however.

DR. GREENBERG: Thank you. That was helpful. So following history we start over there in the right-hand corner. Dr. Edwards.

DR. EDWARDS: Yes.

DR. GREENBERG: We're doing 1(A) now. Just 1(A). I'm going to read the question to you again. Can we use existing immunologic correlates to predict protection -- we took out existing. Good. Can we use immunologic correlates to predict protective efficacy of meningococcal conjugate vaccines for individuals for which the current polysaccharide vaccine is licensed?

DR. EDWARDS: Yes. With the data that was presented and the fact that we have a product that appears to be superiorly immunogic from the previously licensed product makes me comfortable in saying yes.

DR. GREENBERG: Dr. Daum.

DR. DAUM: I want a new seat.

DR. GREENBERG: Pardon me?

DR. DAUM: I want a new seat.

DR. GREENBERG: No way. This is the big leagues.

DR. DAUM: What about question zero?

DR. GREENBERG: I think we have an idea of

how this is going to be used. In fact, nobody is -- you know, this is assumed that this data is going to be used to give the manufacturers some feeling about what the informed and appropriate academic or regulatory constituency thinks will be needed for moving forward.

DR. DAUM: Well, do you want just one word or do you want --

DR. GREENBERG: I want one word and a relatively concise explanation of your word.

DR. DAUM: I feel wishy washy about this question because I heard data that suggested that two different kinds of assays have promise of being very valuable tools for assisting in what I think should be done which is an efficacy trial in young infants. Am I convinced that --

DR. GREENBERG: This is adults. This is 1(A).

DR. DAUM: This is 1(A). So my answer is a qualified yes but I would like to have more data and more clinical situations and address such issues as duration of antibody response of primanian and carriage to go with. It's a yes, I think we're on the right track but I would like more.

DR. GREENBERG: I would just like to remind

people if I understand things right, this question of correlates was already crossed with the polysaccharide vaccine where efficacy was not demonstrated with the Y and whatever the other value is --

DR. FERRIERI: W135.

DR. GREENBERG: -- because the same question, it's impossible to do a study so correlates were used for those already. You are not blazing totally new ground here.

DR. FRASCH: It was also used when we went from a 14 ml meningococcal vaccine to a 23 ml meningococcal vaccine.

DR. GREENBERG: Dr. Griffin.

DR. GRIFFIN: I think for the -- yes for the license because we do have a background of a license vaccine for which we know the kinds of responses we can get which we can compare directly to the conjugate vaccine. I'm comfortable with 1(A).

DR. GREENBERG: Dr. Snider.

DR. SNIDER: Yes, for the reasons that have been articulated thus far. I would say that to the extent that it seems reasonable to use more than one immunologic correlate and I would supplement it with whatever additional data on animal challenge Phase IV data from the U.K. might be available at that time.

DR. GREENBERG: Dr. Stephens.

DR. STEPHENS: Yes.

DR. GREENBERG: Ms. Fisher?

MS. FISHER: This is for adults?

DR. GREENBERG: This is 1(A). This is question 1(A) which is adults. The question is for the people for whom the polysaccharide vaccine is currently licensed.

MS. FISHER: I believe there should be clinical trials. No.

DR. GREENBERG: Okay.

MS. ESTES: Yes, and I echo Dixie's comments.

DR. GREENBERG: And I finally realize that there is one good thing about being the chairperson and that is you get to vote last.

DR. FAGGETT: Okay. I share Ms. Fisher's concerns but I'll vote yes and really, Barbara, my reason for it is I'm hearing that they are not equating clinical trials with the correlates. There is no way of equating. You know, there's not an equal weight been given that clinical trials were mainly gold standard and that's why I'm voting yes.

DR. GREENBERG: Dr. Karzon.

DR. KARZON: I vote yes. I would like the

FDA to look into the various methodologies used in the assay controls and make certain that they are the best possible to defend because there were differences that were unresolved, various groups claiming excellence or different levels of excellence.

For part A I don't happen to know what permissiveness is stated in this category. Does that mean all people right now?

DR. GREENBERG: Over the age of two.

