concerns regulations, and
16 not only that which is reportable, but what about
17 isolates should be sent to the State lab, and I think
18 it should be left that way.

19 CHAIRMAN WILSON: Dr. Thrupp.

20 DR. THRUPP: But there is another whole
21 parameter to the issues behind the questions behind
22 post-market surveillance and test device tracking,
23 aside from the notification of public health issues,
24 namely is there a new strain that is not being
25 recognized by devices.

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1 Or is there a device that allegedly works
2 in the PMA or in the grandfathering, or whatever, and
3 is not working currently, and that is not being well-
4 recognized, except focally, and is there a mechanism
5 or should we recommend a mechanism for tracking by
6 performance standards, and tracking the utilization
7 results to pick up errors in a way that would allow
8 the agency or the CDC to act proactively.

9 This is a somewhat poor analogy, and I am
10 not really sure that it is the same, but when it was
11 apparent a few years ago that certain automated
12 susceptibility testing devices were not detecting
13 penicillin resistant pneumococci, and this was not
14 necessarily broadly recognized, but several labs did.

15 And that was consider enough of a public
16 health issue that the FDA at that point had to step
17 in. Now, there is lots of pneumococci -- well, there
18 are not going to be very many bacillus anthracis
19 strains being tested, and so I am not sure we can make
20 a practical recommendation to put in here, but if you
21 think we should try.

22 DR. GUTMAN: Well, you are certainly
23 welcome to. You have to realize, whether you put it in
24 or not, there is medical device reporting in place
25 right now. So that if a lab entity gets it, and they

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1 see some strange thing happening that could hurt
2 people, they are supposed to report it now.

3 And I think that the laboratory community
4 is now highly attuned to that reporting mechanism and
5 are actually committed to a long term goal to improve
6 the awareness of that system.

7 So it would be my hope that something
8 really outrageous happened, in terms of some strange
9 behavior that you are not predicting at the table, and
10 that would come to life.

11 But again if you wanted to put on the
12 table that we would be a little bit more proactive, I
13 would certainly not be opposed to that, or we would
14 not be at all opposed to trying to figure out a way to
15 do it. I don't know how it would fit as a special
16 control --

17 MS. SCHULMAN: And depending on what it
18 is, it can either go into the special control guidance
19 document, or just a special control itself. And how
20 we would implement it, we would work on that later,
21 and just take your recommendations.

22 DR. THRUPP: Would it be helpful --

23 DR. GUTMAN: And the alternate in terms of
24 tracking this would be if someone did come up with
25 proficiency testing, and you had some survey form for

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1 watching that, and that might not deal with a new
2 strain problem.

3 But it would at least give you some
4 insight into how the test is actually working in the
5 real world, and that would be beyond our capability.
6 It would not be beyond the capability perhaps of
7 USAMRIID or CAP and maybe even CDC.

8 DR. THRUPP: Would it be helpful for us to
9 come up with a politically acceptable and very general
10 statement along just what you suggested; that the FDA
11 would be encouraged to partner with CDC, USAMRIID, and
12 other appropriate agencies that are involved in
13 laboratory performance issues to establish practical
14 ways to evaluate the performance --

15 DR. GUTMAN: That would seem politically
16 correct, and you could even make it stronger, and that
17 after collaborating that there weren't good
18 surveillance mechanisms, or reasonable surveillance
19 mechanisms in place, that you would recommend that we
20 try and do something more proactive.

21 DR. THRUPP: I would make that motion.

22 CHAIRMAN WILSON: All right. We have a
23 motion, and do we have a second? Okay. We have a
24 motion and a second. Do we have any other discussion?
25 All those in favor?

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1 (Chorus of ayes.)

2 CHAIRMAN WILSON: Any opposed?

3 DR. ZABRANSKY: A question. This is going
4 to be attached to the post-market surveillance or
5 other?

6 CHAIRMAN WILSON: I think this would come
7 under other wouldn't it? Okay. Are there any other
8 --

9 DR. NACHAMKIN: I don't like the concept
10 of -- I don't think it needs to be tracked in a formal
11 sense, but there again, I -- well, I would abstain.
12 I am not strongly opposed to it, but I am not really
13 for it either.

14 CHAIRMAN WILSON: Okay. Thank you. Are
15 there any of the other special controls under Item
16 3(b) that anyone wants to make a recommendation for?
17 Dr. Reller.

18 DR. RELLER: I think it has been very
19 useful going through these specific points, because we
20 have
21 -- at least I have learned that the performance
22 standards that would require specific rules that could
23 be very cumbersome would be counter-productive of what
24 we want to see happen, namely the widespread use
25 availability and extension under guidance of these

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1 reagents from before 1976.

2 Given Dr. Nachamkin's concerns and Dr.
3 Thrupp's -- the successful motion for keeping track of
4 what happens with these reagents is what you are
5 interested in, that that also could be done most
6 readily without some new structure to do it within the
7 content of the limited distribution.

8 And including even -- because we don't
9 have the capacity scientifically by virtue of numbers,
10 and it would be counter-productive to have specific
11 rules having to do with performance.

12 That does not mean that those -- for
13 example, Level A laboratories that were incorporated
14 into the laboratory response network, deputized, or
15 however you want to look at it, could not have as part
16 of the process of being the extension of the public
17 health, that how these tests perform in their hands
18 would be collated and monitored by the laboratory that
19 got the reagents to them as part of the extension
20 process.

21 And then there would be some control
22 mechanism put in place so that if Stan Reynolds got
23 the reagents to me, and I didn't get the information
24 back to him on how it worked in my laboratory, he
25 would have the capacity to say no more reagents until

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1 you do what you are supposed to.

2 And I think that it doesn't have to be an
3 adversarial thing. I think it would be a public
4 health -- I realize that I am naive, or an optimist,
5 but I am an optimist. I am a bright side person.
6 That it would be an honor to be a part of the network
7 serving the public's health.

8 And maybe the encouragement of that
9 mentality on the front line would also be a positive
10 thing. I don't think when we come to the restricted
11 distribution that it is not the intent that it is a
12 restricted use, but rather a comprehensive,
13 coordinated approach that includes the communication
14 between infectious disease practitioners, and their
15 clinical colleagues on the front line, and physicians
16 and others who have expertise in the laboratories in
17 getting the needs of the individual patient, as well
18 as the public's health, met.

19 And in a way that the data is collected
20 that you can make some sense out of it, both in terms
21 of diagnostics, as well as having the organisms, and
22 having the typing, and having the database for the
23 epidemiological, for the control mechanisms, et
24 cetera.

25 So that there is a rapid, but a measured,

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1 unified, and controlled response to these things,
2 rather than some of the chaos that has happened
3 before.

4 CHAIRMAN WILSON: Air right. Dr. Thrupp.

5 DR. THRUPP: I would interpret Barth's
6 comments as an expansion of what I had suggested,
7 filling in some of the operational details, and I hope
8 that you didn't mean that we did not want the FDA
9 included in these loops.

10 I think historically that there have been
11 instances when the CDC and the FDA, and USAMRIID have
12 not always communicated all data as readily as quite
13 the ideal.

14 And I think that is one reason why I was
15 suggesting that it might be helpful to the FDA to have
16 a very general statement that in such a network as Dr.
17 Reller is describing, and fully what I intended, that
18 the FDA work with these networks and the appraise of
19 the data that is being exchanged.

20 DR. RELLER: Actually, Lauri, I agree with
21 you, and I think that having this in Category II with
22 restricted distribution actually puts the FDA in a
23 more important position than it would be if it were
24 one just without a restriction. Is that correct, Dr.
25 Gutman?

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1 DR. GUTMAN: Yes.

2 CHAIRMAN WILSON: If there are no further
3 motions on Item 3(b), we move next to Item 4(a).

4 MS. SCHULMAN: One second. So we have
5 agreed upon the guidance guidelines?

6 CHAIRMAN WILSON: Other.

7 MS. SCHULMAN: Other. Okay.

8 CHAIRMAN WILSON: And Item 4(a) states is
9 a regulatory performance standard needed to provide
10 reasonable assurance of the safety and effectiveness
11 of a Class II or III device. And since we recommended
12 that this be classified in Class II, we have to
13 address that question. Dr. Gutman, can you --

14 MS. SCHULMAN: One point of clarification.
15 That just applies to foreign standard guidelines. So
16 we can skip 4(a), 4(b), 5, and 6.

17 CHAIRMAN WILSON: Okay. So next would be
18 Question 7(a) then. Can there otherwise be reasonable
19 assurance for the safety and effectiveness without
20 restrictions on its sale, distribution, and use,
21 because of any potentiality from harmful effect when
22 a collateral measure is necessary for the devices use.

23 And so in this case, this is one where you
24 have to vote the opposite of what you think it is. It
25 is a negative question in other words.

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1 MS. SCHULMAN: Right, and because we are
2 classifying a pre-limit device, which was
3 prescription, the answer would be no, which makes it
4 a prescription device, and then we go to 7(b) for the
5 added restrictions.

6 CHAIRMAN WILSON: Correct. Do we have a
7 motion?

8 DR. THRUPP: Yes.

9 CHAIRMAN WILSON: And your motion is?

10 DR. THRUPP: That we vote know.

11 CHAIRMAN WILSON: Any further discussion?
12 All in favor?

13 (Chorus of ayes.)

