

1 begin with, as they required in the randomized portion. Is
2 that true?

3 DR. SWEDLOW: They were theoretically done with
4 the same entry criteria. Theoretically. In analysis, they
5 appeared to have a lower incidence of mild to moderate
6 variables -- sorry, a higher incidence of mild to moderate
7 variables.

8 DR. IAMS: Is that as opposed to more serious
9 decelerations so that the net effect was that the randomized
10 trial was conducted in perhaps a slightly higher risk for
11 the distress?

12 DR. SWEDLOW: Or for dystocia.

13 DR. GARITE: I mean, that is what it turned out to
14 be but, certainly going in it was very clear that the
15 motivation to enroll patients was driven by the severity of
16 the pattern in the randomized phase, whereas in the baseline
17 phase it just enrolled everybody who had the mildest of
18 patterns, and the documentation for that is the increased
19 frequency of the milder variable decelerations.

20 CHAIRMAN BLANCO: All right, let's move on. Diony
21 had asked a question about patient comfort and apparently
22 there is a reference about patient comfort with the FSpO2
23 sensor.

24 MS. PORTER: I am Martina Porter with
25 Mallinckrodt, and I am an advanced practice nurse. The

1 references are not from the United States. They are from a
2 group that was in Australia, and an Australian midwife did
3 look at the mothers' perception of participating in a
4 research study and one of the questions that she asked
5 during that study was about patient comfort. There were 77
6 patients that responded to her questionnaire, and 22 percent
7 of those patients did not have an epidural, and of those 22
8 percent only one patient reported negatively on the
9 experience of the sensor placement.

10 In your module, module 10 and, unfortunately I
11 don't have a page for you but it is section 10.9, and the
12 references are numbers 155, 156, 195 through 197.

13 CHAIRMAN BLANCO: Thank you. Unless there are
14 other points from before that we want to bring up, let's go
15 ahead and move on to the next number, and I believe that is
16 labeling, number four:

17 The sponsor has provided proposed professional and
18 patient labeling, volume 3 of your PMA panel package. The
19 sponsor has proposed the following essential components for
20 its indications for use statement, a modification from the
21 indications statement in the panel package:

22 Adjunct to fetal heart rate monitoring; term fetus
23 with a non-reassuring fetal heart rate pattern; improves
24 assessment of fetal oxygen status; directly measures fetal
25 oxygen saturation; permits the safe continuation of labor

1 during non-reassuring fetal heart rate patterns and
2 reassuring fetal oxygen saturation, thereby reducing the C-
3 section rate for non-reassuring fetal status without
4 increased injury to fetus or mother; provides better
5 sensitivity and specificity for matching delivery indication
6 to immediate neonatal condition.

7 a) Is each element of the indications for use
8 statement supported by the data presented in the pivotal
9 study?

10 b) Has the sponsor adequately and appropriately
11 identified the population that will benefit from this
12 device, what the readings will mean and how they should be
13 interpreted, based on the clinical study?

14 c) The oximeter is designed specifically to be
15 used as an adjunct to the fetal heart rate tracing. Is the
16 proposed labeling clear about this?

17 d) Has the sponsor adequately described proper
18 insertion and use of this device?

19 e) The sponsor describes the bias and precision
20 of the device as given in question one and as fully
21 described on the attached sheet. This information is not in
22 the information for prescribers. What information about the
23 accuracy of the device should be in the information for
24 prescribers?

25 With that, I open the floor for panel comments.

1 Yes, ma'am?

2 DR. SHARTS-HOPKO: I have a couple of things. I
3 raised the issue of vertex presentation this morning. You
4 have to be clear in all of this material that it is for
5 vertex full-term infants, etc., etc.

6 It was mentioned in the text at one point but I
7 believe in the contraindications you need to specify that it
8 is inappropriate in women with HIV.

9 The only other comment I have is that I was really
10 curious about when it was expected that the eight-minute
11 patient video would be used -- I think not when a person is
12 in a non-reassuring fetal heart rate pattern. I gather from
13 the video that it is intended for use before labor. I have
14 a lot of worry about how much people are set up for
15 adversity when you approach a low risk birth with high risk
16 information. But, at any rate, I think that it is not
17 appropriate for use at the time that the woman in labor is
18 determined to have this non-reassuring pattern.

19 CHAIRMAN BLANCO: Well, why don't you elaborate on
20 that so we can give some guidance to the FDA. Do you think
21 there should be a video? Yes or no? What should it
22 include? If not, what kind of informed consent information
23 should be given to the patient?

24 DR. SHARTS-HOPKO: I think if you think clinically
25 about how these things play out, you know, the woman is on

1 the fetal heart monitor and, all of a sudden, people start
2 going oh-oh -- so, she is going to pick up on that from your
3 faces or your lack of talk or whatever you do say. I think
4 at that point if the practitioner is inclined to use this
5 device, then you say we have a monitor, and here is one that
6 you can hold, and go over the points in the video. But I
7 think that that has to be done verbally, as most consents
8 are, at the time.

9 CHAIRMAN BLANCO: Any specific issues that you
10 think need to be or should be addressed?

11 DR. SHARTS-HOPKO: The little red marks on the
12 face, which are indicated in that video, that are transient.
13 You know, that there has been research to support the
14 usefulness and safety of the device. But I think that that
15 video is kind of ludicrous.

16 CHAIRMAN BLANCO: All right, Diony?

17 MS. YOUNG: Yes, I also was concerned about some
18 of the things with it. One point in particular about the
19 video and the information contained in it, there is the
20 statement -- and I am quoting exactly -- the new N-400
21 system provides valuable additional information about how
22 well a baby is doing during labor, end quote. Now, there is
23 no statement at all in that informational video about what
24 the indications for use are for the device, nothing at all
25 that I could find in there. So, the woman actually hasn't

1 been given any reason for its use.

2 Now, you are indicating that, yes, it is an
3 adjunct and saying it has valuable additional information.
4 You have talked about the electronic fetal monitor and you
5 have talked about various other procedures that may be done,
6 but then you go straight into the device without saying why
7 it might be used, not even indicating that if we are
8 concerned about the baby's heart rate, etc.

9 CHAIRMAN BLANCO: Okay. Subir, do you have
10 something you want to say?

11 DR. ROY: I was concerned about these bullets in
12 the sense that the first one, adjunct to fetal heart rate
13 monitoring, seemed to stand alone and I think we need to be
14 very careful about that because I think what we have seen is
15 the coupling of that comment in terms of assessing term
16 vertex presentations who have a non-reassuring fetal heart
17 rate pattern. Within that coupled statement I would
18 collapse the two; I would combine the two. I would not
19 enable the sponsors to separate for the simple reason, as
20 brought about by Nancy and Diony, that if they have a
21 monitor that says that this will improve the ability to
22 assess what is happening to the fetus, then the patients
23 will come in demanding its use where we don't have any
24 evidence that it is really indicated to be used.

25 CHAIRMAN BLANCO: Any comments from anyone else?

1 MS. YOUNG: Can I just add one other area where
2 you do need to clarify? That is on page three of the
3 patient information video. It says that the monitors and
4 sensors in the Nellcor product line are non-invasive. And,
5 if it is non-invasive to the fetus, then say that it is non-
6 invasive to the fetus.

7 DR. SWEDLOW: Point taken.

8 CHAIRMAN BLANCO: Any other comments? I would
9 like to elaborate on Subir's point because I think through
10 the reading of the PMA and the manuscript there is a lot of
11 added information which is great for us to make a
12 determination, but I think in the labeling it needs to go
13 back to a very specific indication for use in a very
14 specific setting that the data purports to show that it
15 gives a specific result. I think this is trying to address
16 some of Dr. O'Sullivan's issues about the broadening of the
17 use of this particular instrument into other avenues, and we
18 need to try to make sure that what data the company has gone
19 out to seek and to obtain is what gets put as the indication
20 and as what the benefits and safety are.

21 DR. O'SULLIVAN: Since we are on that, even in the
22 section where it says improves assessment of fetal oxygen
23 status, it should say in "the presence of."

24 CHAIRMAN BLANCO: I would go so far as to say it
25 shouldn't even say that.

1 DR. O'SULLIVAN: That is fine. I would have no
2 problem with that whole section coming out because even the
3 sensitivity and specificity issue I think is not answered
4 100 percent.

5 CHAIRMAN BLANCO: Well, that is not what they went
6 to look for. That is the point I am trying to make.

7 DR. O'SULLIVAN: So, that whole section, you
8 think, comes out?

9 CHAIRMAN BLANCO: Yes, I think the recommendation
10 to the FDA should be that they went for a very narrow, very
11 specific indication, which is great because it made the
12 endpoint easy to determine, but now they, you know, have to
13 live by that endpoint, and not try to then say the data that
14 you obtained, that you weren't necessarily looking for,
15 allows you to do all these other things. If someone
16 disagrees, come on back.

17 DR. CHATMAN: Along the same lines, your
18 colleagues are going to extend the definition of non-
19 reassuring fetal heart rate pattern. You know that too,
20 right?

21 CHAIRMAN BLANCO: But then that is the issue -- I
22 think pretty much everyone has agreed -- that the matrix
23 with this definition needs to be part of the indications for
24 use and needs to be part of labeling.

25 Dr. Schultz, you were going to make a comment?

1 DR. SCHULTZ: Well, I was just ask, at some point
2 during your discussions, if you would be willing to try to
3 provide us with an indication for use statement that clearly
4 and succinctly translates what you have been discussing, and
5 eliminates what you think ought to be eliminated and
6 contains what you think ought to be contained. That would
7 be extremely helpful.

8 CHAIRMAN BLANCO: You want to make us work?

9 DR. SCHULTZ: Well, we brought you all the way
10 here, and put you up --

11 CHAIRMAN BLANCO: In sunny D.C.!

12 DR. ROY: Could I also ask is the word "directly"
13 actually correct as used here, in terms of directly measures
14 fetal oxygen saturation? Isn't it indirect?

15 CHAIRMAN BLANCO: The company is shaking their
16 heads. I would say it doesn't make any difference either
17 way. They didn't address whether this correlates with the
18 baby's pO2. So, why put that it does that?

19 Again, what I am looking for is if you look at
20 their PMA application, right in the beginning of your volume
21 one, indications for use -- and this isn't trying to answer
22 Dr. Schultz's question, the Nellcor N-400 fetal oxygen
23 saturation monitoring system continuously monitors fetal
24 oxygen saturation and is indicated for use as an adjunct to
25 fetal heart rate monitoring to better assess fetal oxygen

1 status in the presence of a non-reassuring fetal heart rate
2 pattern during labor and delivery.