DR. KARZON: So at the moment this means all individuals above the age of 2.

DR. GREENBERG: Yes.

DR. KARZON: And it hasn't really been used that way. Has it?

DR. GREENBERG: I think it has been used that way.

DR. KARZON: I don't know many pediatricians who at the age of two --

DR. GREENBERG: Not generally used that way but if there's a case in a house and there's a kid over the age of two, I think they --

DR. KARZON: So this is used on call with concerns of epidemics?

DR. GREENBERG: No.

DR. FRASCH: The children of this country

beginning at age two are not being immunized with this product. What I'm concerned about is what we are permitting and what will be done under this 1(A). Will this be a go-ahead to mandate or recommend that all children beginning at two should have this product?

DR. GREENBERG: I don't see -- I can't imagine anybody anywhere coming away from this conversation with that interpretation of what has happened here.

DR. FRASCH: But the other thing is the FDA approves the CDC ACIP actually is the one who exactly has a dyconomy about of these subjects.

DR. KARZON: Well, I think my thoughts have been registered.

DR. GREENBERG: Yes. Good. Dr. Huang.

DR. HUANG: Oh, I agree with Dixie and Walt's comments and I would only go so far as to say that when these correlates are used and today because we've heard about different types of correlates, that there needs to be some standards set or outcomes testing that would be extremely important for accepting these kinds of correlates. My response is yes.

DR. GREENBERG: Dr. Breiman.

DR. BREIMAN: I agree with that comment. I also would want to echo what Dr. Griffin said that really I think for 1(A) we're talking about immunologic noninferiority based on the information we have now anyway. If we look at it that way, I'm comfortable.

DR. GREENBERG: And Dr. Ferrieri.

DR. FERRIERI: 1(A) I vote yes for all the reasons articulated by Dixie Snider and others.

DR. GREENBERG: And, for the record, I incur and think that you've all done a very good job of putting all the caveats that are important on that answer. I would like to now move --

DR. FAGGETT: One question. Could we go back to Barbara and see if she has had a change of heart?

DR. GREENBERG: We can. I actually know very little about parliamentary procedures. I do not know whether legally I can do that but I'm happy to do it. I think people vote their conscience and that is fine with me.

DR. FAGGETT: I was just interested if she had any different opinion.

DR. GREENBERG: Fine.

DR. FERRIERI: We like diversity of votes.

DR. GREENBERG: So I would like to now move to question 1(B) and, of course, Dr. Edwards. You know, we picked who sits in that seat. Let me read the question again for you and that is can we use immunologic correlates to predict protective efficacy of meningococcal conjugate vaccines for infants and toddlers below two years of age?

DR. BREIMAN: Can I just ask -- I'm sorry. One more clarification. Is this like saying might it be possible someday to?

DR. GREENBERG: Carl?

DR. BREIMAN: Is that what's meant or, again, given the data that were currently presented -- I mean presented that are currently available.

DR. GREENBERG: So we took out existing.

DR. BREIMAN: I know but I just would like Carl's nuance.

DR. GREENBERG: Carl, could you give us your feeling about that?

DR. FRASCH: Once upon a time the -- I think the question is very general, can we use immune correlates. It doesn't really specify a time or exactly the ones we heard today.

DR. GREENBERG: Bill.

MR. EGAN: Bill Egan from FDA. Yeah, I

think to get to the bottom line what we're talking about is how to set up a trial that could be used to demonstrate efficacy that could then be used for licensure. The question turns out to be does an immune correlate exist? First, for older individuals and then for children under two that could be used to support licensure. I mean, that's what we're talking about here.

I think this addresses Dr. Karzon's comment as well, what are you supporting and it's basically the decided conduct of the trials to support licensure. Ms Fisher was quite correct that vaccines are licensed on the basis of their demonstrated safety and efficacies.

DR. GREENBERG: Kathy.

DR. ESTES: I think, as everyone agrees, this is a difficult question. I think it's maybe even more difficult by the epidemiologic data for the U.S. that is shown where a good percentage of the disease is B. Certainly we are further behind in the generation of a B vaccine. I think for the U.S. it's going to be almost inconceivable that such a study could be conducted here given the epidemiology disease.