14 CHAIRMAN WILSON: Any opposed? Okay. The
15 vote carries unanimously. Item 7(b) states that we
16 need to identify the needed restrictions if Item 7(a)
17 is no. And there are four options.

18 The first is only proper written and oral
19 authorization of a practitioner licensed by law to
20 administer the use of the device.

21 The second is to use only by persons with
22 specific training or experience in its use. Third is
23 to use only in certain facilities, and the fourth is
24 the other category. Do we have any recommendations
25 for any of these?

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1 DR. ZABRANSKY: What is meant by
2 practitioner?

3 MS. SCHULMAN: It is dependent upon the
4 State. The State makes the rules on who can make --

5 DR. ZABRANSKY: Does that make a lab
6 director a practitioner if he his not a physician, he
7 or she?

8 MS. SCHULMAN: Afraid so.

9 DR. THRUPP: I think that is kind of moot,
10 because if we do to Number 2 and Number 3, and other,
11 that would override Number 1 anyway.

12 CHAIRMAN WILSON: Do we have a motion?

13 DR. THRUPP: Two and Three are removed.

14 CHAIRMAN WILSON: Do we need to be more
15 specific than that, Dr. Gutman?

16 DR. GUTMAN: I don't want to read your
17 minds. I presume from the discussion --

18 DR. THRUPP: Number 3 applies what Bart
19 Reller was discussing. Well, we should just vote
20 that and that would be under other, I think.

21 CHAIRMAN WILSON: But do you want any more
22 specific recommendation from us, or --

23 DR. GUTMAN: No, I would appreciate the
24 understanding of exactly what you have in mind here.
25 I will give you a choice and you can tell me if I have

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1 guessed right or not?

2 CHAIRMAN WILSON: Dr. Reller.

3 DR. RELLER: Actually, I had thought that
4 we had a motion before that we had a consensus on it,
5 and not unanimity, that there was the request to
6 consider it, or revote on it, and once we got through
7 all the appropriate check boxes to 7(b).

8 And the essence of that motion was just
9 what Ron outlined in Item 2 and 3 having to do with
10 the facilities, and the specific training. And I can
11 go ahead and make the motion again in the broad
12 context.

13 That all three of these reagents tests
14 having to do with bacillus anthracis be limited in
15 their distribution, and the accountability, and the
16 oversight if you will, be in the public health
17 laboratory group.

18 That could be State health laboratories,
19 and it could be the New York City laboratory, for
20 example. It could be Federal laboratories. I mean,
21 those details could be worked out.

22 And that these laboratories be encouraged
23 or certainly no restrictions in the content of a
24 laboratory response network of including first
25 responding laboratories, and it would not necessarily

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1 be limited to academic medical centers, but wouldn't
2 necessarily include all of them, because in order to
3 be such a designated primary testing site, that one
4 would have the understanding and agreement that there
5 would be appropriate training, and the interpretation
6 in following all the procedures that would be as best
7 as we know necessary to get a valid test result with
8 appropriate controls, et cetera.

9 And that there would be also the
10 understanding that when the reagents were distributed
11 to them under the authority or authorization of the
12 relevant next level public health laboratory, that the
13 testing results, performance, et cetera, that all
14 reporting of what is found be done in accordance with
15 existing local and State reporting regulations.

16 But in addition that the performance of
17 these reagents in that laboratory hand be systemically
18 collated by the public health laboratories for
19 interagency review that would include, and not be
20 limited to, but it would include the FDA, whose
21 regulatory authority in the first place authorized
22 them to categorize these agents in such a way that
23 achieves this end, namely two, with restrictions. How
24 about that?

25 CHAIRMAN WILSON: Okay. We have a motion,

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1 and I believe that Dr. Thrupp seconded it already.
2 Any further discussion? Okay. All those in favor?

3 (Chorus of ayes.)

4 MS. POOLE: Six and one abstention.

5 CHAIRMAN WILSON: Okay. Ms. Schulman, is
6 there anything else on this one that we need to vote?

7 MS. SCHULMAN: No, not on that form.

8 CHAIRMAN WILSON: Okay. Would you like to
9 walk us through what we need to do on this one then?

10 MS. SCHULMAN: Number 3, device and
11 implants, yes, and no, and we can say no, and number
12 4, the indications for use. That was the preamendment
13 indication. Was that given out?

14 In the packet there is a preamendment
15 indication. Okay. Roxanne is going to put it up on
16 the overhead, and then we can vote, and then on the
17 sheet you can just write as discussed.

18 CHAIRMAN WILSON: All right. Can the
19 members of the audience see that okay?

20 MS. SCHULMAN: This the pre-amendment one,
21 and just vote that you accept it or change it.

22 CHAIRMAN WILSON: Do we have a motion to
23 accept that? We have to vote on this and so I need a
24 motion.

25 DR. THRUPP: Where is this supposed to go

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1 on the for?

2 CHAIRMAN WILSON: Number 4, indications
3 for use, the intended use.

4 DR. NACHAMKIN: I will make a motion that
5 we accept the description as is.

6 CHAIRMAN WILSON: We have a motion. Do we
7 have a second?

8 DR. SMITH: Second.

9 CHAIRMAN WILSON: We have a motion and a
10 second. Any further discussion?

11 DR. NG: I have a question

12 CHAIRMAN WILSON: Dr. Ng.

13 DR. NG: I'm sorry, but this only
14 addresses the FA and the gamma phage. What happened
15 to the antigen?

16 CHAIRMAN WILSON: Ms. Shively, is the
17 indication for the antigen on there?

18 DR. SHIVELY: Actually, I don't believe it
19 is.

20 DR. NACHAMKIN: I'll amend my motion.

21 CHAIRMAN WILSON: Go ahead.

22 DR. NACHAMKIN: I will amend it to accept
23 this description, the description of the gamma phage
24 fluorescent antibody reagents only.

25 CHAIRMAN WILSON: Okay.

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1 DR. NG: I'll second.

2 CHAIRMAN WILSON: All right. How do we
3 handle the antigen test?

4 MS. SCHULMAN: That was part of the
5 preamendment discussion, right, to bundle?

6 DR. NACHAMKIN: I will recommend that we
7 accept these descriptions for the FA and gamma phage
8 reagents and develop a description for the antigen --
9 or for the antibody assays.

10 CHAIRMAN WILSON: Okay. Speak into the
11 microphone, please.

12 MR. REYNOLDS: -- bacillus species
13 serological reagents because five is not really a
14 serological reagent.

15 CHAIRMAN WILSON: You're correct. They're
16 not.

17 DR. NACHAMKIN: How about striking
18 "reagents"?

19 DR. ZABRANSKY: Well, hold on. You would
20 have to strike more than that because the rest of
21 discusses "consists of antisera to differentiate." So
22 that whole first sentence would have to be reworded
23 that it includes the phage.

24 DR. NACHAMKIN: Are we counting the other
25 reagents consisting of a bacterial virus as being

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1 phage? If you would like us to add specificity, we
2 would be happy to edit that.

3 DR. TUAZON: Why can't you just use
4 "bacillus species diagnostic devices"?

5 DR. ZABRANSKY: -- are used to
6 differentiate.

7 DR. TUAZON: Yes.

8 CHAIRMAN WILSON: Is that a friendly
9 amendment then to the motion? Dr. Nachamkin.

10 DR. NACHAMKIN: So how about: Bacillus
11 species diagnostic reagents are devices that consist
12 of antisera or phage that are used to differentiate
13 bacillus species and presumptively identify anthracis
14 from culture isolates, or something like that.

15 CHAIRMAN WILSON: Okay. Do we need a
16 specific wording for FDA, Steve? All right.

17 DR. NACHAMKIN: Then I will make an
18 amendment that we accept this with further amendments
19 by the FDA staff to meet the definition.

20 CHAIRMAN WILSON: Okay. Do we have a
21 second?

22 DR. NG: Yes.

23 CHAIRMAN WILSON: All those in favor?

24 (Chorus of ayes.)

25 CHAIRMAN WILSON: Any opposed? Okay.

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1 Good. The change is unanimous. Ms. Schulman.

2 MS. SCHULMAN: No. 5, the identification
3 of the risks of health presented by the device.
4 Roxanne, is there an overhead for that? Could you put
5 that up and vote on that or make any changes or
6 additions.

7 My mistake. There was not an overhead.
8 You can simply vote as discussed in the panel meeting
9 or any additions that were not discussed.

10 DR. THRUPP: Actually, the second part,
11 the last couple of sentences in the one that we just
12 looked at talks about the types of risk to health and
13 about the forms of disease and the fact that
14 inhalation anthrax can be fatal. So some of that is
15 implied in there. I'm not sure that it needs to be
16 brought out separately.

17 CHAIRMAN WILSON: Dr. Nachamkin.

18 DR. NACHAMKIN: It doesn't seem that there
19 is any specific hazard with the devices themselves,
20 and where the hazard comes in is working with the
21 organisms to which the device is going to be applied.

22 So wouldn't you have to put something in
23 there like: Appropriate biosafety handling of the
24 diagnostic specimens must be followed, or something
25 like that.

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1 CHAIRMAN WILSON: Okay.