3 Well, we don't really want that because that is
4 what we are saying they didn't set out to do. What we would
5 like the indication to say, I think and other panel members
6 please chime in, is when used in conjunction with fetal
7 heart rate monitoring under a specified protocol the N-400
8 fetal oxygen saturation monitoring system has been
9 demonstrated to be safe and effective at reducing the rate
10 of C-sections performed for non-reassuring fetal status,
11 period.

12 DR. ALLEN: That is really the second bullet here,
13 it permits the safe continuation of labor during non-
14 reassuring fetal heart rate patterns, etc. It is the second
15 bullet of the three.

16 CHAIRMAN BLANCO: Yes.

17 DR. ALLEN: I would keep that.

18 CHAIRMAN BLANCO: Anybody want to add or subtract
19 from that, or change it?

20 DR. IAMS: One question about semantics of vertex
21 versus cephalic. Should it be cephalic? Would you use this
22 on a brow? Face? Other cephalic presentations? So, the
23 proper obstetrical word would be cephalic.

24 CHAIRMAN BLANCO: Other comments on a)?

25 DR. O'SULLIVAN: The only problem I have with that

1 is can you use it on a face? How are you going to get it
2 on?

3 DR. SWEDLOW: Can I answer?

4 CHAIRMAN BLANCO: Please.

5 DR. SWEDLOW: As long as you can find a patch of
6 skin it will read. It could be here; it could be on the
7 shoulder. It doesn't really matter where it is.

8 CHAIRMAN BLANCO: What I think that brings up,
9 cephalic, I think the issue that brings up is, you know, you
10 want to be -- and I know this may seem self-evident, but you
11 want to have a situation where you are aiming towards a
12 vaginal delivery.

13 DR. O'SULLIVAN: Yes.

14 CHAIRMAN BLANCO: And, I don't know whether we
15 should put that in there somehow. But I think part of the
16 point you are making is, you know, can it be used in brows?
17 Well, in certain types you are not going attempt a vaginal
18 delivery anyway, so you might not. Do we want to be that
19 detailed with that indication or leave it more broad? What
20 do you think, Dr. O'Sullivan?

21 DR. O'SULLIVAN: Well, you are very seldom, if
22 ever, going to use it on a brow because most of those at
23 term are not going to deliver vaginally. Certainly if you
24 have any chance of that happening, it has to be very high.
25 Face can still deliver vaginally. Occipital will deliver

1 vaginally; military attitude will deliver vaginally. The
2 only thing I think probably won't is the brow.

3 CHAIRMAN BLANCO: I think the issue is, you know,
4 at this point I could make the statement, well, the only
5 thing they used it was on vertex --

6 DR. O'SULLIVAN: Right.

7 CHAIRMAN BLANCO: But, you know, I don't think
8 anybody is every going to put a study together looking at
9 brow, face or anything else --

10 [Laughter]

11 DR. O'SULLIVAN: Right. So, you know, if you want
12 to use the term cephalic, that is fine but I think the study
13 they did was vertex.

14 CHAIRMAN BLANCO: Dr. Schultz?

15 DR. SCHULTZ: Just as a comment, in terms of
16 fashioning the labeling, we can use both positive statements
17 in the indications for use as well as negatives in the
18 warnings and precautions. So, you don't have to try to fit
19 everything into the indications for use statement. If you
20 think that there are specific areas that should be warned
21 against or cautioned against, we can certainly do that as
22 well.

23 CHAIRMAN BLANCO: I think we have heard several
24 mentions. Hopefully, somebody is keeping track. Okay, any
25 other issues on the indications for use a)? No? Then, I

1 guess we shall move on to b):

2 Has the sponsor adequately and appropriately
3 identified the population that will benefit from this
4 device, what the readings will mean and how they should be
5 interpreted, based on the clinical study?

6 Anyone care to comment? No takers? Well, to me,
7 by using the matrix basically fulfills the need for what is
8 being asked here. Does everybody agree with that?

9 DR. O'SULLIVAN: I agree.

10 CHAIRMAN BLANCO: Well, that was an easy one.

11 Let's go on to c). Everybody ready for c)?

12 The oximeter is designed specifically to be used
13 as an adjunct to the fetal heart rate tracing. Is the
14 proposed labeling clear about this?

15 DR. O'SULLIVAN: I think as we have changed it, it
16 is.

17 CHAIRMAN BLANCO: I think that it wasn't before
18 but it probably is now. Any other comments? Moving right
19 along:

20 d) Has the sponsor adequately described proper
21 insertion and use of this device? Comments?

22 DR. O'SULLIVAN: Since I have never used it, I am
23 going to take the tack of saying that he who doesn't know
24 anything has a right to say something.

25 [Laughter]

1 The sponsor is talking about insertion of this
2 device for an OA position, and I guess it has something to
3 do with the fact that I hardly ever see that in the
4 population that I deal with, and, therefore, I would take
5 argument with the fact that one should assume -- if one does
6 not know that the position is OA, one should assume that it
7 is OA and insert it in that fashion. I think that is
8 inappropriate. I think we have to describe exactly how it
9 should be done, whether it is OA, OT, or OP.

10 CHAIRMAN BLANCO: For your benefit, that is a
11 quote from the video for physician insertion. Isn't that
12 correct, Dr. O'Sullivan?

13 DR. O'SULLIVAN: Yes, that is what the physician
14 is going to be looking at when he is getting his education,
15 or her.

16 CHAIRMAN BLANCO: I would like to broaden the
17 comment. Obviously, you looked at the video as well and I
18 think most of the panel received the video. I didn't think
19 it was very instructive, quite frankly. I thought it was
20 kind of a sales pitch more than instructive. I mean, I
21 didn't see anybody saying how you put it on your hands.
22 While that may seem self-evident to physicians who put in
23 IUPCs, this is a little bit different. It is a little bit
24 bigger device. You have to jiggle it. You have centimeter
25 markings that are supposed to go different places. I think

1 it needs to be a little bit more detailed. What do the
2 other panel members think? Anybody else view it and think
3 it was clear?

4 DR. EGLINTON: I also think that it is
5 inappropriate to say if the fetal head position cannot be
6 determined, place the sensor posteriorly. That is a quote
7 from the placement guide. I think you have to know the head
8 position.

9 DR. SWEDLOW: We will tune it.

10 CHAIRMAN BLANCO: Dr. Wolfson, did you have a
11 comment?

12 DR. WOLFSON: I was just going to comment that I
13 thought the video was sufficiently instructive. Again,
14 maybe that is based again on my bias of experience of having
15 used a lot of IUP catheters so it looks quite
16 straightforward and it looks like simply the same process,
17 just a little different sensor.

18 CHAIRMAN BLANCO: Yes?

19 MS. YOUNG: I just think that it has to be made
20 clear in describing how to use the device -- Dr. Garite
21 answered my question this morning when I asked maternal
22 position, and I know that there is some mention, and I think
23 it was in the question and answer period, about maternal
24 ambulation and he answered that question as well. However, I
25 think it needs to be made clear in the instructions for use

1 of it what position the mother may or may not be in. And,
2 if she is in the supine position, then say that she should
3 be in the supine position. But if she can also be put on
4 her side, then say she can be put on her side. If there is
5 any necessity, perhaps say how long she should remain in one
6 position, or should she remain in just one position that is
7 either on the side or supine. I mean, the operator needs to
8 know what level of flexibility there is as far as the
9 maternal positioning is concerned.

10 DR. IAMS: I just have a question about whether
11 you think the device, if it ever became dislodged or was
12 inadvertently removed, does that require insertion of a
13 second, new device? And, that ought to be in there too.

14 CHAIRMAN BLANCO: Any other comments on this
15 particular number? We had two dissenting views on the video
16 for physician insertion. So, I would like to hear some
17 comments from some other folks on whether they thought that
18 was sufficient or we needed more information. Does anybody
19 else care to make a comment?

20 MS. YOUNG: Well, I am not a practitioner and I do
21 think more information would have been helpful for a
22 practitioner.

23 DR. CHATMAN: I thought it was adequate.

24 CHAIRMAN BLANCO: We are just splitting right down
25 the middle so I guess we will get off of that.

1 [Laughter]

2 Anyone else have a comment?

3 DR. SHARTS-HOPKO: Well, actually this flexibility
4 of position, if you hope to attain more vaginal deliveries
5 and people may assume varied positions for birth, if that is
6 going to be okay I would say so specifically, otherwise they
7 will be prohibited by their practitioner.

8 CHAIRMAN BLANCO: So, the question is whether
9 birth position plays some role --

10 DR. SHARTS-HOPKO: If there is any restriction on
11 birth position.

12 MS. YOUNG: Can I just follow-up a little bit
13 further on that? Can the mother be propped, or should she
14 be dead flat?

15 DR. SWEDLOW: You mean perfectly flat?

16 MS. YOUNG: Can she be propped with pillows in an
17 inclined, forty degrees position? That information is
18 helpful.

19 DR. GARITE: The answer is yes. Yes, that is
20 fine.

21 CHAIRMAN BLANCO: It seems that you probably tape
22 this to the thigh and the woman can do pretty much
23 everything she wants to do in bed, once she is there. It is
24 just a matter of not ambulation.

25 MS. YOUNG: Well, can she get on her hands and

1 knees?

2 DR. GARITE: We don't have the data.

3 CHAIRMAN BLANCO: No, no, you shouldn't throw your
4 hands up. I mean, that is a technique that is utilized for
5 labor in women.

6 DR. SWEDLOW: If it is taped to her thigh, my
7 guess is yes but if it falls out I would say no. I mean, it
8 is the kind of thing that we are going to have to find out
9 during the clinical use. Honestly, we can't answer these.

10 DR. CHATMAN: Excuse me, is it common for patients
11 with epidurals to get on their hands and knees?

12 CHAIRMAN BLANCO: No, I don't think so.

13 DR. CHATMAN: I didn't think so. The picture that
14 I see here though is one -- I think you talked about
15 medicalization of labor and delivery where the patient has
16 O2 going, an IV going, a catheter in the bladder, a catheter
17 in the epidural space, and IUPC, the scalp clip on and the
18 Nellcor 400 on as well. So, she would be hooked up totally
19 so she wouldn't be able to move --

20 [Laughter]

21 Dr. Roy said that the patient is going to look
22 something like that --

23 [Laughter]

24 CHAIRMAN BLANCO: Well, we always have a good time
25 at these panel meetings. All right, I think we are ready to

1 move on to e) here, if everybody agrees:

2 The sponsor describes the bias and precision of
3 the device as given in question one and as fully described
4 on the attached sheet. This information is not in the
5 information for prescribers. What information about the
6 accuracy of the device should in the information for
7 prescribers?