Then you would say, well, maybe this study

could be conducted in Africa looking at A. Then you would have to suppose that the correlate of A immunity is probably the same as C and D be correct.

I guess I'm struggling with the fact that yes, as with apple pie and motherhood, it's always better to have a randomized clinical trial, but also I'm struggling with whether it's really doable with the epidemiology of the disease that we have.

I guess what I would say I think that we should prefer to have a randomized trial to determine the efficacy and also to have serologic studies done so that if possible we can determine a correlate. But if that's not feasible, I don't think that we should say no and the vaccine could not be licensed without using other correlates.

I feel that we really need to make certain that all stops have been pulled out to try and get the efficacy trial that we so deserve or desire, but that we also have to be somewhat reasonable. If that's totally inconceivable, then we should use additional data such as immunologic correlates.

DR. GREENBERG: So your answer is a yes with lots of --

DR. ESTES: Caveats.

DR. GREENBERG: -- qualifiers.

DR. ESTES: Right.

DR. GREENBERG: Thank you. Dr. Daum.

DR. DAUM: I think Kathy and I are really at the same place. The only thing that I would, I guess, like to raise again is if the word existing were in that question for this age group, my answer would be no. Otherwise, I agree with the philosophy and flavor that Kathy espoused.

DR. GREENBERG: I think that is a very important thing to get down, Nancy, because I wager that if we put existing, and, Carl, you should be listening to this, if existing were in that statement, I'm willing to poll if you want it but I would bet the answer to this will be no if we put existing in that question. So I think that is just an important message for everybody to hear.

Diane.

DR. GRIFFIN: I agree, for me at least, because I do not feel currently comfortable, particularly in this age group will I don't think that we have a full understanding of what protection is and that it may be different than it is in the older age group. It may not be.

I mean, I think one possibility is you could say, okay, if you've got the levels -- if you've got

exactly the same immunity as you get in adults, then that would be great but that's highly unlikely we're not going to get that in that group. I have a very highly qualified -- I mean, to be highly qualified no or a highly qualified yes but I'm very comfortable with saying yes to this.

DR. GREENBERG: Okay. Dixie.

DR. SNIDER: Yes, with the qualifiers that have already been stated.

DR. GREENBERG: Dr. Stephens.

DR. STEPHENS: Yes, with the emphasis on the clear need to develop a standardization of these assays which I think is the message that we are all kind of echoing.

DR. GREENBERG: Ms. Fisher.

MS. FISHER: No, I don't think there's enough information. I think you cannot deal in theoreticals. I think that we have to maintain the highest standards as possible and that would include particularly in children in a clinical trial to demonstrate efficacy.

DR. GREENBERG: Dr. Estes.

DR. ESTES: I'm actually going to vote no on this. I think the evidence that I've seen to date does not convince me. At some point in the future I

might be convinced but I would vote no at this point.

DR. GREENBERG: Dr. Faggett.

DR. FAGGETT: Yes, I kind of agree with those two previous speakers that this indeed is another instance of a need for more clinical trials in the pediatric age group. The way this question is stated, however, in that we talk about using the correlates to predict efficacy, then I will give a qualified yes.

DR. GREENBERG: Okay. Dr. Karzon.

DR. KARZON: This is a very difficult – decision to make. At one time, on the one hand, this age group is at very great risk and they need this vaccine eventually more than any other single group. Yet, we have no experience with any vaccine of this sort in infants at this point. There's a big conflict in me to just go ahead.

We usually have more data on adverse events before we proceed to full use licensure. In this age group sometimes there are adverse events that may be unique. I'm very reluctant at this time. I think maybe the best pattern is to go ahead with the older groups where we have some experience with these vaccines and get more data.

I didn't want to say so when I was

suggesting what we have to do as a preamble, but if we get material from the U.K., I didn't want that in the record. Since somebody has brought it up, I would be more comforted too. I am concerned about adverse events that we can't imagine at this point. Most of them we can't imagine that do show up. So I would go and make that a second step.

DR. GREENBERG: So to get a precise answer here, do you --

DR. KARZON: A precise answer would have to be no. I think the basis of it is important because it is much needed.