2 DR. THRUPP: You are addressing laboratory
3 safety.

4 DR. NACHAMKIN: That's correct.

5 DR. RELER: I think the primary intent --
6 that would be a subcategory. But my interpretation
7 was that the primary purpose of this paragraph five is
8 the public's health or an individual patient's health,
9 in terms of --

10 DR. NACHAMKIN: It could be either.

11 CHAIRMAN WILSON: I think it is both isn't
12 it, Dr. Gutman?

13 DR. GUTMAN: Yes, it would be both.

14 CHAIRMAN WILSON: All right. So we can
15 put down -- Ms. Schulman said we can put down "as
16 discussed." Do you want to add that language
17 specifically? So we will accept that as a motion. Do
18 we have a second? We have a second. All right. Any
19 other discussion? All in favor?

20 (Chorus of ayes.)

21 CHAIRMAN WILSON: Any opposed? Dr.
22 Beavis, would you care to comment?

23 DR. BEAVIS: Yes. As much as the point of
24 this forum is related to a Biosafety Level II
25 organism, I think it is incumbent on laboratories to

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1 have these for all organisms, and I don't see the need
2 to specially make a special point on it for this
3 organism.

4 CHAIRMAN WILSON: Okay. Go ahead.

5 MS. SCHULMAN: No. 6, recommended advisory
6 panel classification. The priority of the
7 classification is Class II. The priority you would
8 vote on would be high, medium, and low, and that would
9 be how fast you would want us to write the draft
10 guidance for comment and the draft regulation
11 classifying these devices.

12 CHAIRMAN WILSON: Are there any specific
13 -- if you classify it as high, medium, or low, what is
14 the difference in the timetable between those
15 categories?

16 MS. SCHULMAN: There is no specific time
17 frame, but if you classify it as high, we would put
18 that on as one of the first things that we would try
19 to address.

20 But then again the regulatory requirements
21 and time frames of investigational device exemptions
22 could come up before that, but it would be one of the
23 first things that we would work on before any other
24 classification or reclassification effort.

25 CHAIRMAN WILSON: Okay. So you need a

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1 vote on high, medium, or low. Does anyone care to
2 make a motion? Dr. Reller.

3 DR. RELER: I would think it would
4 behoove the FDA to have this as a high priority.

5 DR. THRUPP: Second.

6 CHAIRMAN WILSON: We have a motion and a
7 second. Any further discussion? All in favor?

8 (Chorus of ayes.)

9 CHAIRMAN WILSON: Okay. The vote carries
10 unanimously.

11 MS. SCHULMAN: No. 7, if the device is an
12 implant that is life-sustaining or life-supporting and
13 has been classified in a category other than Class
14 III, explain fully the reasons for the lower
15 classification, with supporting documentation and
16 data. That can be answered also "as discussed in the
17 panel meeting" if you feel it has been covered.

18 CHAIRMAN WILSON: Do we need to vote on
19 that?

20 MS. SCHULMAN: No, we do not.

21 DR. THRUPP: Is that question really
22 applicable to this? It's implying that they are
23 talking about implants.

24 MS. SCHULMAN: Or life-supporting or life
25 sustaining. It is not just necessarily implants.

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1 CHAIRMAN WILSON: Okay.

2 MS. SCHULMAN: No. 8, the summary of
3 information, including clinical experience and
4 judgment, upon which the classification recommendation
5 was based. If that was fully discussed in the panel
6 meeting, you can say it was discussed in the panel
7 meeting.

8 CHAIRMAN WILSON: Is everyone comfortable
9 with that? Okay.

10 MS. SCHULMAN: No. 9, identification of
11 any needed restrictions on the use of the device. If
12 we feel that we have fully covered that on the general
13 questionnaire in No. 7(b), then we can say it was
14 covered in 7(b), or anything else can be added at this
15 time.

16 CHAIRMAN WILSON: Anyone care to add
17 anything to what we have discussed previously? Okay.

18 MS. SCHULMAN: Okay, No. 10. Because we
19 have a change in the law, it does say: If it is in
20 Class I, recommend whether the FDA should exempt it
21 from registration lists and premarket identification
22 records and reports, good manufacturing practices.

23 But because of the change in the law since
24 FDAMA, a Class II can be exempt. So you would have to
25 vote whether you want it exempt from premarket

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1 identification in Class II, yes or no.

2 CHAIRMAN WILSON: Okay. Do we have a
3 motion on that?

4 DR. ZABRANSKY: The motion is no.

5 CHAIRMAN WILSON: We have a motion for no.
6 Do we have a second?

7 DR. BEAVIS: Second.

8 CHAIRMAN WILSON: We have a motion and a
9 second. Any further discussion? All those in favor?

10 (Chorus of ayes.)

11 CHAIRMAN WILSON: Any opposed? Good. The
12 vote carries unanimously.

13 MS. SCHULMAN: And No. 11 is whether you
14 can identify any existing standards applicable to the
15 device, device subassembly components, the device
16 materials, parts, or accessories. If we discussed
17 that before, we can say that, or any can be added at
18 this time.

19 CHAIRMAN WILSON: Is there anything that
20 anyone would care to add to what we have discussed
21 previously? Okay.

22 MS. SCHULMAN: That is the forms and you
23 can vote on whether you are accepting them as was
24 written or not, the entire thing.

25 CHAIRMAN WILSON: Do we vote on both forms

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1 together?

2 MS. SCHULMAN: Yes. One vote.

3 CHAIRMAN WILSON: All right. Do we have
4 a motion to accept what we have done on the two forms?
5 We have a motion. Do we have as second? Is there any
6 discussion about any of the points on either form that
7 anyone would like to bring up? Anything that we have
8 left out or not thought of? Okay. All those in
9 favor?

10 (Chorus of ayes.)

11 CHAIRMAN WILSON: Any opposed? Okay. We
12 are just a little bit behind schedule, and we are not
13 in too bad a shape today. Let's go ahead and break
14 for about 10 minutes. So if you could be back at
15 about five after 3:00. Thank you.

16 (Whereupon, at 2:54 p.m., a recess was
17 taken, and the meeting resumed at 3:11 p.m.)

18 CHAIRMAN WILSON: This part of the
19 afternoon is a similar process to what we have been
20 through, only this time we are going through it for
21 **Yersinia pestis**. I would like to begin the process by
22 having the FDA presentation, and Ms. Roxanne Shively
23 will give that as she did this morning for the
24 *Bacillus anthracis*. Ms. Shively.

25 DR. SHIVELY: Good afternoon. A lot of

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1 the information I am going to be going over now will
2 be somewhat repetitious from this morning, but it is
3 a different bug. We've gone to Gram-negative now.

4 Yersinia pestis has worldwide reservoirs,
5 including 13 Western states. In the United States,
6 there is an increased risk to humans from its
7 urbanization into natural and zootic plague foci.

8 I skipped a slide, but I was just going to
9 go over what we were going to do again, but it's what
10 we just did. So I think maybe we don't need to do
11 that. Okay. So going back to Yersinia pestis, the
12 bug of the afternoon.

13 Pneumonic plague is highly fatal when not
14 recognized early, and early symptoms are nonspecific.
15 Laboratory identification can be difficult. This is
16 a slower growing organism, often taking 48 to 72 hours
17 to appear on culture plates.

18 Yersinia pestis is difficult to
19 distinguish from Yersinia pseudotuberculosis, which is
20 a common environmental enteric, and also from other
21 biochemically inactive Gram-negative rods.

22 In humans, the serologic response may take
23 10 to 14 days to develop. So such testing is usually
24 retrospective.

25 The first preamendments product was a vial

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1 of specific bacterial virus used in a culture plating
2 method to distinguish Yersinia pestis from Yersinia
3 pseudotuberculosis.

4 In 1950, WHO recommended a bacteria phage
5 as a reference method, and provided C bacteria phage
6 to other laboratories.

7 In 1953, Cavanaugh and Quan published a
8 report about using filter paper strips with
9 lyophilized phage, and this product was available from
10 the CDC for quite a number of years.

11 Factors affecting results with this test
12 were again: variant phage strains that behaved
13 differently; the media used; the length and
14 temperature of incubation; phage titer and stability;
15 and also the inoculum density of the test organism.

16 Technologist experience with interpreting
17 lysis is also critical, especially when there are
18 mixed cultures.

19 The second product type is a vial
20 fluorescein-labeled antibody against the F-1 antigen,
21 and this is used to microscopically visualize specific
22 binding with cultured organisms, or organisms in
23 infected specimens.

24 This provides presumptive evidence for the
25 identification of yersinia pestis. Rabbit hyperimmune

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1 serum was available from the Lederle Labs in the
2 1970s, and in 1970, WHO recommended a method using
3 this type of reagent, specifically antisera from
4 rabbits inoculated with plague vaccine.

5 Earlier, in 1959, Winter and Moody had
6 described the original method that was applied.
7 Factors that affect results with this particular
8 product include that other species can express the F-1
9 antigen, and different strains of the Yersinia pestis
10 can have variable expression of the antigen.

11 And also this expression can be reduced
12 with storage and certain growth conditions. Inoculum
13 density and the method of fixation also impact on
14 results.