8 There is no attached sheet to this. It is in
9 question one. It is the issue that we talked about, the 4.7
10 percent and the 67 percent.

11 DR. IAMS: I would leave that out. That confused
12 us for -- what? -- thirty minutes this morning. I think you
13 would end up with all sorts of misinformation floating
14 around about the device.

15 DR. EGLINTON: I agree.

16 CHAIRMAN BLANCO: I think you just need to make
17 sure that the endpoint you use, 30 percent, that folks are
18 clear on it and, again, whether you need to have that for
19 some period of time and what period of time.

20 DR. D'AGOSTINO: If you include it, it gives the
21 appearance somehow or other of more precision than what we
22 really think is going on. So, I definitely would go with
23 excluding it.

24 DR. NEUMAN: I have a different opinion, not as a
25 practitioner but as someone involved in science. It seems

1 to me, as we were saying earlier today, that the error
2 associated with the measurement is an important piece of
3 information and I think without having some statement to
4 that effect people might assume that there is no error
5 associated with the measurement.

6 CHAIRMAN BLANCO: Well, how about a suggestion of
7 a disclaimer, using Dr. Schultz's suggestion before, not in
8 the indications but somewhere describing that there is
9 evidence for some error rate, and describe the error rate
10 and that while the machine may read above 30, you may
11 actually be below 30 and that you cannot use the machine for
12 correlating to true pO2 in the fetus. Would that sort of
13 correlate the two viewpoints or compromise the two
14 viewpoints? Is that acceptable to you Dr. D'Agostino?

15 DR. D'AGOSTINO: Yes.

16 CHAIRMAN BLANCO: Mike?

17 DR. NEUMAN: Yes.

18 CHAIRMAN BLANCO: Okay, so I think somewhere a
19 disclaimer that this is not a machine with accuracy to
20 believe that number to mean anything in terms of the pO2 of
21 the fetus. You have to remember that 30 number, and if it
22 is above or below, for how long and whether you section or
23 not. Anyone else? Any other comments on that?

24 DR. SHARTS-HOPKO: Jorge, I don't know the answer
25 to this but other people around the table will. You know,

1 in prior meetings we have had to deliberate on the errors of
2 residents, and I wonder if there is anything anybody can
3 think of that an inexperienced person, alone in the middle
4 of the night might do wrong that you can anticipate.

5 CHAIRMAN BLANCO: Well, I can imagine a lot of
6 things --

7 [Laughter]

8 -- but I don't know that we can anticipate them.
9 I don't know, I think it is a procedure that will have to be
10 learned, just like all the other things are learned, and I
11 think again the issue is making very concise, very clear
12 indication matrix, how it is used, what the number is, and
13 disclaimers to the fact that it can't be used to reassure
14 anybody that you know what the pO2 is in the fetus. Yes,
15 Dr. Allen?

16 DR. ALLEN: This would go to the concern I had
17 about establishing landmarks. If you had a first year
18 resident who is not sure of the landmarks I don't think they
19 should just put it on posteriorly. I mean, we have had
20 residents who haven't been able to identify a breach from a
21 vertex, a face from an OA. I think the landmarks are very
22 important, especially in teaching institutions.

23 CHAIRMAN BLANCO: Well, I think it was pretty
24 clear that we thought that the landmarks needed to be known
25 so that you put the monitor in appropriately.

1 DR. IAMS: Would it be appropriate to ask that
2 proficiency in application of fetal scalp electrodes and/or
3 intrauterine pressure catheters be recommended before
4 somebody begins to try to learn this?

5 Everybody who has it is going to have that
6 technology applied already. So, I think that is not
7 unreasonable from an actual point of view, but from a
8 placement point of view, you don't want somebody learning
9 this technique while they are learning the other one.

10 CHAIRMAN BLANCO: Right.

11 DR. IAMS: They should already have mastered that
12 one.

13 CHAIRMAN BLANCO: Very good point. Okay? Any
14 other points? Anything else that anyone cares to add? If
15 not, we are going to move on to the last question.

16 Post-approval studies, question five, does the
17 panel recommend additional post-approval studies? If so,
18 please describe.

19 I would just add my own editorial comment at this
20 point, I think we can discuss some that we think are needed,
21 and then once we get into the voting phase, depending on how
22 things are voted, at that time we may resurface to the issue
23 of whether certain things need to be looked at in more
24 detail that we think need to be monitored. So, I will open
25 it up for the panel discussion at this point. Anything that

1 comes to mind at this point for folks?

2 DR. D'AGOSTINO: There is the usual safety type
3 surveillance which is automatic, I presume, but there have
4 been a number of questions about how one actually makes
5 decisions which aren't that clear in terms of the timing and
6 what-have-you. It would very be important I think to have
7 those type of studies on the actual use of the instrument.
8 As opposed to just seeing what happens, actually design
9 studies to get a handle on that.

10 CHAIRMAN BLANCO: The FDA needs some real
11 specifics in terms of what we think those issues are. So,
12 let's try to go over some of those. If you remember some of
13 them, if not I will try --

14 DR. D'AGOSTINO: You know, we have that matrix but
15 there were questions about how long must it be below 30,
16 what is the actual operational use of the matrix. I am
17 talking specifically about getting that matrix and turning
18 it into an operational set of definitions and operational
19 procedures, and I don't think I need to say very much more
20 about that.

21 CHAIRMAN BLANCO: I guess what I was saying is not
22 so much the matrix but some things that may be interesting
23 to look at that would address some of the issues. It would
24 be, as you mentioned, the length of time below 30 percent
25 because that was a variable. I think some other issues

1 might be the length of time -- well, now I have blanked out
2 but the prolongation in terms of the insertion of the
3 monitor to getting a reading. Does anyone else have other
4 things that they think need to be looked at?

5 DR. O'SULLIVAN: I think you might include the
6 frequency of its use. You might want to look at what the
7 cesarean section rate really is for fetal distress or non-
8 reassuring fetal heart rate patterns versus dystocia, and
9 whether there really is a difference or not. You might want
10 to look at the infection rate, and sort that out from those
11 with or without IUPCs, and I suspect that, of course, that
12 will be a problem because most people are using IUPCs.

13 DR. D'AGOSTINO: You don't want to encourage off-
14 label use obviously, but there will be, from previous
15 discussion, and how it actually gets used in terms of what
16 decisions are actually being made I think would be very
17 important.

18 DR. IAMS: I think we should be pretty rigorous
19 about that actually. Given the number of cesareans, as I
20 said before, in this country, it should not take long
21 although it may be fairly intensive. I think you should
22 track the number of cesareans and the indications for their
23 use, and given the expected off-label -- expansion of the
24 indications, my definition of a non-reassuring tracing and
25 yours at this table may be clear but once it is introduced

1 into the marketplace -- everybody wants to have the newest,
2 latest technology and that will mean very mild decelerations
3 will be declared non-reassuring by some practitioners.

4 So, I think there ought to be very specific -- I
5 am not sure what category of study, you can help us with
6 that, but some fairly close tracking and fairly prompt turn-
7 arounds. You should know -- if it gets the kind of wide use
8 you would expect -- certainly within a year or maybe even
9 quicker than that. You might know that it increases the
10 rate of cesarean because women with very benign
11 decelerations which are declared to be worrisome, and then
12 accompanied by a transient dip below 30, are now getting
13 cesareans. So, I think you ought to have a fairly quick and
14 exhaustive tracking and fairly quick review to catch this
15 pretty early so we don't end up repeating some of our messy
16 experiences with previous technologies. I think the
17 potential is tremendous but the potential for mischief is,
18 unfortunately, there also and I wouldn't want to see this
19 device lumped on that pile of bad technologies that we
20 talked about before.

21 DR. DIAMOND: The issue of infection was brought
22 up. I think that is particularly an issue in that although
23 the rates were not significant, there was a 20 percent
24 increase in fever overall and about a 50 percent increase by
25 the study parameters. So, I think that is important to look

1 at.

2 The scalp pH as a function -- in those patients
3 who had the oxygen fall below 30 and scalp physician are
4 done, what that correlation is to give points on that curve.

5 Most of these patients had epidurals, so what were
6 the results in non-epidural patients?

7 DR. O'SULLIVAN: Use of oxytocin.

8 DR. DIAMOND: Use of oxytocin. The other thing I
9 would like to see would be more information on the
10 correlation of the values with each other when the oxygen is
11 low and when it is 30, which is the cut-off, as opposed to
12 40 where, we were told, most of the values they have are.

13 CHAIRMAN BLANCO: Anything else? Anyone else?
14 Some suggestions? Well, it looks like we have exhausted the
15 discussion on the questions. I appreciate your answers and
16 your bearing with us on all the bombarding of questions. We
17 certainly appreciate that, and now it is time for the panel
18 to get together for the discussions.

19 Before we start, let's remember where we are
20 trying to aim. Eventually, after we hold some discussion, I
21 will ask for one of the voting panel members to produce a
22 motion. The motion should be one of three things: One
23 would be a motion for non-approval. One would be a motion
24 for approval. Then, one would be a motion of approval with
25 conditions. Then, if we have a motion for approval with

1 conditions that is seconded, we need to discuss the
2 conditions one by one, vote on them for inclusion or
3 exclusion one by one, and then on the overall package.

4 Before we vote we will have another opportunity
5 for public comments from the audience. I am sure there are
6 some folks out there that, after hearing us all day, would
7 like to make some comments. So, we will have that
8 opportunity, but just so that the panel members are aware of
9 where we need to end up when we are all through with the
10 discussion.

11 Does anyone want to start the discussion and make
12 some comments as to where we should go? Now we are looking
13 for approval, conditions, whatever. I am not asking for a
14 motion; I am asking for discussion. Anything that people
15 want to discuss about this PMA? Dr. Eglinton, maybe you
16 could start off with some thoughts.

17 DR. EGLINTON: I think we have heard lots of
18 discussion. I don't have any other thoughts.

19 [Laughter]

20 It has all been said.

21 CHAIRMAN BLANCO: Well, I think if nobody else has
22 any discussions we can move to the public comment, and then
23 we can move to a motion for a vote. So, let's see where we
24 go. Everybody is ready for that?

25 [Several panel members answers affirmatively]

1 All right, are there any members of the public
2 that would like to make comment? Please come forward,
3 identify yourself, identify whether you have any conflict of
4 interest and whether you are supported by any company who
5 could possibly be either the company in question or a
6 competitor, and then make your statements and do keep them
7 succinct.