DR. GREENBERG: Dr. Huang.

DR. HUANG: Not being a pediatrician, I notice that our pediatric colleagues voted two to one so I go along with yes.

DR. BREIMAN: Well, in the absence of more standardized tests and also a better defined threshold, I just want to make it clear that I would vote no. Again, I'm reading this question as saying assuming those things can be developed, would we at some point use this approach to establish or predict efficacy.

My belief is that we are going to need to do that because, as I said before, the variety of

products that we are going to be evaluating. I think the answer again is a qualified yes. At some point we will need to use that but not until these other steps are accomplished.

DR. GREENBERG: Dr. Ferrieri.

DR. FERRIERI: Well, I've given a lot of thought to this and my final vote is a yes but with qualifications so that my answer yes is on the basis of acquiring more information on the immune response and the translation of that to clinical efficacy from any of the immunologic correlates. My vote of yes does not support or exclude in any way the use of clinical efficacy trials.

DR. GREENBERG: Okay. And, for the record, I vote yes with at least as many qualifications as everybody else has added. I think that it would be a mistake for anybody to come away from this thinking anything other than we would like a lot more proof of correlation before passing on a vaccine in infants for licensure. That case was not made sufficiently here is what I would say. That can be gotten, I hope.

Okay. I'm hoping that the next two questions will flow from that first one very simply, not the least of which is because I want to get out of here. I am going to --

DR. FERRIERI: These are tougher.

DR. GREENBERG: So I thought we needed to discuss that first one. It's a very hard question. The second question is for both age groups can the presence of bactericidal antibodies be used as a measure of functional and, therefore, presumed protective activity. I would just like to say Carl has said for both age groups. It seems to me that to shortcut this discussion, you just heard that people have a lot greater feeling about the older age group than the younger age group in the use of, I assume, since the bactericidal looked like the better correlate, that they feel much more comfortable in that older age group. In some sense saying for both age groups is obscuring this question a little bit but we'll go with it the way you have written it. Do I have --

DR. STEPHENS: Can we discuss this question? We haven't.

DR. GREENBERG: Not really so let's discuss the question if you want to discuss it.

DR. FERRIERI: I would like to make a point regarding this issue and that is the relative protection from disease within the first two months or so of life is a reflection of placental transfer and

maternal antibody in individuals who fall within various Fothergill Wright types of curves. So by inference, even in the youngest age groups we might presume that the serum bactericidal activity is a correlate of protective activity independent of age.

DR. GREENBERG: Dr. Stephens.

DR. STEPHENS: Can I ask for a clarification? Do you mean antibodies or do you mean activity, Carl? Although we presume that these are bactericidal antibodies, and I think that's right, it's activity that the assays, in fact --

DR. FRASCH: It's bactericidal activity. However, I would like to make a comment. I think my impression is that some people are confusing the correlate with how they are going to measure the correlate, i.e., the rabbit complement or human complement or the dilution and so on. I don't want to get involved with the how as much as the correlate itself.

DR. GRIFFIN: I guess I would ask for one clarification. Do you mean as the sole measure here? It says as the measure.

DR. GREENBERG: No. It was changed. Any other discussion of this question? Dr. Daum.

DR. DAUM: I would like to ask, I guess, my

sort of standard question. Do you mean existing information or do you mean -- I mean there are two ways you can interpret this. One, a prospective randomized trial was done today and sera were taken from the control group and from the experimental group. The kids who were protected all had bactericidal activity. The kids that were not protected didn't. Would I accept that? Of course I would.

In the absence of such a trial with just what we've heard and just what exist, is there enough information to say that I know what the protective bactericidal activity level is and I'm comfortable predicting efficacy from it? That's a different question.

DR. FRASCH: I don't think I see the word level in the question.

DR. DAUM: So we're talking presence or absence.

DR. FRASCH: Yes. We're not trying to pin down any level. I thought we just heard earlier today a very convincing study from Ft. Dix. They bleed all the recruits when they arrived, they figured out who had bactericidal at the initiation of their training. They waited to see who got disease and who didn't get

disease. Then they sorted out whether they fell into the group with or without bactericidal activity.