15 And the last product type that was
16 preamendments is a vial of purified Fraction-1 antigen
17 that was used to sensitize sheep red blood cells for
18 passive hemagglutination testing. And this was used
19 to detect antibody responses to the F-1 antigen.

20 A titer increase with paired specimens can
21 retrospectively confirm Yersinia pestis infection.
22 These vials of F-1 sensitized sheep red blood cells
23 were provided by the Walter Reed Army Medical
24 Institute of Research in the 1970s.

25 Multiple publications describe use of this

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1 type of product and the method, and WHO did adopt the
2 PHA test as a standard method.

3 Factors affecting results include the
4 purity of the antigen preparation; concentration of
5 the F-1 antigen; obtaining a serum sample too early
6 during the course of infection, and also there can be
7 rare infections with non-encapsulated strains of
8 Yersinia.

9 Protosome effects can also occur, and this
10 type of test is unable to differentiate recent from
11 past infection. Endpoints can be very subjective to
12 read, and there can be nonspecific reactivity due to
13 heterophiles.

14 I would like to go over a few historical
15 notes and just a general summary. Plague is an old
16 historically significant disease that is still with us
17 Early diagnosis does reduce mortality.

18 Preamendments, diagnostic laboratory
19 testing was limited to specialized and public health
20 laboratories. Reagents were developed within these
21 laboratories and prepared and distributed between
22 those labs, both nationally and internationally.

23 Naturally caused human disease that is
24 zootic plague is not common. Public health efforts
25 were and continue to be important for controlling and

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1 preventing natural sources of infection.

2 Yersinia pestis is also a Category A
3 biothreat agent. I'll remind you that classification
4 is based on an assessment of risks and the level of
5 controls that can mitigate those risks.

6 And I will just repeat that for an *in*
7 *vitro* diagnostic test the risks are those that are
8 associated with misdiagnosis and epidemiological
9 misinformation due to false positive or negative
10 results.

11 As we discussed this morning, the controls
12 can be general or also include special controls. And
13 I won't go through those controls again. I think you
14 know them pretty well by now. Dr. Wilson, should we
15 do questions now or do you want to start the
16 discussion?

17 CHAIRMAN WILSON: Does anyone have
18 questions of Ms. Shively? Thank you. At this point,
19 we would like to go to the open public hearing.
20 Again, this portion of the meeting is open to the
21 public to present information relevant to unclassified
22 preamendment devices to identify Yersinia pestis.

23 If there are any speakers, they are asked
24 to state whether or not they have any financial
25 involvement with the manufacturers of these devices.

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1 So at this time, if there is anyone who would like to
2 make a public comment, would they please come forward.
3 Please identify yourself.

4 MS. HIMES: I am Rosemary Himes of the
5 Association of Public Health Laboratories, and I
6 apologize that I wasn't able to make some of my
7 comments this morning during the anthrax discussions.

8 But I just wanted to reemphasize a point
9 that Dr. Reynolds made, that during the last crisis
10 much of what the public health labs had to deal with
11 was environmental testing.

12 And also we don't know what would happen
13 in a case of plague -- we do anticipate we are talking
14 about this with smallpox even -- but based on the
15 events of anthrax, people are going to be hysterical
16 and want environmental testing.

17 The reagents that you are talking about
18 here, although you are talking about them in terms of
19 clinical use, we know that environmental labs, and
20 even public health labs are going to be called upon to
21 use them in environmental circumstances.

22 So I would ask you to consider that when
23 you talk about labeling, or indications for use, both
24 back in the Bacillus anthracis test and in the
25 Yersinia pestis test as well, because we know that

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1 this is going to be of significant concern.

2 CHAIRMAN WILSON: Thank you. Dr. Reller.

3 DR. RELER: I have a question. What
4 environmental specimens would you envision might
5 inundate public health laboratories in the event of
6 concern over Yersinia pestis outbreak infections?

7 MS. HIMES: As a microbiologist, I would
8 not anticipate that any should be done, but when you
9 look at what happened with anthrax, the list of
10 specimens that the public health labs were asked to
11 test was just unbelievable.

12 And most of it was supposed to be dealt
13 with through law enforcement, in terms of what was a
14 credible threat. But in many places across the
15 country, law enforcement hands are tied by what was
16 considered politically correct testing.

17 So the public health laboratory is being
18 asked to do testing not based on scientific merit, but
19 based on public perception and public hysteria. So
20 you could consider with any of these agents people's
21 concern about dissemination from other sources.

22 And with pestis you might consider animal
23 sources and you might consider environments where
24 those animals were. I mean, people were bringing
25 their mailboxes to the public health labs to be

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1 tested.

2 So you might think of people bringing
3 specimens from their yards where animals may have
4 been, those kinds of things.

5 And I would not even at this point begin
6 to guess what might come in based on what happened,
7 and Dr. Smith certainly could speak to that as well.

8 DR. RELER: What is the role and
9 responsibility of public health laboratory directors
10 not underestimating the issues of political pressure,
11 but what is the responsibility for the science in
12 educating and delineating what should be -- I mean, I
13 am not naive, but this really shouldn't be in the
14 political arena.

15 I mean, people should not be making
16 decisions about something that they don't understand.

17 MS. HIMES: And I would agree with you,
18 and I would say that in most cases strong efforts are
19 made to try and educate, and turn away testing, or at
20 least prioritize it.

21 Where the big concern would be is -- and
22 we received many calls about this at the association
23 -- people who wanted testing done and law enforcement
24 did not deem it to be a credible threat and would not
25 bring it to the public health laboratory.

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1 So people were looking for private
2 environmental labs to do this testing for them. What
3 ultimately happened then is the specimens may have
4 gone to a private environmental lab, and the
5 environmental lab did an initial screening and could
6 not rule out anthrax, so then sent the isolate to the
7 public health lab, who then ended up having to test it
8 anyway.

9 So I would see the same thing happen if
10 these reagents are going to be available. They are
11 going to be used by environmental labs that are not
12 accredited and that the FDA has no oversight over.

13 But they are going to be used in those
14 settings, and it would be the labeling requirements
15 that might help to discourage that. The other
16 consideration would be in the labeling to include the
17 fact that the control strains for these tests are
18 going to be select agents, and that all users must
19 comply with the Federal Select Agent law.

20 DR. RELLER: Actually, this line of
21 questions -- and I think you already realized that I
22 am on your side-- will help us, in accord with the
23 previous discussion, to maybe some options here.

24 Maybe we are in a little better shape with
25 our education, knowing that this is basically a

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1 fragile organism. We don't have some of the hardiness
2 in contaminating the environment that we had with the
3 earlier agent.

4 I know that some very conscientious
5 practitioners in our state actually forward through
6 the MedWatch alert system to the FDA some egregious
7 abuses for private gain of diagnostic testing devices
8 for environmental isolates for the public that were an
9 egregious abuse of public concern, for personal
10 private gain.

11 And I think that the way that we do these
12 things has an important role in educating everyone who
13 needs education about what is really the risk, and why
14 it is so important to have competent laboratories,
15 including public health laboratories that are
16 adequately funded to do the job right and to educate
17 everyone, including the politicians, on what really
18 protects the public's health, and enables diagnoses
19 swiftly for individual patients, as well as the public
20 health responses to real events with competent testing
21 and oversight on how reagents are used.

22 CHAIRMAN WILSON: Dr. Thrupp.

23 DR. THRUPP: Dr. Reller's comment would
24 really come under the same kind of restrictions that
25 we voted for under section 7, which ought, if

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1 enforced, to minimize the amount of this testing in
2 private labs and outside of the public health arena.

3 MS. HIMES: Or at least make it more
4 difficult for them to access those reagents to do that
5 level of testing. Thank you.

6 CHAIRMAN WILSON: Dr. Gutman.

7 DR. GUTMAN: You are more than welcome to
8 make any recommendations about labeling that you like,
9 and I suggest that you vote your heart and soul, but
10 I have to be honest. I believe in truth in labeling.
11 You are pushing the FDA paradigm beyond where I
12 believe it legally stands, and though I think it is a
13 really important issue that is raised here -- and
14 again you can recommend what you want -- I don't wish
15 to suggest that I actually believe the FDA is going to
16 be a big help here.

17 Maybe we could go back and re-explore, but
18 right now mail and mail boxes are simply not part
19 of our menu.

20 CHAIRMAN WILSON: Mike.

21 DR. ZABRANSKY: You are a four-corner
22 state, but I don't know much yersinia you see up where
23 you are, right?

24 CHAIRMAN WILSON: A little bit.

25 DR. ZABRANSKY: Do you know what they are

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1 doing in the Colorado State lab as far as that?

2 CHAIRMAN WILSON: Concerning yersinia?

3 DR. ZABRANSKY: Yes.

4 CHAIRMAN WILSON: Last I knew, basically
5 DFA cultured traditional testing, but generally -- we
6 have the luxury of having the Fort Collins branch of
7 the CDC just 60 miles away, and most specimens end up
8 there.

9 DR. ZABRANSKY: What about Arizona and New
10 Mexico? Does anybody know what they are doing there?

11 CHAIRMAN WILSON: Mr. Ticehurst, did you
12 want to make a comment?

13 MR. TICEHURST: John Ticehurst, from Johns
14 Hopkins University's medical institutions. I wanted
15 to, like Roxanne, without going through the litany of
16 what I said this morning, reemphasize a couple of
17 points that from my point of view, I was a little
18 disappointed, weren't touched on much in the
19 discussion this afternoon on anthracis.