8 **Open Public Hearing**

9 DR. ROSS: Michael Ross, I am from UCLA Medical
10 Center. I am a consultant to Respiroics which has a
11 potentially competing product. As many of you know, I have
12 been here on the other side of multiple products.

13 I really have some sincere questions about the
14 discussion today and I think it is important to bring some
15 of that together. It really is a concern about the product
16 and its utilization. So, I would like to divide those into
17 some issues of variance that we talked about, the
18 interpretation, the outcome, some of what I think is a
19 little circular reasoning, and then recommendations, and I
20 will try to do that briefly.

21 The variance, first of all, and I have done some
22 experiments on scalp oximetry devices -- the variance that
23 we talked about, the 5 percent issue, is really due to an
24 issue of offset, and that is that different probes are
25 offset at different percentages from what would be the norm.

1 That, in fact, does not regress to a zero error if one takes
2 a lot of points over time. It, in fact, stays probably as
3 the same 5 or 6 percent variance in offset. So, that is a
4 little statistical artifact.

5 The fact that the average bias may be listed as
6 0.6 percent is the fact that if you take a number of
7 different patient curves or animal curves and set your
8 calibration curve at the middle of all of them and if you
9 have a series of offsets, you are going to come out to a
10 very small mean error across the board but your individual
11 case is going to have a significant offset.

12 We don't, in fact, know the specific variance at
13 the 30 percent point, and this is a key threshold point. We
14 see some human data, none of which goes down to a 30 percent
15 level. And, that is a critical threshold criterion. In
16 fact, if the reading is 30 percent based upon this variance,
17 over one-third of the cases will actually have greater than
18 34 percent or less than 25 percent. I think you need to
19 define the variance.

20 The interpretation -- we have heard discussion
21 about a very soft definition of when to act and when not to
22 act, and I think that there needs to be a defined duration
23 below the threshold and a degree below the threshold. As
24 was pointed out, 20 percent is very different from 29
25 percent, and 1 minute very different from 10 minutes.

1 Furthermore, we only have signal 66 percent of the
2 time. That is if one counts only the time between
3 contractions. If you count the time including the
4 contractions you have even a lower percentage. Furthermore,
5 as we know from lots of animal studies, there is a marked
6 individual variation in when fetuses actually do develop
7 hypoxia-mediated metabolic acidosis. The 30 percent is a
8 nice general threshold, and that is probably reasonable to
9 use, but there is lots of variance within that depending
10 upon their hematocrit and blood volume, heart rate, and so
11 forth. So, it is all the more important to have an accurate
12 definition of the threshold including the duration and the
13 degree.

14 Moving on to the outcome issue, we have seen that
15 there is a decrease in the cesarean sections for non-
16 reassuring fetal heart rate tracing but an increase for the
17 dystocia or the mixed indications -- the dystocia or fetal
18 intolerance -- as primarily behavioral change. It appears
19 to be associated with a slight shift in the study group and
20 perhaps an increased rate of C-section for fetal compromise
21 in the control group as compared to the pre-study period.
22 This really seems like it is mostly a behavioral shift, a
23 Hawthorn effect, but not data-driven events because we don't
24 have a defined threshold and we don't have defined criteria.

25 In fact, one may propose five years from now if

1 one or more of these products is out, that I have a
2 wonderful treatment to reduce the rate of dystocia, and that
3 is to remove the scalp oximetry device because you would see
4 the shift back to more fetal compromise.

5 With that in mind, we have a little bit of
6 circular reasoning that has gone on. We have heard a
7 defense of the variance and the threshold and the
8 interpretation -- that we should sort of dismiss that and
9 not worry about it because it really doesn't matter because
10 we have reduced the C-section rate for fetal distress. That
11 is the important point. Yet, when we heard a discussion
12 about the increase in C-section rates for dystocia, we
13 dismissed that because we said it couldn't possible be fetal
14 distress because we had the oximeter on.

15 So, my recommendations, and not on behalf of
16 Respironics, would be that one needs to confirm the accuracy
17 and the variance of this device at the fixed threshold which
18 is going to be the recommendation to the community, that
19 being 30 percent, or define better what that threshold would
20 be and confirm with a rigorous study fixed criteria of time
21 and degree of drop, duration and degree of drop at which it
22 should be above or beyond that threshold to both make the
23 decision for cesarean section or to hold your hand and not
24 do the cesarean section.

25 Thank you.

1 CHAIRMAN BLANCO: Thank you. Any other comments
2 from the public?

3 [No response]

4 Does FDA have any comments that they would like to
5 make, any of the involved individuals? No? And, does the
6 sponsor have any comments that they would like to make? n

7 DR. SWEDLOW: Yes, thank you. On behalf of
8 Mallinckrodt, I would like to say that we greatly appreciate
9 the thoughtful and grueling review -- grueling for us and
10 grueling for you review of this very complex multi-center
11 study. We know it was very difficult to hold all the
12 information in your minds at the same time and, really,
13 right on target in picking out exactly the right questions
14 to deal with. We really appreciate the effort that you all
15 put into it.

16 I also want to assure the panel that the company
17 is absolutely dedicated to the concept of working with the
18 FDA on clarifying, or clearing up, or fixing, or whatever
19 verb you want to use incongruities and ambiguities in the
20 labeling and indications, etc. We absolutely stand firm on
21 that concept. In particular, we are very, very concerned
22 that it only be used in a population where it is appropriate
23 and it be used with fetal heart rate monitoring and it be
24 used in the right population. Again, I thank you for your
25 patience and attention.

1 CHAIRMAN BLANCO: Thank you very much. Well, the
2 time has come -- and it is wonderful because I don't get to
3 vote so you guys get to vote. I will at this point
4 entertain a motion. As we discussed, it needs to be one of
5 three, approval, non-approval or approval with conditions.
6 We will then entertain a second and we will proceed from
7 there. Do I hear a motion?

8 DR. O'SULLIVAN: I move that we vote to approve
9 with conditions.

10 CHAIRMAN BLANCO: Do I hear a second?

11 DR. SHARTS-HOPKO: Second.

12 CHAIRMAN BLANCO: All right. Before we take any
13 vote we need to outline each of the conditions and vote on
14 the conditions to be added, and then proceed from there. I
15 believe we are going to have someone from the FDA writing
16 these down on an overhead so we keep track of them. Dr.
17 O'Sullivan, you made the motion so why don't you go through
18 some of the conditions that you would put on the approval of
19 the PMA, please?

20 DR. O'SULLIVAN: I think that, for one thing,
21 there has to be a post-market surveillance, and that the
22 post-market surveillance has to include, amongst probably
23 some other things, the frequency of its use and the
24 conditions under which it has been used in the market. That
25 is, how rigorous -- I don't know how to word this but how

1 rigorously is the protocol and matrix being followed.

2 CHAIRMAN BLANCO: All right, so one of the
3 conditions that you would put on is to keep track of the
4 indications for use and identify what would be off-label use
5 or inappropriate use. Is that what you are saying?

6 DR. O'SULLIVAN: That is correct, yes.

7 CHAIRMAN BLANCO: Let's take them one at a time.

8 DR. D'AGOSTINO: The word surveillance, post-
9 marketing surveillance can be broad and sometimes it just
10 means sort of passive observations. We had talked a moment
11 ago -- at least I had talked a moment ago about more of a
12 post-marketing study --

13 DR. O'SULLIVAN: That is right.

14 DR. D'AGOSTINO: -- as opposed to a surveillance
15 with the protocol so that you would extract this
16 information.

17 DR. O'SULLIVAN: I think what I really mean is a
18 protocol, not just surveillance per se. Something more
19 rigorous than that.

20 CHAIRMAN BLANCO: Well, there is a difference.
21 Let's try to clarify what we mean and make sure that we are
22 clear in the suggestion. What I would interpret from a
23 surveillance would be essentially that the company would
24 need to track each individual patient and get some
25 information back from each individual patient where this

1 product is utilized, and then keep a tabulation of that
2 information that would be reviewed after a certain amount of
3 time.

4 What I understand from what Dr. D'Agostino is
5 suggesting is not that. What he is suggesting is a totally
6 new study, to some extent, that would look at some of the
7 specific issues that were raised by the study.

8 DR. D'AGOSTINO: Exactly, and it is not going to
9 be -- at least my suggestion is not going to be a
10 replacement of this study that is before us or as rigorous,
11 but I am thinking of a prospective type of post-marketing
12 study where you actually are within the hospitals, within
13 the clinics, and so forth, generating protocol sheets that
14 people will, in fact, use so it isn't just sort of
15 recollection of what is happening or sort of rather passive
16 or inactive. It is not meant to be a clinical trial, and so
17 forth, but with the thoughts of what information you are
18 going to extract, not just waiting for the information to
19 come.

20 CHAIRMAN BLANCO: But is that the same thing? I
21 think what Dr. O'Sullivan -- and correct me if I am wrong,
22 Dr. O'Sullivan -- what you would like to see is whether it
23 is being utilized appropriately for appropriate indications.
24 Is that correct?

25 DR. O'SULLIVAN: Whether it is utilized

1 appropriately and also whether the outcomes in the post-
2 market use, or the experience in the post-market use
3 confirms that which has already occurred in the randomized,
4 controlled trial.

5 CHAIRMAN BLANCO: Okay. In order to get that
6 information you really have to do it as a surveillance,
7 almost, as Dr. Iams suggested, as a registry because --

8 DR. O'SULLIVAN: A registry you can't rely on
9 because a registry depends upon individual physicians
10 feeding in the information. This has to be more rigorous
11 than that.

12 DR. IAMS: Yes, we need some standardized
13 definitions here --

14 DR. O'SULLIVAN: Right, standardized definitions,
15 standardized data collection sheets, that kind of thing.

16 DR. IAMS: Yes, I mean surveillance versus study
17 versus registry, whatever. I agree. We need to be able to
18 track what happens to the cesarean rate. So, if you simply
19 record what happens to each individual patient who gets a
20 clinically prescribed device you really don't know what
21 happened in the hospitals in which the device is used and
22 those who didn't have such a device. So, you almost need to
23 ask for some sort of formalized study to track -- in those
24 hospitals that choose to use it -- to track the cesarean
25 section rate by indication for the first 6-12 months, or

1 whatever, until you get an N that appeals to the
2 statisticians around the table.

3 CHAIRMAN BLANCO: So, number one, you would have
4 to have the sponsor be the one that provides the data, not
5 the physicians that use it.