DR. DAUM: There weren't many children in that study.

DR. FRASCH: I don't think we're talking specifically children.

DR. GREENBERG: It says for all age groups there, or for both age groups.

DR. FRASCH: I'm just saying the study that he's talking about was done in adults and not in children but the study was done. I think we had this same problem initially with hemophilus in that we didn't really know or didn't accept that because bactericidal is protective in the older population that it is protective in the infant. I think these are some of the same problems we had then.

DR. GREENBERG: Dr. Karzon.

DR. KARZON: I'm a little puzzled in the sense that two we voted on when we voted for one.

DR. GREENBERG: Well, not --

DR. KARZON: We --

DR. GREENBERG: Dr. Egan.

DR. EGAN: If I could try to just shed a little bit of light in this again. The question one was really asking does the correlate of immunity exist

now for older kids, for younger kids. We voted on that. If you said yes to one, then I think the second question is asking is this the correlate of immunity. Is that right, Carl?

DR. FRASCH: Yes. Exactly.

DR. EGAN: So now you're asking for everyone who voted yes is this the correlate of immunity.

DR. STEPHENS: I think it's not the word "the."

DR. EGAN: A correlate. I stand corrected. A correlate of immunity. There may well be more than one. Is this a correlate of immunity.

DR. GREENBERG: And a correlate of immunity doesn't mean a sufficient correlate of immunity in my mind.

DR. EGAN: Well, a correlate of protection.

DR. GREENBERG: Well, I mean, I think that is the critical question here as to whether we are saying this is a sufficient correlate of protection to be used for registration.

DR. EGAN: If I want to go back to follow Ann and talk about history, the first three Hib conjugate vaccines were used in infants. Those were licensed on the basis of efficacy trials. The fourth one, the Pasteur Merieux Connaught conjugate vaccine,

that was based on a correlate of immunity, namely the level of serum antibodies, the .15 and 1 microgram per ml that Carl mentioned before.

DR. GREENBERG: I think --

DR. GRIFFIN: But it's different having had those three trials.

DR. GREENBERG: Oh, you bet it's different. I am reading this as it is a measure. We're not saying it is a sufficient measure for basing licensure. I think we can go ahead and ask the question now.

DR. ESTES: For both age groups I think it's quite clear that bactericidal antibodies are functional assays. That's how they are measured. As was said before, the protective antibody against encapsulated bacteria is a bactericidal antibody. I think I would answer yes to this question.

DR. GREENBERG: Dr. Daum.

DR. DAUM: I can't help it. I end up confused about what the question is really asking. I don't want to raise the points again because we've already raised them. I think that this bactericidal activity can be used probably to predict efficacy and outcome and I still would like to see a trial where this is one of the things that is measured and

particularly for young children.

DR. GREENBERG: So I would say your answer is yes but you're concerned that it's not sufficient for registration.

DR. DAUM: Particularly for young children.

DR. GREENBERG: Yes. Dr. Griffin.

DR. GRIFFIN: Yes, necessary but not sufficient.

DR. GREENBERG: Dr. Snider.

DR. SNIDER: I'd say yes. The presence of the bactericidal antibodies can be used as a measure. I think other measures should be used. Even in regard to that measure, people are going to bring data before this committee. I think that we would like to see, as a personal opinion, that the laboratory that was performing it, either there was more than one laboratory performing it or there was some kind of quality assurance to give us reassurance that what that one laboratory was measuring could be validated in another laboratory.

DR. GREENBERG: Dr. Stephens.

MS. CHERRY: Before we go, I'm sorry. I missed the first couple of votes. Can I have the one-word answers?

DR. GREENBERG: They were yes, yes, yes, and

yes.

MS. CHERRY: Okay.

DR. GREENBERG: Dr. Stephens.

DR. STEPHENS: Yes, I think it can be used. The presence of bactericidal activity -- again, I want to emphasis that point -- can be used as a measure of functional protective activity. I think there are a lot of caveats that have already been echoed and I support those caveats.

DR. GREENBERG: Ms. Fisher.