20 One is that I would hope that the panel
21 would recognize the inability to do clinical studies
22 the way that FDA would traditionally hope they would
23 be done. And in making recommendations about special
24 controls that would include guidance documents, if
25 they can provide some ideas to the FDA as to what

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1 kinds of things could be done as surrogates, that
2 would help.

3 Because there is really no regulatory
4 mechanism to deal with getting these kinds of things
5 on the market without clinical studies, and I think I
6 will stop at that on that one.

7 The other thing is that -- I will be a
8 little more blunt than I was this morning -- the
9 general controls that deal with good manufacturing
10 practices and quality systems regulations probably
11 don't cut it here.

12 A colleague that I used to work with at
13 the FDA I think was very good about this. If you can
14 put teeth in, perhaps strongly recommending or making
15 it a requirement that good manufacturing practices not
16 be self-regulated, but perhaps be inspected by the
17 FDA. then at least you have the assurance that the
18 products are going to be made consistently. If the
19 product is being made inconsistently, then it throws
20 all these other variables that you are concerned about
21 even into more disarray.

22 And then, lastly, just so you recognize
23 that even though there are these MedWatch
24 requirements, I am going to say something a little
25 more strongly than what Steve Gutman said before.

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1 In the six years that I worked at the FDA,
2 I am only aware of a couple of times where post-
3 marketing surveillance issues about lab assays came
4 up, and it's because that group is disassociated in
5 terms of the structure within CDRH from the group that
6 does the premarket evaluations.

7 And they put most of their emphasis
8 perhaps more appropriately on things like problems
9 with heart valves.

10 And the only thing that it ever even came up in
11 a panel meeting that I was aware of was when there
12 were deaths associated with improper use of a lousily
13 performing Group B strep antigen test.

14 So if that is something that the group
15 feels should have more emphasis, you are going to have
16 to put a stronger recommendation on that. Basically,
17 to put it another way, post-marketing surveillance for
18 laboratory assays usually doesn't hit the radar screen
19 in CDRH's post-market surveillance groups.

20 They just don't have the people to do it,
21 and I would make the argument that this is an arena
22 where the public health importance is so high, and
23 because you can't do the right kinds of clinical
24 studies pre-market, that you could put a lot of strong
25 arms on the right kinds of post-marketing

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1 surveillance.

2 But again the resources would have to be
3 put there to do it right.

4 DR. NACHAMKIN: John, I really don't quite
5 understand your comment about monitoring GMP.

6 DR. TICEHURST: I mean enforcing it.

7 DR. NACHAMKIN: But this panel doesn't
8 enforce those rules. That is an agency issue. My
9 understanding is that, for the device we voted on
10 earlier, we didn't exempt them from GMP.

11 They are required to use good
12 manufacturing practices. What else -- are you
13 suggesting that we do something additional in terms of
14 our comments to force inspection? I mean, isn't that
15 part of the process?

16 DR. TICEHURST: I think the reality is --
17 and somebody could correct me from the audience or
18 from the FDA if I am wrong -- that companies that have
19 Class I or Class II products, because they don't get
20 inspected for GMP, are then self-regulated, and a lot
21 of them basically don't do it.

22 DR. GUTMAN: The GMP requirement is
23 stronger for Class II than for Class I. I am probably
24 not as worried as John is about this one because there
25 is so much attention and money going into

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1 bioterrorism, including field hires, that I would be
2 astounded if this weren't a high priority. I mean,
3 you are more than welcome to recommend it, but I think
4 the agency got the message that this might be one of
5 the more important things on its plate.

6 It's probably not just coincidental that
7 we are having this panel meeting right after September
8 and October. So my guess is that there will be an
9 internal vigilance.

10 I also think that there is a lot of re-
11 engineering activity going on. And, again, I won't
12 make false promises because I don't know how they are
13 going to actually pan out, but there is a lot of soul
14 searching and reassessment about the whole post-market
15 piece.

16 So my hope would be that -- I can't
17 dispute what John has said, that historically the
18 post-market has not had the appeal of even
19 bronchoscopes, much less heart valves. But in the
20 agency's defense, some of the highest penalty fines
21 both civil and criminal, have been directed at the
22 industry, though it is perhaps not as strong as all
23 us would like.

24 DR. TICEHURST: Can I respond or should I
25 not?

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1 CHAIRMAN WILSON: No, go ahead.

2 DR. TICEHURST: I think that if I were in
3 your shoes, I would think -- and as Steve said, you
4 can recommend anything that you want. I would
5 recommend consistent manufacture be enforced, that if
6 you are not going to go with a Class III, that you
7 recommend it be enforced as a special control.

8 The pendulum swings back and forth, I
9 think in terms of the level of regulation, when there
10 aren't those strong things in place.

11 CHAIRMAN WILSON: Thank you. Is there
12 anyone else who would like to make a public comment?
13 If not, then -- Dr. Thrupp.

14 DR. THRUPP: Do we have information on
15 what the current status of the status for the last 20
16 years has been with regard to the supply of these
17 reagents analogous to the questions with regard to
18 anthrax reagents?

19 CHAIRMAN WILSON: Dr. Ezzell, can you
20 respond to that?

21 DR. EZZELL: The reagents for the bursts
22 in antibody against the F-1 antigen has been available
23 for a number of years, and that is not really a
24 problem.

25 DR. THRUPP: From Fort Collins?

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1 DR. EZZELL: From Fort Collins and also
2 from USAMRIID. And our reagents differ from those.
3 We have monoclones, a number of monoclones, to F-1
4 antigens. And the reagents that Fort Collins uses,
5 that is a monoclonal specifically against F-1 antigen
6 and recognizes those organisms that are drawn at body
7 temperature, at 35 or greater, 35 to 37 centigrade
8 because F-1 antigen is only expressed at elevated
9 temperatures and not at room temperature.

10 The USAMRIID reagent is one that
11 recognizes both F-1 positive and F-1 negative yersinia
12 tests, and that reagent has been available for --
13 well, we have large quantities of that.

14 And that has been available for at least
15 15 years, and we have it now. We have plenty of it.

16 DR. RELLER: Let's say a state lab in Utah
17 or Colorado or Arizona, where do they get their
18 reagents?

19 DR. EZZELL: Now they are getting them
20 from CDC, which is specifically for F-1 antigen.

21 DR. RELLER: From Fort Collins?

22 DR. EZZELL: Yes, the Fort Collins
23 antibody.

24 DR. RELLER: Who actually manufactures
25 these reagents and what sort of GMP oversight does

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1 USAMRIID and the CDC have or Fort Collins? Who looks
2 over that?

3 DR. EZZELL: That is something that they
4 are switching, and I am not sure of the status of that
5 right now. That is something that is being worked out
6 within CDC, the CDC in Atlanta, with Richard Kellogg
7 and his group down there.

8 DR. RELER: Do these federal agencies
9 outsource the production of reagents?

10 DR. EZZELL: I haven't heard about
11 outsourcing, but I think that CDC has been trying to
12 do a lot of their reagent development and what have
13 you in-house. They have a production group down there
14 that is producing a lot of these reagents.

15 What their plans are in the future to
16 outsource, I am not aware of those. But we do use
17 Cook, Hart, and Perry for our conjugations and
18 purifications, and we do provide reagents to the CDC.

19 We did use a commercial operation where we
20 provided all the antibody and Cook, Hart, and Perry
21 did the purification within the conjugations under
22 their specific guidelines to meet a quality standard.

23 DR. BROWN: You are probably not going to
24 like my answer because I am going to try and beg off
25 on you. You are asking a question about current

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1 activities; whereas, our understanding is that the
2 charge of the panel was to consider historical
3 devices.

4 Looking forward to the future, we well
5 understand and have made a commitment to follow the
6 regulations that exist, and I think it is fair to say
7 that the CDC has made that commitment also.

8 But neither Dr. Ezzell nor I should be
9 speaking for the CDC on those points. Again, the
10 Army, the whole DoD, would receive those reagents from
11 the CDC. It would not be an independent manufacturer.

12 DR. EZZELL: And, as USAMRIID, we operate
13 as one of the two Level-B laboratories within CDC, and
14 so we have all of the CDC reagents. But we have also
15 Army reagents, too. So we are working with them with
16 their reagents, and we have our own reagents as well.

17 CHAIRMAN WILSON: Dr. Gutman.

18 DR. GUTMAN: The agency recognizes the
19 importance of having these products made available,
20 and we actually do have a commitment to collaborate
21 with the folks at the CDC and USAMRIID as well to make
22 sure that they understand the requirements and do come
23 into compliance.

24 And, again, you are free to make a
25 recommendation and we pay particular attention to

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1 that, but we actually have our eye on that ball even
2 now.

3 CHAIRMAN WILSON: Okay. Does anyone else
4 have a question for Dr. Brown or Dr. Ezzell? Dr.
5 Nachamkin.

6 DR. NACHAMKIN: Do you have any anecdotal
7 performance data on any of these reagents? We are
8 going through the same thing as we did this morning,
9 and we have not actually heard anything about how good
10 are these tests.