6 DR. O'SULLIVAN: Correct.

7 CHAIRMAN BLANCO: Number two, you would have to
8 have more information than just the patients where it is
9 utilized. Correct?

10 DR. O'SULLIVAN: Correct.

11 DR. IAMS: You have to have some reference
12 population. I don't know exactly whether you would recruit
13 observational matched controls, like the next two people in
14 the same hospital that had the cesarean, or whatever. I am
15 not quite sure how to design that or what to say about it,
16 but there is a real concern here on my part, and I think it
17 is shared by many on the panel that in a fairly short order
18 we could see this device used in broadened indications that
19 would look like what was in the list of indications but they
20 would be relatively relaxed, and we would end up having
21 unleashed something that isn't going to do what seems like
22 happened in this trial. So, somehow or other, I think we
23 ought to pay a lot of attention to what happens in the first
24 year or so of use so that you can say, "ye, wait a minute,
25 what we thought was going to happen isn't happening."

1 DR. WOLFSON: Jay, don't you want to do both then?
2 Don't you really want to have a surveillance so that every
3 time a device is placed --

4 DR. IAMS: I want to know about every device, but
5 I also want to be able to have some kind of reference
6 population because we have been through this with electronic
7 fetal monitoring. I was there when that happened and I was
8 there when lots of other things happened. We said we were
9 doing much better but, of course, we weren't.

10 DR. WOLFSON: I understand that. It seems to me
11 though that you do need the surveillance process because it
12 is still going to tell you about utilization and indications
13 for use on an individual basis. Because how it is going to
14 permeate in a given institution is going to be a progressive
15 process, I mean, you are going to have some early adapters
16 who are going to go in and one will get the training right
17 off the bat, and they are going to be the trainers who
18 train, and then it is going to permeate at given
19 institutions at varying rates. So, I don't know -- it
20 sounds like a very complex type of study to try to create if
21 you are doing it prospectively.

22 CHAIRMAN BLANCO: We are looking at two issues.
23 Mike, I know you have been wanting to say something so go
24 ahead.

25 DR. DIAMOND: I understand where Dr. O'Sullivan

1 and Dr. Iams and the others are coming from and I agree with
2 them. But I think to put together a registry with this sort
3 of information you are now describing, number one, is
4 extremely burdensome on the sponsor. Number two, it would
5 create a huge cost which will increase the expense of these
6 device. Number three, you are asking the sponsor to be
7 responsible for providing this data on each and every
8 patient when really that is going to be out of their
9 control. It will be in the hands of the doctors and the
10 hospitals in which it is going to be utilized.

11 So, I don't know that this is going to truly be
12 functional. Plus, let's say you get the data and your
13 concerns, Dr. Iams, are met -- the cesarean section rate is
14 up. This product is already approved for general use. What
15 is going to happen then? To my knowledge, I am not aware
16 that very often, if at all, of a product once approved has
17 ever been recalled for those sorts of reasons.

18 Perhaps a better suggestion would be a study to be
19 conducted addressing the issues you are talking about in a
20 limited number of places prior to general approval to be
21 able to get the detailed data that you are looking for,
22 appropriately powered and appropriately controlled, without
23 having to be doing it in every single hospital across the
24 country.

25 CHAIRMAN BLANCO: Let me try to address some of

1 those issues and, Dr. Schultz, you may want to make a
2 comment, but I think it is the role of the FDA to regulate
3 what devices are there, and if it shows that it does not do
4 what it is supposed to do, then they recall it. Am I not
5 correct on that?

6 DR. SCHULTZ: I think you are both correct. We do
7 have the authority to do that. We don't do it very often,
8 and we need pretty good reasons to do it. I think that we
9 can work with the company to try to design a study that,
10 hopefully, will allow us to compare what happens as this
11 device is taken to the market. I think there may be other
12 avenues to collect that type of information, but I think we
13 get the sense from the panel that if, indeed, the panel
14 votes for approval that they feel that additional data needs
15 to be collected and that we need to work on that with the
16 company and with whatever other resources may be available
17 to collect that information.

18 CHAIRMAN BLANCO: Yes, I think there are two
19 issues, and I think that is why we are going back and forth.
20 There are two bits of data that the panel has concerns
21 about, if I can try to summarize it. One is the spread of
22 its use in non-indicated settings. And, that is one of the
23 things that you brought up, Dr. O'Sullivan, and then what
24 Dr. Iams has brought up, which is the issue of the data
25 having some questions to it because of the issue of the

1 increased rate over baseline and the increase of dystocia.
2 So, yes, it may be burdensome to the sponsor but if those
3 aren't there, they might not get approved at all. It might
4 get approved; it might not. So, I think that the issue is,
5 you know, there is some need to clarify the C-section rate
6 data because what has been provided has some issues with it,
7 as I see it if I can summarize, and then there is the issue
8 of expanding its indications.

9 DR. SCHULTZ: Yes, the point I was going to make
10 was that in addition to recall which, obviously, is a fairly
11 drastic step, many times what we do is use information that
12 is collected post-market to modify the label. That
13 certainly would be something that would be extremely
14 important. As Dr. Iams is suggesting, you know, if the C-
15 section rate, for instance, were to double using this device
16 and we put that on the label, obviously that would have a
17 fairly dramatic impact on the use of the product. So, I
18 think that there are ways to deal with that short of actual
19 recall.

20 DR. IAMS: I am afraid I don't have a lot of
21 confidence in obstetricians to follow those kinds of labels,
22 because if you labeled the electronic fetal heart rate
23 monitor that is what it would say -- you know, if you use
24 this product it is going to increase your rate of cesareans
25 and most of them will be -- I won't say most but many of

1 them will be of no particular benefit to the mother or the
2 fetus. And, I don't want to be in the position of okaying
3 that thing happening again, especially for a product whose
4 clear potential is to reduce what happened with heart rate
5 monitoring.

6 CHAIRMAN BLANCO: In all fairness to the FDA, I
7 believe that electronic fetal heart rate monitoring was in
8 the market prior to the amendment that created their
9 regulatory ability over devices. Am I not correct on that?
10 Colin, where are you? I think you are the one who told me
11 that.

12 MR. POLLARD: Yes.

13 CHAIRMAN BLANCO: Thank you. The other good thing
14 is that we have some very intelligent and smart folks at FDA
15 and the sponsor, and we don't have to give them detail by
16 detail. I think the conditions are, number one, we are
17 concerned about whether this really decreases it because of
18 some of the way the data is. Number two, we are concerned
19 about spread of indication of use. And, something needs to
20 be done about monitoring those two, and whether the
21 instrument will worsen those two settings. Is that fair
22 enough for you, Dr. O'Sullivan? Dr. Iams? Dr. Diamond, do
23 you buy that?

24 DR. DIAMOND: Do we want to make a suggestion
25 about a study prior to approval or after, or are we going to

1 leave that open to the FDA?

2 CHAIRMAN BLANCO: I think we can do that.

3 DR. DIAMOND: Leave it open to the FDA?

4 CHAIRMAN BLANCO: No, no, the thing is if you
5 request another study, then why are you going to approve the
6 device? If the pivotal study that they presented before us
7 does not prove to you satisfactorily that it is clinically
8 significantly efficacious, then your vote should be to not
9 approve the device, it seems to me.

10 DR. DIAMOND: Perhaps if the study were
11 appropriately designed, and conducted, and the results were
12 positive it would save the sponsor having to come back to
13 panel for further suggestions a year or two from now from
14 the panel. So, it would give them the opportunity to avoid
15 that.

16 CHAIRMAN BLANCO: Okay, I am not sure where that
17 goes. Any other comments?

18 DR. WOLFSON: Didn't we also talk about monitoring
19 infection rate?

20 CHAIRMAN BLANCO: Yes, why don't we get all the
21 conditions and then we can vote on them one by one.

22 DR. WOLFSON: Because the list I have says
23 frequency of use, infection rate, cesarean section rate,
24 incidence of dystocia as an indication for abdominal
25 delivery, knowing the results in non-epidural patients and

1 specifying what is truly a positive finding, meaning the
2 length of time less than 30 percent.

3 CHAIRMAN BLANCO: It seems to me, if we are doing
4 surveillance, that those are items that you would want to
5 check in the surveillance. So, what I think what we
6 basically have are two conditions. One, monitoring of the
7 individual indications for use of every device and, two,
8 monitoring in some way to look at what happens to the
9 cesarean section rate when this device is utilized. Did I
10 summarize that appropriately for everyone? Indications for
11 use for the device. That would be one. I am trying to
12 paraphrase, Dr. O'Sullivan, so jump in if you don't think I
13 am doing right. One is the surveillance of each device, the
14 indications for its use and then, number two, surveillance
15 for cesarean section rates in sites where the instrument is
16 utilized. Then there is a set number of information that
17 Dr. Wolfson would like followed, or suggested should be
18 followed within probably that second surveillance. Do you
19 want to go over that list again for us, please?

20 DR. WOLFSON: The list I have from before is
21 frequency of use in sites, infection rate, incidence of
22 dystocia for cesarean section. I think those are the only
23 ones that are applicable really to surveillance as you have
24 stated there. The two that are outlying was the length of
25 time below the 30 percent level for criteria for

1 intervention, and the other one was experience in non-
2 epidural patients but I don't know how you would put that in
3 there.

4 DR. DIAMOND: Another factor I would like to see
5 in there would be adequacy of labor as defined by
6 intrauterine pressure catheter monitor for frequency of use.

7 DR. WOLFSON: That would be part of dealing with
8 patients with dystocia.

9 CHAIRMAN BLANCO: Anything else?

10 DR. IAMS: Jorge, does this list include some
11 responsibility on the part of the sponsor to track cesarean
12 section rates in the hospitals in which this is introduced?

13 CHAIRMAN BLANCO: I think we need to put that as
14 part of number one.

15 DR. IAMS: The worst possible catastrophe for the
16 sponsor would be to have this thing associated with a rise
17 in C-section rates, with a giant argument, about which there
18 would be insufficient data, to the incident -- yes, it has
19 gone up but it is not our fault, etc., that kind of stuff,
20 and then have it come back to some extremely messy hearing
21 somewhere and get suspended, pulled back, or whatever. I
22 think it is in the sponsor's best interest to make sure that
23 if this product, through no fault of theirs, is used
24 inappropriately they have enough data at the end of the year
25 here is why the section rate went up. It is not what we

1 said on our monitoring list here, list of indications; it is
2 because this, this and this happened. Otherwise, I think
3 they run some risk of being tarred. So, I don't feel bad at
4 all about asking them to spend what could be a little money
5 up front to save a huge, drawn out, controversial experience
6 if, in fact, the product is somehow linked to a rise in
7 section rates.