MS. FISHER: It would seem that the evidence that was present today does suggest that the presence of bactericidal activity is involved in immunity. However, I'm having trouble with how the question is asked here because I do think that it is very strong in suggesting that could be used as the only correlate when we don't know if there are other factors involved in truly enduring immunity.

DR. GREENBERG: I think you are correct and I think everybody else. You can say yes and say but I don't think it's sufficient to judge for efficacy. It is a measure. Or you can vote no.

MS. FISHER: If I vote yes, then with that kind of caveat is that on the record or -- I mean, are all these caveats on the record?

DR. GREENBERG: I hope so. We are being recorded. Every hiccup I make is on the record I hope.

MS. CHERRY: Yes, there is a transcript. This is an open meeting. The transcript will be on the Internet.

MS. FISHER: Because intellectually I think my answer would be yes, there is evidence that it is involved in immunity but clearly we have large gaps in knowledge in knowing if it is the only factor involved in true immunity, particularly in children.

DR. GREENBERG: Okay. Thank you.

MS. CHERRY: That's a qualified yes?

MS. FISHER: Yes.

DR. GREENBERG: Dr. Estes.

DR. ESTES: I also vote a qualified yes with the qualifications that have been said.

DR. GREENBERG: Dr. Faggett.

DR. FAGGETT: I agree that the presence of bactericidal activity is a measure and I do give a qualified yes to that fact.

DR. GREENBERG: Dr. Karzon.

DR. KARZON: I say yes with the same caveats.

DR. GREENBERG: Dr. Haung.

DR. HUANG: Yes with the same caveats.

DR. GREENBERG: Dr. Breiman.

DR. BREIMAN: And I would say yes, we can use it but we don't know how to use it.

DR. GREENBERG: And, for the record, I vote yes with all of the same -- oh, I'm sorry. Who did I miss?

DR. FERRIERI: We will remember.

DR. GREENBERG: I'm sure of it.

DR. FERRIERI: I vote yes, Harry, and I want for the record to indicate that I think we need more information on the younger children.

DR. GREENBERG: And I agree and I vote yes. So we are now down to the last question and we'll see how quickly we can deal with this. Can total antibody quantitative by ELISA be used as a surrogate for functional bactericidal antibody and, therefore, for protection? That's the question. Do I have any discussion?

DR. HUANG: Harry, I think this one the wording is such that total antibody and that immediately reminds us of the comparisons between the high avidity ELISAs and the IgG versus total antibody. It is clear that total antibody does not correlate with functional bactericidal activity and does not

correlate with protection. I think this is fairly straight off now.

DR. FERRIERI: I agree with Alice.

DR. GREENBERG: Do I have any other discussion of that before we have a vote? Dr. Daum, do you want to discuss it?

DR. DAUM: I have two very brief comments. First of all, we heard about three different ELISAs, at least broadly speaking. I think the answer might not be the same to all three. At least mine wouldn't. Secondly, I think it was Dr. Huang that said it doesn't correlate with bactericidal. I think it did correlate but much less. I think there was still a correlation.

DR. HUANG: Total antibody did not.

DR. DAUM: Even total correlated but it's just would we be happy with it. The answer to that is clearly no because the correlation was much lower but it was still a correlation.

DR. HUANG: Not in quantitation. That's the second word you have to read.

DR. GREENBERG: Okay. Any other comments about this question?

DR. FERRIERI: Well, I would like to clarify something Carl put up at the end, the data on the

British Columbian study in children two to six years. If I understood the data then, Carl, and this is what unsettles me so much, in the children two to six years, of whom a very high percentage had antibody greater than two micrograms by ELISA, there was a disfunction, lack of correlation with those who had a bactericidal titer that was -- this is where I'm not sure of -- greater than 1 to 4 or greater than or equal to 1 to 4?

DR. FRASCH: No, greater than.

DR. FERRIERI: Greater than 1 to 4. I guess we need it broken down for those who are just 1 to 4. I find that as well as other data presented today to undermine my confidence and this is why I don't feel I can vote yes for this.

DR. FRASCH: I think since you mentioned the slide from Vancouver, I think clearly the ELISA that was used for that assay did not correlate.