11 DR. EZZELL: In our hands ,with our
12 antibodies, we have had -- there is cross-reactivity
13 some cross-reactivity with the CDC's proteases and
14 polyclonal serum we're using. But if you go to the
15 monoclonal, there is no cross-reactivity because the
16 F-1 antigen is highly specific for -- when it is used
17 in monoclonals, it is highly specific -- the one we
18 use now -- are highly specific to Y tests, strong at
19 elevated temperatures.

20 But they were in the past, many years ago
21 prior to 1976, and there were polyclonal sera that
22 cross-react with CDC strains. Ms. Shively has
23 incorporated that in the presentation that she just
24 gave. But some of the present reagents are highly
25 specific for the F-1 antigen.

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1 CHAIRMAN WILSON: Does anybody use the
2 phage that was mentioned?

3 DR. EZZELL: The phage has gradually
4 caught on. May Chu has been one of the primary users
5 of the phage, but we have the phage, and also there
6 was a lot of the use of phage by Dan Kavanaugh and Jim
7 Wheelings when they many years ago were at WRAIR, at
8 the Silver Spring facility.

9 And in the Yersinia pestis lab, they were
10 using phage, which we now have at USAMRIID, but we do
11 not use it routinely. So I do not have a long
12 historical or a lot of historical data on the use of
13 phage. But May Chu has used the phage extensively and
14 has much better data than I do

15 DR. NACHAMKIN: Is the phase as easy to
16 use, for example, as gamma phage for anthracis?

17 DR. EZZELL: It is fairly easy to use
18 because this phage for Yersinia pestis can be dried
19 down on strips. The gamma phase does not lend itself
20 readily to being dried down and to be applied to the
21 strip.

22 But the phage, as it comes for yersinia
23 pestis, is a stable phage, and it can be applied as a
24 strip and standardized in that manner. And that is
25 the way May Chu handles it and how other people in the

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1 past have used the phage. It is a very stable phage.

2 DR. RELLER: So this is like putting it on
3 a plate, like an XV factor strip?

4 DR. EZZELL: Exactly. Exactly.

5 DR. GUTMAN: The classification is very
6 important, and performance is also very important.
7 But it doesn't necessarily drive us since we are
8 expecting to get submissions and ask questions of that
9 nature at the time that we give the submissions.

10 CHAIRMAN WILSON: Does anyone have any
11 other questions for Dr. Brown and Dr. Ezzell? Okay.
12 Thank you. Before we move on to the final
13 recommendation and vote, we want to open this up for
14 an open committee discussion and for panel members to
15 voice any concerns they have, and to ask any last
16 questions from either the representatives from
17 USAMRIID or FDA.

18 So at this point I would like to begin the
19 open committee discussion. Are there any issues that
20 we didn't cover this morning that are applicable to
21 both agents or the things that are unique to the
22 Yersinia pestis? Dr. Thrupp.

23 DR. THRUPP: Are we going to bundle?

24 CHAIRMAN WILSON: We have not gotten there
25 yet. Are there any specific issues where you feel you

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1 need more information?

2 CHAIRMAN WILSON: Okay. This form has
3 been put up on the screen, and for those of you who
4 can't read it from a distance, the question is, is the
5 in vitro diagnostic product information derived from
6 its use potentially hazardous to life, health, and
7 well-being when put to its intended use.

8 DR. NACHAMKIN: I'm sorry, but are we
9 going to be hearing them separately?

10 CHAIRMAN WILSON: We can do that. I am
11 assuming we are going to bundle them again, but I can
12 put that up to a vote.

13 DR. NG: I move for a bundle vote.

14 CHAIRMAN WILSON: Okay. We have a motion
15 for a bundle vote. Do we have a second?

16 DR. THRUPP: Yes.

17 CHAIRMAN WILSON: All in favor?

18 (Chorus of ayes.)

19 CHAIRMAN WILSON: All right. Would anyone
20 care to make a motion on the first question?

21 DR. THRUPP: Yes.

22 CHAIRMAN WILSON: Dr. Thrupp moves yes; is
23 there a second?

24 DR. NACHAMKIN: Yes.

25 CHAIRMAN WILSON: We have a second. Any

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1 further discussion? If not, all in favor?

2 (Chorus of ayes.)

3 CHAIRMAN WILSON: Okay. The vote carries
4 unanimately. Okay. The second question states is
5 there sufficient information to determine the general
6 controls are sufficient to provide reasonable
7 assurance of the safety and effectiveness of this
8 device.

9 In other words, if you vote yes, that
10 would be classified as a Class I device. Is there a
11 motion? Dr. Nachamkin.

12 DR. NACHAMKIN: I move that we vote no.
13 Again, for the same general reasons, in terms of the
14 implications of testing, and public health concerns,
15 et cetera.

16 CHAIRMAN WILSON: Okay. Thank you. Do we
17 have a second?

18 DR. THRUPP: Second.

19 CHAIRMAN WILSON: We have a second. Any
20 discussion? All in favor?

21 (Chorus of ayes.)

22 CHAIRMAN WILSON: Again, the vote carries
23 unanimately. Question 3(a) Considering the nature and
24 complexity of the product, and the available
25 scientific and medical information, is there

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1 sufficient information to establish a special control
2 or set a special control to provide reasonable
3 assurances of the safety and effectiveness of the
4 device.

5 And the implications of this question is
6 if you vote yes, it is classified as a Class II; and
7 if you vote no, it is classified as Class III. Do we
8 have a motion? Dr. Ng.

9 DR. NG: I move we vote yes.

10 DR. THRUPP: Second.

11 CHAIRMAN WILSON: We have a motion and a
12 second. Is there any discussion or comments? All in
13 favor?

14 (Chorus of ayes.)

15 CHAIRMAN WILSON: Again, a unanimous vote.
16 So, therefore, our recommendation is that the device
17 be classified in Class II. Moving on to 3(b), again
18 we have to specify the special control or controls
19 needed to provide such reasonable assurances. Would
20 anyone like to make any recommendations regarding
21 this? Dr. Thrupp.

22 DR. THRUPP: Yes. It seems that the
23 status is really very similar to where we were this
24 morning. I don't really think we have enough
25 information to establish quantitative performance

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1 standards.

2 And specific post-market surveillance
3 could be handled under the kind of motion that we set
4 up for restricted uses before. And so I would suggest
5 that as we did before that number three, testing
6 guidelines, could be derived from available
7 publications and experience, and should be both for
8 specimens, for procedures, for interpretation, and for
9 public health report.

10 CHAIRMAN WILSON: Is what you are
11 proposing that we essentially duplicate what we did
12 for the Bacillus anthracis under this question?

13 DR. THRUPP: Well, under part three,
14 testing guidelines, yes.

15 CHAIRMAN WILSON: Okay. We have a motion.
16 Do we have a second?

17 DR. NG: Second.

18 CHAIRMAN WILSON: We have a second. Any
19 further discussion? All in favor?

20 (Chorus of ayes.)

21 CHAIRMAN WILSON: The motion carries
22 unanimously. And we now skip the next several
23 questions, correct?

24 MS. SCHULMAN: Exactly.

25 DR. THRUPP: Could we come back to other?

1 CHAIRMAN WILSON: I assumed that we are
2 going to duplicate both of those.

3 DR. THRUPP: Well, I must admit that I
4 think we should respond with at least a little more
5 discussion to Dr. Ticehurst's comments, because in the
6 anthrax, we did not say anything about drug
7 manufacturing guidelines, and whether the FDA should
8 be encouraged to be more proactive in evaluating
9 actual production, especially should it go commercial.

10 So I wonder if we should add something to
11 this or perhaps to this morning's, because I have a
12 feeling that his comments were thoughtful and not just
13 off the cuff.

14 CHAIRMAN WILSON: Dr. Reller.

15 DR. RELLE: I don't know whether by
16 protocol we can go back, but I think the general -- or
17 perhaps I think we may get a general endorsement that
18 we would like to see special emphasis on enforcement
19 of GMP by FDA to these reagents for Yersinia pestis,
20 as well as for the reagents for Bacillus anthracis,
21 which are such a high priority for the public's
22 health.

23 MS. SCHULMAN: Very good, and that will be
24 part of the record.

25 CHAIRMAN WILSON: Dr. Nachamkin.

1 DR. NACHAMKIN: I have a few concerns
2 about putting in words for special emphasis for GMP,
3 and the reason is that since we are restricting the
4 distribution of these products to public health or
5 through the public health infrastructure, public
6 health laboratories are going to be in a very good
7 position to assess the quality of the reagents that
8 they are getting for subsequent distribution through
9 the infrastructure.

10 And to me that is probably better control
11 over what is being produced, and trying to enforce,
12 and the reason that I say that is because why should
13 we say, look, FDA, we want you to make a special
14 emphasis on monitoring the production of these
15 reagents when we have a whole laundry list of other
16 diagnostic devices that you are not doing now.

17 I would rather see them put their effort
18 into other diagnostic devices. I just don't know what
19 the priority is for this, in terms of assigning that
20 inspection process over what they already have on
21 their plate.

22 So, again, because of these other
23 restrictions, they may actually do a better job in
24 ensuring better quality production than if it is just
25 out there for regular laboratories.