8 CHAIRMAN BLANCO: I guess the only thing that I
9 would point out, just because it keeps coming back with Dr.
10 Diamond sort of asking for a new study and --

11 DR. IAMS: I don't care how that gets done.
12 Whether Dr. Diamond's pre-market introduction works or
13 whether there is some post-market surveillance, or a gradual
14 roll out -- I don't know; I don't really care but somehow I
15 think there needs to be --

16 DR. D'AGOSTINO: But it makes a big difference,
17 doesn't it? Premarketing type of studies, that means we
18 vote to not approve.

19 CHAIRMAN BLANCO: Well, that is the point. That
20 is where I am going. You are saying that you are not sure
21 whether this actually, instead of lowering the C-section
22 rate, actually increases it. So, if I could play devil's
23 advocate for a minute, I mean, I would almost say then why
24 are we talking about approving this particular instrument if
25 the company hasn't convinced us that they actually have an

1 instrument that lowers the cesarean section rate? And, that
2 is the point that they went after.

3 DR. IAMS: What you have just articulated is the
4 argument against doing another rigorous study with sites and
5 investigators. I wouldn't argue for that because that would
6 be subject to the same kind of research protocol versus real
7 world. I really believe in watching what happens to the
8 rates of the endpoint you are trying to influence. We are
9 trying to see the cesarean section rate go down, and we
10 should be able, given the frequency of that endpoint, to see
11 that happen fairly soon. Maybe you can forgive the first
12 few months of people kind of trying to figure it out, but in
13 a fairly short order. This is a very frequent event. We
14 ought to see some decline in the places that use this
15 compared to what they were doing before or compared to what
16 they are doing in women who aren't getting the monitor, or
17 whatever. It shouldn't be that hard, and I don't think it
18 is at all inappropriate to say the sponsor should
19 participate in paying for that.

20 CHAIRMAN BLANCO: I don't think anybody is saying
21 that, Jay. The point is that if you feel that you require
22 that, then you are not convinced that they have proven the
23 hypothesis that they set out to show.

24 DR. IAMS: Jorge, it is just the difference
25 between the real world and the research world. I live in

1 both worlds and I see things happen in research protocols
2 and then you try to take them to the clinician and you see
3 that the product gets used in a different way. This product
4 has potential to make huge benefits. It looks like it
5 might, but it also has potential to be used, again through
6 no fault of the sponsor, in ways that could have exactly the
7 opposite effect.

8 DR. O'SULLIVAN: It is extremely important because
9 the other side of that is that we don't also need to put
10 physicians of ourselves, or anybody else, in the position of
11 having to go to court because we didn't use the monitor.

12 CHAIRMAN BLANCO: Yes, but I guess again I have to
13 go back, as the chairman and a non-voting person, and remind
14 you that medical-legal issues don't play a role. This is a
15 regulatory body. We are making a regulatory recommendation
16 and there has to be sufficient data presented to this body
17 that convinces you that there is a clinically significant
18 benefit that outweighs any risk of using this product. So,
19 you have to say I am convinced this lowers cesarean section
20 rates in a clinically beneficial way that is clinically
21 significant for approval. We are trying to redo the study,
22 it seems to me. Dr. Schultz, go ahead.

23 DR. SCHULTZ: Well, let me just say this is not an
24 uncommon scenario at this point in the day when you are sort
25 of struggling with this kind of issue, you know, where you

1 have seen something and, from a legal standpoint, what we
2 really need you to tell us is, is there reasonable assurance
3 that this device is safe and effective based on the data
4 that you have seen.

5 Now, that doesn't mean that all the questions have
6 been answered, and that there are not still lingering doubts
7 as to what will happen when this device, if it is approved,
8 goes into widespread use. We understand that, and as I
9 tried to say earlier, I think that we can work with the
10 company to try to address the types of issues that you have
11 indicated you want to see addressed.

12 Now, that could be done with different types of
13 studies. I mean, there may be more intensive studies done
14 at selected sites to gather some types of information, and
15 there could be widespread surveillance looking at how the
16 device is being used on a broader basis, perhaps collecting
17 less data on all of the patients in whom the device is being
18 used.

19 Again, I think one of the things to keep in mind
20 as well as that, yes, the company has some responsibility;
21 we have some responsibility, but there are also other
22 interested parties who may be very interested in the way
23 this device performs once it hits the market. So, I think
24 that there are a lot of different options.

25 Again though, the question that you need to answer

1 at this point, and certainly I don't want to try to do that
2 for you, is at this particular time, given that we will make
3 every conceivable effort to collect the information that you
4 are interested in collecting post-market, you still need to
5 decide at this particular time do you have reasonable a
6 assurance that this device is going to be safe and
7 effective. Once you have made that decision, then we can
8 talk about a post-market study.

9 DR. ALLEN: I know you want us to make a decision
10 on whether we like what we have heard and whether we want to
11 approve this or not, but I would like some guidance from
12 your experience. Is there a better, more rigorous way that
13 works in collecting good data? I agree with Dr. O'Sullivan
14 that registry data, my sense of it, is poor. Is there
15 something better short of another prospective study?

16 DR. SCHULTZ: Again, as I tried to say, I think
17 that there are certain questions that only prospective are
18 designed to answer. There are certain questions that only
19 those types of studies are designed to answer. There are
20 other questions that are amenable to being answered in a
21 surveillance type of study. I think that there is an option
22 here to use a combination of prospective data and
23 retrospective data to answer some of the kinds of questions
24 that Dr. Iams was talking about, looking at C-section rates,
25 say, over the previous year and then looking forward into

1 the next year.

2 Again, I think that there are a number of
3 different ways that different kinds of questions can be
4 answered, and obviously it is not going to be easy to design
5 that kind of a study but, you know, what I think you have
6 very clearly told us is that you expect this type of data to
7 be collected in one way or another, and we and the company
8 will then have to sit down and figure out how to do it.

9 CHAIRMAN BLANCO: All right. Gary, we haven't
10 heard very much from you. Do you want to make some comments
11 on these conditions? What do you think?

12 DR. EGLINTON: I think that, as Dr. Schultz said,
13 we face this at this point in the afternoon every time. We
14 do need to address these issues. What I am worried about,
15 again as Jay talks about the real world -- in the real
16 world, how are we going to get these data? I mean, how many
17 hospitals are there in this country where obstetric care
18 takes place? There are almost four million deliveries.
19 There are almost a million cesareans. How many hospitals
20 are there?

21 So, what are we really talking about? The sponsor
22 is going to be dependent upon the provider in each
23 individual hospital to write down on a piece of paper,
24 "inserted this device because the indication was non-
25 reassuring fetal status," and that is what the doc is going

1 to do. Or, actually what is really going to happen the
2 nurse is going to check something; that is what is going to
3 happen. So, how much real data are we going to get here?

4 One way we are going to get real data, as real as
5 we can get big survey data, is from the National Hospital
6 Discharge Survey, published in January or February every
7 year. It is on the web site at CDC, and it will detail the
8 number of cesareans, what the indications are for the
9 cesareans, and it runs -- I can't remember now whether it is
10 two years behind or three years behind. It is two or three
11 years behind. That is how we are going to find out.

12 I mean, if I go home from this meeting and I go
13 talk to my hospital CEO and tell him, "okay, now I've got to
14 talk you into buying Nellcor circuit boards for all our new
15 pH monitors so we can do FSpO2 monitoring," I have an uphill
16 battle and I suspect every other chairman of an OB
17 department has the same uphill battle. Where is the money
18 going to come from to buy these things? So, it is not going
19 to spread out.

20 The little device you just stick in the uterus may
21 not cost a lot of money but it is going to cost more money
22 to buy the monitors as free-standing units, and it is going
23 to take some length of time before this technology spreads
24 out in actual use. So, I think we are probably going to be
25 looking at the hospital discharge survey to get the

1 information rather than this. It will take years to do
2 this. We are not going to have very many of these things
3 inserted next year. They certainly won't be in my hospital
4 because I can't buy the darned monitors.

5 CHAIRMAN BLANCO: Well, let me address another
6 issue. I hate to put you on the spot but I know you have
7 done this longer than I have so you have been there before.
8 If we need all these conditions are you convinced that the
9 data that the sponsor has presented is sufficient to allow
10 this to be approved in some way?

11 DR. EGLINTON: I believe that the null hypothesis
12 was rejected in a properly designed and properly executed
13 randomized, clinical trial. I also agree with the need for
14 some post-market surveillance. I just think that we have to
15 be careful about how we craft that requirement and not place
16 unrealistic expectations. So, I agree with Dr. O'Sullivan's
17 motion.

18 DR. WOLFSON: I wanted to add maybe one more thing
19 to that list as I think about it. We haven't talked about
20 neonatal outcome, and that is wanting to address the issue
21 of a falsely reassuring O2 sat. At this point, I am not
22 exactly sure how to do that, or which parameters to follow,
23 but I would suggest that somewhere in there we look at the
24 neonatal outcome or we track that along with whatever
25 studies are designed under the surveillance -- possibly

1 arterial pO₂. I don't like Apgar scores; they are way too
2 flaky --

3 DR. O'SULLIVAN: Cord gases.

4 DR. WOLFSON: Yes, cord gases is what I was
5 referring to. That is probably all we have because I don't
6 think scalp pH is going to be a very valuable finding or
7 very prevalent.

8 CHAIRMAN BLANCO: I think that is broadening the
9 question. I mean, what you are now looking at is the issue
10 of the correlation and whether the monitor can be used in
11 some other way.

12 DR. WOLFSON: No, not just that, Jorge. My real
13 concern is because we don't have real rigid criteria for
14 what is the time to intervene in the face of this -- my
15 concern is that people will walk out a labor too far because
16 of ambiguity in this criterion and, as a result, we will end
17 up with babies that might end up being more acidemic
18 potentially, so end up with a higher false-negative rate
19 than what we are expecting.

20 CHAIRMAN BLANCO: So, you are interested in
21 gathering the data on the babies where the monitor was
22 utilized --

23 DR. WOLFSON: And cord gases were obtained.

24 CHAIRMAN BLANCO: Okay, you want to add that to
25 one of the conditions. We need to vote on these.

1 DR. D'AGOSTINO: Just to the question of no
2 approval or approval with conditions, if I understand
3 correctly, what the FDA is saying is that they believe that
4 they, in fact, can work with the company. So, it is not a
5 matter of hospitals have to purchase this and then see what
6 happens. You do that with the post-marketing surveillance,
7 but you can also select hospitals, select settings and give
8 them the instrument and design these prospective studies
9 that don't duplicate the clinical trial.