DR. GREENBERG: Before we start voting, I'd like to make one statement for the record. That is, in this type of discussion that is actually relatively technical and very data driven rather than notion driven, I find it hard to analyze the data for the first time at this meeting and to be as on top of it as I could be.

The next time we do this, if we could get the serology and the comparisons beforehand. Instead of if I sit there on the airplane getting bored and not wanting to do my reviews, I might be a better informed panel member. I know that is sometimes difficult. This type of stuff with a 30-year history of serology, we could have been better prepped. Now I will ask Dr. Edwards.

DR. EDWARDS: I think using the data that the PMC, for instance just as one example, clearly shows that there is a disconnect between the ELISA and the bactericidal assays. Given all the data that was presented about the problems with the ELISA, I think that I strongly feel that I must answer no to this, that the total ELISA antibody does not appear to be a surrogate for functional activities because we really weren't shown that.

Now, whether it may ultimately buy additional assays or refinements or other things, that is another issue. But with what we were shown today, no, there does not appear to be a correlation or it cannot be a surrogate.

DR. GREENBERG: Dr. Daum.

DR. DAUM: I concur with Kathy's comments but would like to say one other thing. That is, that

I saw data from two other ways of doing the ELISA which looked like they were promising. Those were presented from Chiron and Dr. Granoff and many others who worked on that. Also from Dr. Medor from Wyeth.

I would like to see more data about those two approaches. I don't understand why high avidity antibody would correlate better and why low avidity antibody wouldn't. Without understanding that, I'm reluctant to get real excited about saying yes to that.

They certainly put up on a graph with a — bactericidal antibody and high avidity antibody, or Dr. Medor's company's technique. Those look like they have promise. While the total antibody ELISA, clearly I would not be enthusiastic about the correlation which looked fairly poor to me. The other two techniques looked like with explanation and underpinnings and more data might be useful.

DR. GREENBERG: So the answer was no with those caveats. Correct?

DR. DAUM: The answer as it's written.

DR. GREENBERG: Yes. Dr. Griffin.

DR. GRIFFIN: No, I don't think we have the data currently to be able to make that correlation.

DR. GREENBERG: Dr. Snider.

DR. SNIDER: Well, I mean, I think basically the answer is no if we're talking about just total antibody. I mean, we heard one quote "total antibody" that upon questioning seemed to be high affinity antibody. I mean, as stated the answer is no. I don't know why do that. Why try to make the leap, at least at this particular point in time when there are better correlations.

DR. GREENBERG: Dr. Stephens.

DR. STEPHENS: I think the answer to the question is no. I'm just wondering why the question was even asked.

DR. GREENBERG: I'll let you ask that off the record. Ms. Fisher.

DR. FISHER: No. Conflicting data and not enough data.

DR. GREENBERG: Dr. Estes.

DR. ESTES: No, but I saw data today that I thought was potentially encouraging and so I think there is a chance in the future that this might be able to be developed.

DR. GREENBERG: Dr. Faggett.

DR. FAGGETT: Presently stated the shoe does not fit. I vote no.

DR. GREENBERG: Dr. Karzon.

DR. KARZON: I would have to say no on this one until the issue is clarified.

DR. GREENBERG: Dr. Huang.

DR. HUANG: I agree with Drs. Daum and Estes. I vote no.

DR. GREENBERG: Dr. Breiman?

DR. BREIMAN: No.

DR. GREENBERG: Dr. Ferrieri?

DR. FERRIERI: No.

DR. GREENBERG: For the record, I vote no as well. Does this bring the meeting to a close?

MS. CHERRY: This brings the meeting to a close except for one quick announcement.

DR. GREENBERG: So this brings the meeting to a close as far as I'm concerned. I would like to thank the panel for dealing with such a hard question. We will probably see you all in November. Hopefully there won't be another hurricane on its way. Happy travels.

(Whereupon, the meeting was adjourned at 2:45 p.m.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: MEETING SESSION 7

Before: VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

Date: SEPTEMBER 15, 1999

Place: BETHESDA, MARYLAND

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

irene gray