1 CHAIRMAN WILSON: Dr. Thrupp and then Dr.
2 Reller.

3 DR. THRUPP: Certainly I would agree with
4 what you are saying, and that at the present time,
5 especially if the networking of data and follow-up to
6 all the things that we have discussed is implemented,
7 the chances are that nothing is going to go wrong.

8 But from a generic standpoint, given the
9 comments that actual FDA inspection has not been that
10 proactive, even for Class II's, and might be ideal,
11 and given that this is such a major BT agent, and two,
12 are such potentially major problems, and three, that
13 they could go commercial in terms of other
14 manufacturers aside from CDC or USAMRIID, I would
15 think that in a generic sense it would be prudent for
16 the FDA to have some encouragement to be more
17 proactive in case of broader developments in
18 manufacturing.

19 I am not questioning that the public
20 health labs aren't doing a good job at the present
21 job, but we don't have data, and the FDA doesn't have
22 data. It is kind of in-house with them, not that they
23 are not perfectly competent I'm sure.

24 I think it would provide an extra measure
25 of flexibility for the FDA to have encouragement

1 should they need it.

2 CHAIRMAN WILSON: Dr. Reller.

3 DR. RELLER: Actually, it was this latter
4 point that was my intent in the wording, and not in
5 any way to single out these agents vis a vis other
6 diagnostic reagents.

7 In other words, I agree with Irv, but it
8 is just that the opportunity is with us today for
9 these reagents, and I purposely asked the outsourcing
10 question because what is the source today, and what
11 the source for our public health LRN expanded network
12 tomorrow is, may be different as regards these
13 specific -- and I am not talking about new products
14 that come along for the recognition of Yersinia
15 pestis.

16 I am talking about these, and it seems to
17 me that the opportunity today is to endorse the
18 importance and the regulatory role of the FDA for GMP
19 in diagnostic reagents, whether or not it is another
20 Federal agency that is producing them, or whether
21 there is a decision made by that agency to outsource
22 the manufacturing of some or all components of the
23 reagent.

24 So it is seizing the opportunity to
25 emphasize the importance of special attention to GMP

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1 on these reagents, and not vis a vis other reagents.

2 MS. SCHULMAN: I was just going to add on
3 that that as I said, it will be part of the record as
4 being a Class II device being subject to GMPs and
5 subject to design controls.

6 But we can certainly share your concerns
7 with our colleagues in the Office of Compliance, with
8 panel transcripts and your concerns here with special
9 emphasis on that. But we cannot make it a separate
10 special control like reinspections. That is not done
11 under Class II devices.

12 CHAIRMAN WILSON: Is it legal or practical
13 to try and set up a two-tiered system for compliance
14 with GMP?

15 DR. GUTMAN: Well, two-tiered wouldn't be
16 the way that I would describe it. What I would
17 describe the input as I am hearing it from the
18 committee is to try and look at the way that things
19 are being prioritized, and it seems like this is
20 tempered with the notion that there may be other
21 devices around.

22 We passionately care about GMP, and so
23 this doesn't bother me at all; how we actually
24 translate it is a little bit tricky, if for no other
25 reason than it is done in a separate office.

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1 But we are happy to take that message
2 back, and have Compliance try to figure out how to do
3 the best job they can with what resources they have.
4 And you have the same dilemma you had with heart
5 valves again.

6 And they might choose heart valves before
7 this assay, and maybe this assay should be performed
8 ahead of things. So I think the recommendation is a
9 fair one. It may be hard to figure out what to do
10 with it, but you should make it anyway.

11 CHAIRMAN WILSON: Let me ask. You can't
12 hold one set of manufacturers to a different set of
13 standards than --

14 DR. GUTMAN: The standards are the same.
15 I think what John was referring to was the ability
16 that as you prioritizing how often you visit, no, you
17 can't. QSRs are QSRs are QSRs, and you can be a
18 little bit pragmatic in how you apply them in
19 different settings; but no, you can't change the reg
20 for one manufacturer from another.

21 CHAIRMAN WILSON: Then do we have a motion
22 to include this then as another condition?

23 DR. RELLER: In the wording, I purposely
24 used the enforcement component so that there is not an
25 issue of different GMP. But just an endorsement of

1 the importance of enforcement of GMP for these
2 products.

3 CHAIRMAN WILSON: Okay. Do we have a
4 second?

5 DR. THRUPP: Second.

6 CHAIRMAN WILSON: All right. All in
7 favor?

8 (Chorus of ayes.)

9 CHAIRMAN WILSON: Okay. The motion is
10 passed unanimously. Is there anything else that
11 anyone else wants to discuss under Item 3(b)?

12 Okay. Let's move on to the next one,
13 which I believe is 7(a); is that right?

14 MS. SCHULMAN: 7(a).

15 CHAIRMAN WILSON: Okay. Item 7(a) states
16 can there otherwise be reasonable assurance of the
17 safety and effectiveness without restrictions on the
18 sale, distribution, and use, because of any
19 potentiality for harmful effect or the collateral
20 measures necessary for the device's use.

21 MS. SCHULMAN: And it already is a
22 prescription device and this one will be a
23 prescription.

24 CHAIRMAN WILSON: And again this is a yes
25 or no?

1 MS. SCHULMAN: Right.

2 CHAIRMAN WILSON: And so we have a motion?
3 Dr. Ng.

4 DR. NG: I move and vote no.

5 CHAIRMAN WILSON: You vote no? Okay.
6 There is a second, and do we have any discussion on
7 this item?

8 (Chorus of ayes.)

9 CHAIRMAN WILSON: The motion carries
10 unanimously. For Item 7(b), continues that we need to
11 identify the needed restrictions, and again there are
12 four. The first one we discussed previously and does
13 not really apply to this.

14 So, Items 2 and 3 are used only by persons
15 with specific training or experience of its use, and
16 used only at certain facilities, and other, and is
17 there anything else that we want to add? Would anyone
18 like to make a motion?

19 DR. THRUPP: I'll do it. I would suggest
20 that we use the same phrasing that we used for
21 anthrax.

22 CHAIRMAN WILSON: Is there a second on
23 that?

24 CHAIRMAN WILSON: All in favor? Dr.
25 Beavis.

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1 DR. BEAVIS: This is a clarification for
2 me on this. When new reagents or new tests for this
3 come, will they necessarily be bound by this
4 restriction that everything goes to the public health,
5 or will that question be addressed with each new
6 reagent that is coming to the market?

7 CHAIRMAN WILSON: Dr. Gutman.

8 DR. GUTMAN: We will try to write the
9 language broad enough that it allows some flexibility
10 here.

11 DR. BEAVIS: Okay.

12 CHAIRMAN WILSON: All right. We have a
13 motion and a second. All in favor?

14 (Chorus of ayes.)

15 CHAIRMAN WILSON: Okay. Dr. Beavis, are
16 you abstaining?

17 DR. BEAVIS: I am abstaining.

18 CHAIRMAN WILSON: So, one abstention. We
19 do need a motion to adopt the second and third items
20 under this one as we did for the Bacillus anthracis.

21 DR. THRUPP: So moved.

22 CHAIRMAN WILSON: Do we have a second?

23 DR. NG: I second.

24 CHAIRMAN WILSON: All in favor?

25 (Chorus of ayes.)

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1 CHAIRMAN WILSON: Okay. The motion
2 carries unanimously. Then we can move on to the next
3 one.

4 MS. SCHULMAN: The supplemental data
5 sheet.

6 CHAIRMAN WILSON: Dr. Reller.

7 DR. RELER: Lest there be any confusion,
8 my understanding is that in the discussion of the
9 three reagents with Bacillus anthracis, and now the
10 three with Yersinia pestis, that what we have voted on
11 applies to these as before 1976 used as they are, and
12 used in the present, and manufactured, and we are
13 talking about this.

14 But that if there be in the future tests
15 for the recognition of Bacillus anthracis or for
16 Yersinia pestis that it is possible that they would be
17 categorized, classified, in exactly the same way, and
18 with the same restrictions.

19 That is, through you might say the
20 extended public health network. But that it doesn't
21 obtain absolutely and necessarily that that would be
22 the case. That they would be handled on their own
23 merits. Is that correct?

24 DR. GUTMAN: That is correct.

25 DR. RELER: Good. I think we are all

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1 happy with that. And as new technologies come out, et
2 cetera, and are an entirely different nature, and
3 obviously the target may be the same, but the
4 methodology may be quite different.

5 CHAIRMAN WILSON: All right. Marge, would
6 you like to walk us through the next one?

7 MS. SCHULMAN: Certainly. Number 3 is
8 device and implant, and Number 4, the indications for
9 use.

10 CHAIRMAN WILSON: And there is one comment
11 from Dr. Nachamkin.

12 DR. NACHAMKIN: I was just thinking about
13 when we were talking about having no authority over
14 environmental testing. Does that also mean that for
15 these small shop operations that are coming out with
16 these rapid immuno cards or whatever that are being
17 marketed for mostly to pander to the public hysteria
18 as opposed to any real benefit, can those be -- is
19 there some way for us to include those as diagnostic
20 tests so that they can't escape the review process for
21 -- I am sure there is a gray zone there.