10 In terms of the clinical trial, there are lots of
11 problems with why in the world were the overall rates up
12 there and so forth, but the null hypothesis -- what the
13 study was designed to do, in fact, it did what its major
14 objective was. In fact, it did reduce the C-sections for
15 that particular cause. In doing it, the physicians, or
16 what-have-you, were reacting to other things and it did
17 something bizarre with the overall rate but, still, I think
18 that the clinical trial -- I would say that it is a positive
19 clinical trial but there are all these other questions, and
20 my inclination is to put them in a post-approval as opposed
21 to a pre-approval mode.

22 CHAIRMAN BLANCO: All right. We need to start
23 voting on these so any other conditions that we want to add
24 on these two, or any other subsets and so forth that we want
25 to add here? No?

1 We need to vote on these. Your vote for these
2 does not necessarily mean that you vote the way the motion
3 went. It just means whether this will be included as a
4 condition or not. Then, we need to address a couple of
5 issues about the reason or purpose of the requirement, the
6 number of patients to be evaluated and the reports required
7 to be submitted. I think we have already done for most of
8 these the reason and purpose, and I think it is probably
9 best left up to FDA and the company to look at b) and c). I
10 think you can do a better job than we can at this point of
11 knowing what those numbers are.

12 So, let's have a show of hands of those voting
13 members -- and I probably should go through who the voting
14 members are. Does everybody know? Don Chatman, Subir Roy,
15 Nancy Sharts-Hopko, Machelles Allen, Ralph D'Agostino, Mike
16 Diamond, Gary Eglinton, Jay Iams, Michael Neuman, Mary Jo
17 O'Sullivan and Robert Wolfson. Neither the consumer
18 representative nor the industry representative get to vote.
19 Sorry.

20 If we could see a vote for number one, requiring
21 surveillance for indication for use as a condition of
22 approval? All those in favor, raise your hand.

23 [Show of hands]

24 All those opposed?

25 It looks like that one carries.

1 Number two, surveillance for the various issues
2 that we have discussed and that are written up there,
3 including neonatal outcome and cord pH's, all those in
4 favor, raise your hand.

5 [Show of hands]

6 All those opposed? The motion carries. We are
7 just unanimous.

8 Now the floor is open for any other conditions
9 that may want to be added to the motion for conditions. Do
10 I hear anything else?

11 DR. IAMS: Did we talk about labeling yet?

12 CHAIRMAN BLANCO: No. So we need to bring that
13 up.

14 DR. SHARTS-HOPKO: I was going to say we need to
15 note the issue about vertex or cephalic, whatever you want,
16 presentation as a requirement for use.

17 DR. IAMS: I guess I will take the blame for
18 bringing that up but the study was really done in vertex
19 infants so that is probably the most accurate.

20 CHAIRMAN BLANCO: All right, so let me hear a
21 motion.

22 DR. SHARTS-HOPKO: I move that we modify the
23 indications for use to include -- what did you say? --
24 vertex presentation.

25 CHAIRMAN BLANCO: Do I hear a second?

1 DR. IAMS: Second.

2 CHAIRMAN BLANCO: Okay. Any discussion on that?

3 No? Okay, again, all those in favor, raise your hand.

4 [Show of hands]

5 All those opposed?

6 CHAIRMAN BLANCO: That carries. Now, there are a
7 few more things on indication for use.

8 DR. SHARTS-HOPKO: Well, I am on this kick about
9 contraindicating it in HIV-infected women. I would like to
10 move that that be added.

11 CHAIRMAN BLANCO: Any second?

12 DR. EGLINTON: Second.

13 DR. ALLEN: Well, discussion around that, should
14 it also be contraindicated who have active herpetic lesions,
15 who are hepatitis B surface antigen positive or E antigen
16 positive? Are there other specific infections that should
17 be added?

18 DR. SHARTS-HOPKO: The way they stated it was
19 herpes or other infectious diseases. I just think that HIV
20 is unique.

21 DR. IAMS: I would say this is a situation where
22 the concern about fetal invasiveness versus maternal
23 invasiveness is determinative here. I can understand why
24 the sponsor didn't want to do a study in women who might
25 have those complications but this is not a device that

1 intentionally or even probably unintentionally is likely to
2 break the fetal skin. So, therefore, the risk in
3 transmitting all these infections that we just talked about
4 should not be particularly increased. I can understand your
5 concern about that but I don't think it would be -- unlike a
6 scalp electrode which clearly breaks the skin and which
7 clearly has been associated with herpes and a few other
8 indications where that would be a contraindication. I am
9 not sure that it should be contraindicated in those
10 instances. I think that is something that you can just look
11 at post-surveillance.

12 DR. O'SULLIVAN: I would have a great deal of
13 concern about that, Jay. We don't know what effect, if any,
14 this device would have even on the maternal vaginal mucosa
15 in terms of trauma during insertion and increasing the
16 presentation of CD4 lymphocytes, or monocytes or any viral-
17 carrying organisms into the vagina which would increase
18 viral load in the vagina. And, the numbers are small enough
19 that I just don't see that as an issue --

20 DR. IAMS: Right. I would just defer to your
21 expertise in that area because I know you have quite a bit
22 more than I do. Do you currently not use intrauterine
23 pressure catheters in women --

24 DR. O'SULLIVAN: We do not use intrauterine
25 pressure catheters. We do not use scalp electrodes. We do

1 not puncture membranes.

2 DR. IAMS: You make a distinction between scalp
3 electrodes. I don't think anybody does that, but internal
4 pressure catheters you would not use --

5 DR. O'SULLIVAN: No.

6 DR. IAMS: -- in an HIV-positive woman?

7 DR. O'SULLIVAN: No.

8 DR. IAMS: Would you use them in an HSV-positive
9 woman or a GBS-positive woman?

10 DR. O'SULLIVAN: Well, HSV that has a lesion is
11 not likely to be delivering vaginally anyway.

12 DR. IAMS: No, that is correct.

13 DR. O'SULLIVAN: GBS, yes, I would use it.

14 CHAIRMAN BLANCO: Let's take it one at a time.
15 HIV Any other discussion?

16 DR. ALLEN: What Dr. O'Sullivan mentioned I don't
17 think was heard. The key point is artificially rupturing
18 membranes.

19 DR. O'SULLIVAN: Right.

20 DR. ALLEN: For HIV infection.

21 DR. O'SULLIVAN: Yes.

22 DR. ALLEN: So, if you wouldn't rupture membranes
23 in a particular patient population -- and there is probably
24 a large percentage of providers who aren't up with the
25 current literature with things that may be associated with

1 perinatal transmission, so it might be worthwhile re-
2 mentioning that in the HIV-positive population you wouldn't
3 rupture membranes, i.e., this is a situation where you
4 wouldn't use this device.

5 CHAIRMAN BLANCO: Do you want to amend the motion
6 to make it broader? How would you amend it? What do you
7 want to say?

8 DR. SHARTS-HOPKO: Probably simple is better and
9 just specifically HIV positives without all the rationale.

10 CHAIRMAN BLANCO: All right. So, we are going to
11 vote on HIV-positive individuals. It should not be utilized
12 in HIV-positive individuals. All those in favor, raise your
13 hand.

14 [Show of hands]

15 All those opposed? Okay, so that is added to the
16 labeling. Herpetic lesions? I know, as we said, it is
17 unlikely they would be delivering vaginally but if we are
18 being thorough should we identify it? All those in favor?
19 Oh, a little discussion.

20 DR. SCHULTZ: Dr. Blanco, could I make one comment
21 before you go through all these?

22 CHAIRMAN BLANCO: Yes, sir. You can make two!

23 DR. SCHULTZ: Thank you. I just want to point out
24 that there are degrees of negatives that you can put into
25 the labeling. Contraindications to us means never, no-how,

1 no-way, absolute that it is not to be used. Warnings, on
2 the other hand, may mean that you have identified an
3 increased risk in doing something and, therefore, the
4 practitioner should use utmost caution if he or she decides
5 that in his or her particular patient this may be indicated,
6 but it is not an absolute. Precautions can be in those
7 situations where there is just no information, like you
8 mentioned, where the study did not include those types of
9 patients but there may not be any information pro or con to
10 say that this is either good or bad. So, just so you have
11 those options in mind so that not everything becomes a
12 contraindication.

13 CHAIRMAN BLANCO: Thank you. Does anybody want to
14 revisit HIV or is everybody pretty comfortable that that is
15 a contraindication? Comfortable?

16 DR. O'SULLIVAN: I have to think about that.

17 DR. IAMS: We don't really know, do we?

18 DR. O'SULLIVAN: No, we don't really know. We can
19 only theorize that there is a potential for increasing
20 risks, and the same thing with intrauterine pressure
21 catheters, we don't really know whether, in fact, that would
22 increase risk. Scalp electrodes do. I mean, there is some
23 information to suggest that they do, at least in the non-
24 treated HIV-infected individual. So, perhaps the better
25 terminology may be that -- what was the word you used?

1 CHAIRMAN BLANCO: Warning.

2 DR. IAMS: I would suggest warning for HIV and
3 precautions for all the others, and I wouldn't put Group B
4 strip in there at all because you have a treatment for that.

5 DR. O'SULLIVAN: Yes.

6 CHAIRMAN BLANCO: Would you like to amend the
7 motion? Let me see if I can get this right. The motion
8 would read that HIV and herpes be placed as a warning, and
9 that is it, and not Group B strip in there at all. Is that
10 acceptable to you, Dr. Sharts?

11 DR. SHARTS-HOPKO: That is acceptable but I
12 thought they already addressed herpes in there.

13 CHAIRMAN BLANCO: I don't think they are going to
14 be terribly interested --

15 DR. SHARTS-HOPKO: Okay, I accept it.

16 CHAIRMAN BLANCO: -- in a small number of patients
17 that fit into this criteria. So, we need to vote and move
18 on. So, do you think it is a warning label or a
19 contraindication?

20 DR. ALLEN: Can I ask Dr. O'Sullivan about E
21 antigen status?

22 DR. O'SULLIVAN: Gosh, we never do it. We never
23 look at E antigen --

24 DR. ALLEN: Oh, we do.

25 DR. O'SULLIVAN: So, you probably have much more

1 experience with that one.