22 But I am really concerned that there is
23 going to be a flurry of that kind of stuff that is
24 already out there, and we need to think this out in
25 our review.

1 DR. GUTMAN: There is no way that you can
2 take a company that is marketing it as an
3 environmental claim, and force them to meet diagnostic
4 criteria. You can make recommendations that the
5 agency try to explore ways of dealing with that, or
6 you can contact EPA, or contact your Congressman.

7 But the FDA laws don't really give us a
8 great deal of opportunity here. There are agencies
9 that are supposed to have oversight over this
10 legislation. In terms of scientific validity, we are
11 really at the edge of our regulatory paradigm,
12 although we are cognizant of the issues, they are very
13 real, and we would be interested in collaboration and
14 discussion with others on whether there were
15 mechanisms to explore.

16 CHAIRMAN WILSON: Dr. Reller.

17 DR. RELLER: So that if someone -- it
18 would be basically having a false advertising claim
19 that would come under the FTC, whether or not they
20 have the wherewithal to pursue all of these things.

21 But on the other hand, there is no
22 obligation, I don't think, for a properly led clinical
23 microbiology laboratory or public health laboratory to
24 say no to inappropriate testing.

25 In fact, the CAP requires that there be

1 rejection criteria, right, Mike?

2 CHAIRMAN WILSON: That's correct.

3 DR. RELLER: And this provides another
4 venue, at least in the clinical laboratory, to say
5 this is inappropriate. We reject a lot of specimens
6 that are just inappropriate.

7 So if somebody sent us the flag off of a
8 mailbox, we wouldn't test it. Full stop.

9 DR. THRUPP: But that does not address --

10 DR. NACHAMKIN: That wasn't really my
11 question. Well, for device development, and intended
12 use.

13 DR. GUTMAN: It doesn't address
14 environmental hand-held tests that might be sold
15 either to fire people as environment tests, or even
16 over the counter, I suppose, environmental tests would
17 be legal, and if you wanted to push us, I suppose we
18 could demonstrate some intent to sell that to health
19 care practitioners for use in labs for diagnostic
20 purposes, and we could explore the possibility.

21 But if I were a clever manufacturer, I
22 just wouldn't do that. I would make it very clear
23 that it was an environmental test.

24 DR. NACHAMKIN: But I guess the purpose is
25 that if somebody or a company is producing this little

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1 device to say you should screen your environment for
2 Yersinia pestis, what is the user supposed to do with
3 that if they find it is positive.

4 And doesn't that have some adverse health
5 implications if they do get false positives, and then
6 you are making them jump from just an environmental
7 test to some potential impact on health care, and to
8 me that crosses the line between environmental testing
9 and at least in diagnosis, I guess.

10 And I think that might be a way to get at
11 some of these devices.

12 DR. GUTMAN: I would really prefer not to
13 argue with that line of reasoning. I am not sure I
14 disagree with it, and again I would suggest that if
15 you are passionate about this to go ahead and make a
16 recommendation. Again, I don't want to make promises
17 that I can't keep.

18 DR. NACHAMKIN: Well, I guess I am just
19 asking for advice, and is there some wording that we
20 could use in this document?

21 DR. GUTMAN: Well, I know where you are
22 going and I understand your concerns, and they are not
23 new, and they are not wrong, they are right. I am
24 just not clear whether your legal argument is one that
25 I could convince our legal staff to follow. I will

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1 share this recommendation with people who are more
2 important than me.

3 MS. SCHULMAN: Number 4, the indications
4 for use, and we have it up on the overhead now, and we
5 have given it to you in our panel packet if you want
6 to take a second to check it out and agree.

7 DR. SHIVELY: I would clarify this is the
8 panel packets you were sent, and not the one you have
9 in front of you.

10 CHAIRMAN WILSON: Again, I think the
11 wording on this is similar to what we saw on the
12 Bacillus anthracis usage statement, and so it may need
13 to be modified as we indicated previously.

14 DR. SHIVELY: Actually, this one has the
15 antibodies detection segment in it.

16 DR. RELLER: This one has the antigen, but
17 not the phage. The other one had the phage, but not
18 the antigen.

19 CHAIRMAN WILSON: And it uses the word --

20 DR. SHIVELY: It has phage down here.

21 DR. RELLER: Oh, I'm sorry.

22 CHAIRMAN WILSON: Okay. We do need to
23 vote on this. Would anyone like to make a motion?
24 Dr. Nachamkin.

25 DR. NACHAMKIN: Motion to accept the

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1 prescription.

2 CHAIRMAN WILSON: We have a motion and
3 second? Any discussion on it? All right, all in
4 favor?

5 (Chorus of ayes.)

6 CHAIRMAN WILSON: The motion is approved
7 unanimately.

8 MS. SCHULMAN: Number 5, the
9 identification of any risks to health presented by the
10 device, and we can safely agree what was discussed in
11 the earlier discussions about this device.

12 CHAIRMAN WILSON: And we need to vote on
13 this again. Are there any comments or discussion that
14 people would like to make? Okay. I need a motion on
15 this.

16 DR. THRUPP: We need to come up with
17 separate wording on this one?

18 CHAIRMAN WILSON: We just have to vote
19 that we approved it as discussed.

20 DR. THRUPP: So moved.

21 CHAIRMAN WILSON: All right. I have a
22 motion and a second. All in favor?

23 (Chorus of ayes.)

24 CHAIRMAN WILSON: Okay. Approved
25 unanimately.

1 MS. SCHULMAN: Number 6, recommend an
2 advisory classification prior to the classification,
3 and again we don't have time frames associated with
4 this, and it would be when you would like to see us
5 write the guidance, and the draft regulation.

6 CHAIRMAN WILSON: We need a vote on this.
7 Dr. Ng.

8 DR. NG: I move that we classify this as
9 a Class II of high priority.

10 DR. THRUPP: Second.

11 CHAIRMAN WILSON: The motion is seconded.
12 Any discussion or comments?

13 (Chorus of ayes.)

14 CHAIRMAN WILSON: Thank you.

15 MS. SCHULMAN: Okay. Number 7 is device
16 and implant that is life-sustaining or life-
17 supporting, and has been classified in a category
18 other than Class III, explain fully the reasons for
19 the lower classification and supporting documentation,
20 and data, and you can say if you agree or add anything
21 to it as discussed in a panel meeting with the special
22 controls.

23 CHAIRMAN WILSON: Do you want us to vote
24 on that one?

25 MS. SCHULMAN: We don't have to. There is

1 nothing else to add. Number 8, a summary of
2 information, including clinical experience and
3 judgment upon which the classification and
4 recommendation is based. This can also be answered by
5 as discussed by the panel meeting, unless there is
6 anything else to add.

7 CHAIRMAN WILSON: Is there anything else
8 anyone else would like to add? Okay.

9 MS. SCHULMAN: Number 9, identification of
10 any needed restrictions on these devices, and this can
11 be answered as discussed in 7(b) of the general
12 questionnaire.

13 CHAIRMAN WILSON: Is there anything that
14 anyone would like to add to that? Okay.

15 MS. SCHULMAN: And Number 10, it does take
16 class longer because of the change in the law, and if
17 you want it to be exempt from pre-market notification.

18 CHAIRMAN WILSON: Do we need to vote on
19 this?

20 MS. SCHULMAN: Yes.

21 CHAIRMAN WILSON: Dr. Nachamkin.

22 DR. NACHAMKIN: Motion that we vote now.

23 CHAIRMAN WILSON: And the motion is
24 seconded. Any discussion on that? Any questions?
25 All in favor?

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1 (Chorus of ayes.)

2 CHAIRMAN WILSON: Okay. Thank you.

3 MS. SCHULMAN: Number 11, existing
4 standards, for this device, is there anything that you
5 would like to add about this device?

6 CHAIRMAN WILSON: Is there anything that
7 anyone would like to add to this section?

8 MS. SCHULMAN: Then we need to vote on the
9 form as they are completed and as a Class II device.

10 CHAIRMAN WILSON: And we will vote on the
11 two forms together. We need formal approval to accept
12 the information contained in the two forms. Anyone
13 who would like to make such a motion?

14 DR. THRUPP: I do. So moved.

15 CHAIRMAN WILSON: Do I have a second?

16 DR. NACHAMKIN: Second.

17 CHAIRMAN WILSON: The motion is seconded.
18 Any discussion or last comments? All those in favor?

19 (Chorus of ayes.)

20 CHAIRMAN WILSON: Okay. The motion passes
21 unanimously.

22 MS. SCHULMAN: Thank you.

23 CHAIRMAN WILSON: And thank you. At this
24 point, I think we can conclude the day's business. I
25 would like to thank everyone who attended today --

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1 guest panel members, panel members, and the FDA,
2 particularly Drs. Brown and Ezzell for coming today,
3 and if there is no further business, I would like to
4 adjourn.

5 (Whereupon, at 4:18 p.m., the meeting was
6 concluded.)

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CERTIFICATE

This is to certify that the foregoing transcript in the
matter of: Microbiology Devices Panel Meeting

Before: DHHS/FDA/CDRH

Date: March 7, 2002

Place: Gaithersburg, MD

represents the full and complete proceedings of the
aforementioned matter, as reported and reduced to
typewriting.