2 DR. IAMS: I would just make the comment that this
3 is a device that allows you not to break the skin and find
4 out more about the baby's well-being, whereas the
5 alternative is either cesarean or a scalp sampling, which
6 you are precluded from doing. So, it seems to me that we
7 are being cautious but maybe at the expense of fetal well-
8 being and giving the mother a section which she might
9 otherwise not have.

10 DR. O'SULLIVAN: I think warning is a good idea
11 because I think that we don't have definite evidence.

12 CHAIRMAN BLANCO: Okay, warning for HIV, warning
13 for herpes, warning for hepatitis. Let's vote on one at a
14 time. Let's go back to warning for HIV. All those in
15 favor?

16 [Show of hands]

17 Okay, and no one opposed. Herpes?

18 DR. DIAMOND: With or without a lesion?

19 CHAIRMAN BLANCO: Active herpes lesion. Warning?
20 Somebody brought it up so we have to vote on it.

21 DR. SHARTS-HOPKO: It is in there.

22 CHAIRMAN BLANCO: It is in there, so you agree.
23 Okay. So, they did it already in the labeling. Then, the
24 third one was hepatitis B, E antigen positive.

25 DR. ALLEN: Well, there is so little information,

1 I don't know.

2 CHAIRMAN BLANCO: Well, one way or another.

3 DR. IAMS: Caution.

4 CHAIRMAN BLANCO: Caution? All right.

5 DR. SCHULTZ: I think unless you want to go
6 through a list of all the infections known to mankind --

7 [Laughter]

8 -- I think we get the message and I think we can
9 fashion something appropriate with the sponsor warning and
10 precautioning what you want warned and precautioned.

11 CHAIRMAN BLANCO: All right. That means I am not
12 doing my job. I have to crack that whip and get it going.
13 Okay, any other labeling issues?

14 DR. IAMS: Well, the one that you mentioned
15 before, if I understand labeling, in item four you
16 recrafted, to be used in a term fetus, in a vertex
17 presentation with non-reassuring fetal heart rate tracing as
18 an adjunct to fetal heart rate monitoring to permit the safe
19 continuation, etc., and that paragraph would be in and the
20 rest of them would be out.

21 CHAIRMAN BLANCO: Yes, including the utilization
22 of the clinical matrix.

23 DR. IAMS: And including the utilization of the
24 clinical management matrix, right.

25 CHAIRMAN BLANCO: With the definitions as utilized

1 there. Any discussion on that? Everybody is clear? All
2 those in favor, raise your hand.

3 [Show of hands]

4 Opposed? That passes. Diony, any other items
5 that we have forgotten?

6 MS. YOUNG: No. You know, the ones that I
7 mentioned in terms of adding to the patient information
8 video or information -- specifically what was left out. One
9 was about the indications for use, which should certainly be
10 described to a woman before a device is used. The second
11 one was talking about -- what was it?

12 CHAIRMAN BLANCO: Marks on the baby's cheek?

13 MS. YOUNG: Sorry, the invasive issue, the fact
14 that it is invasive to the fetus -- excuse me, not invasive
15 to the fetus, the mother.

16 CHAIRMAN BLANCO: Do we have a motion on those
17 items?

18 DR. O'SULLIVAN: I have a question. The question
19 really has to do with when or where this video would be
20 shown to the patient. Since the diagnosis or an ominous
21 fetal heart rate tracing is going to be made during the
22 course of labor and I doubt most labor floors have videos on
23 them, nor am I aware the patient is really going to be in a
24 position to see the video -- I am just curious to know when
25 or where these videos are going to be used.

1 CHAIRMAN BLANCO: Well, I don't think that you
2 necessarily have to have a video, but you do have to give
3 some level of informed consent and information to the
4 patient prior to her approval for the use of the instrument.
5 I think we had actually discussed that a video wasn't a good
6 idea for the patient. So, I think it is a matter of what
7 information should be given to the patient prior to the
8 utilization of the monitor.

9 DR. CHATMAN: Theoretically, it will be used if
10 you have a patient who has a non-reassuring heart rate
11 pattern, who is 41 weeks pregnant and you want to get
12 delivered, and before you start Pitocin, you could use it
13 then but there would obviously be very limited applications
14 for a video.

15 DR. WOLFSON: I am going to give a contrary view
16 again. While I agree I would not want to set a negative
17 intention in a patient by introducing her to this material,
18 and what-not, I do believe -- and my understanding at least
19 in our institutions and our community that our birthing
20 classes to speak to the issues of cesarean delivery as an
21 outcome. They do address the use of internal fetal
22 monitoring. And, I can see this video being incorporated in
23 such classes. Granted, I realize it is coming from the
24 sponsor but I can see it also as part of an educational
25 process for the patient prenatally.

1 CHAIRMAN BLANCO: Well, I have a little bit of a
2 concern because I think you are going to then have a lot of
3 patients who are going to say, "oh, it sounds great. I want
4 that. Oh, I don't care if I've got a non-reassuring fetal
5 heart rate or not, it sounds good to me."

6 DR. WOLFSON: Oh, come on, Jorge, we don't have
7 patients running to us asking for fetal internal fetal
8 monitoring.

9 CHAIRMAN BLANCO: Well, maybe you don't but I do.
10 They ask for the section and everything else.

11 [Laughter]

12 DR. WOLFSON: Okays, it comes down to patient
13 education, I will agree with you on that, and it is going to
14 vary from community to community. Just like I was impressed
15 that they had a 95 percent epidural rate, we can barely get
16 40 percent and our patients really want the opposite because
17 of the way in which we approach things clinically and
18 because of the way we educate our patients.

19 CHAIRMAN BLANCO: The feeling I got from the
20 committee is that those folks in which it may be used ought
21 to be the ones that need to be informed about its use. Am I
22 expressing the committee's -- I see a lot of nodding heads
23 so we are going to assume that is the committee's desire.

24 DR. SCHULTZ: Just one more comment, the other
25 thing that I heard and that I think we can work on is to

1 make sure that whatever information is passed along is
2 purely factual, non-promotional, non-suggestive of things
3 that you don't want suggested. So, I think your points are
4 well taken on the issues of who gets it, the timing and the
5 content of both written and whatever other information is
6 passed along to the patient. Those are things that you want
7 worked on. Does that summarize it?

8 CHAIRMAN BLANCO: Yes, and now that you have
9 summarized it so well, let's vote on it?

10 DR. WOLFSON: Could I add one more thing to the
11 labeling issue? We talked earlier about possibly putting, I
12 guess under warning, some information about the accuracy of
13 the instrument. Is that still a desire of the committee? I
14 think Dr. Neuman spoke to that.

15 CHAIRMAN BLANCO: Yes, why don't you hold that
16 thought because we are talking about what we are going to
17 tell the patient and I thought that is what we wanted for
18 physicians. So, hold that thought --

19 DR. WOLFSON: You are correct.

20 MR. JARVIS: What about the statement that permits
21 safe continuation of labor during non-reassuring FHR
22 patterns and reassuring fetal oxygen saturation? Are we
23 going to throw out that statement or leave that statement
24 in?

25 CHAIRMAN BLANCO: Well, it sounds like there needs

1 to be some discussion.

2 MR. JARVIS: We need clarification on that,
3 absolutely.

4 CHAIRMAN BLANCO: Hold that thought and let's vote
5 on what is on the floor at the current time. What we are
6 discussing is Diony's suggestion about the patient
7 education, which Dr. Schultz outlined so well. All those in
8 favor, raise your hand.

9 [Show of hands]

10 All those opposed? Okay, that passes.

11 DR. MITCHELL: Dr. Blanco, will you just look and
12 see if you are happy with the way it is written here before
13 we go on -- patient labeling and video, use only in patients
14 who will need it.

15 DR. SHARTS-HOPKO: I think we changed "video" to
16 patient education --

17 CHAIRMAN BLANCO: Yes, patient education material.
18 Use only in patients who need it, and then the factual
19 information, and then the issue of invasiveness of the
20 mother but not invasiveness of the fetus.

21 MS. YOUNG: And the indications for use.

22 DR. MITCHELL: You mean put the indications for
23 use?

24 CHAIRMAN BLANCO: Let her know the indications for
25 its use is I think what Ms. Young was suggesting.

1 Since we have voted already and we added some
2 things, does anybody have any problem with what we have
3 added? If not, we will just move on.

4 DR. EGLINTON: I am trying to get in the part
5 about don't put it in if you don't know what position the
6 head is in. When do we get to that?

7 CHAIRMAN BLANCO: That is for physicians so why
8 don't we wait for that? Let's get back to indications
9 because we kind of did that one already, and let's clarify
10 it. The issue was when we did indications we really
11 narrowed it down to an adjunct to fetal heart rate
12 monitoring in a term fetus with a vertex presentation and a
13 non-reassuring fetal heart rate, and the issue before was we
14 pretty much threw everything else out. The issue brought up
15 is did we mean to throw out the issue of permits the safe
16 continuation of labor during non-reassuring fetal heart rate
17 patterns and reassuring fetal oxygen saturation, thereby
18 reducing the cesarean section rate for non-reassuring fetal
19 status?

20 My view would be, and let's see if other folks
21 like it, the part I wouldn't put in there is permits the
22 safe continuation of labor during non-reassuring fetal heart
23 rate patterns and reassuring fetal oxygen saturation. I
24 think that is the problem. But I think the issue of
25 reducing the cesarean section rate could be in there. How

1 do other people feel?

2 DR. IAMS: How would you phrase that?

3 CHAIRMAN BLANCO: How would I phrase it?

4 DR. EGLINTON: It is in the book.

5 CHAIRMAN BLANCO: Well, why don't you read it for

6 us? DR. EGLINTON: On page SSED-1.

7 DR. O'SULLIVAN: Which volume?

8 DR. EGLINTON: In volume one.

9 CHAIRMAN BLANCO: That is where I read it from
10 before.

11 DR. EGLINTON: Right, just where you read it from
12 before. Under heading 2, indications for use, the paragraph
13 starts, Nellcor N-400 fetal oxygen saturation monitoring
14 system continuously monitors fetal oxygen saturation, FSpO2,
15 and is indicated for use as an adjunct to fetal heart rate -
16 - all the way down to when used in conjunction with. If we
17 stop at one, reducing the rate of cesarean section rate
18 performed for non-reassuring fetal status, period.

19 CHAIRMAN BLANCO: Is the committee satisfied with
20 that?

21 DR. EGLINTON: Yes.

22 CHAIRMAN BLANCO: Yes? Okay. Anybody who is not,
23 speak now or forever hold your peace.

24 DR. O'SULLIVAN: Are we going to define what non-
25 reassuring fetal heart rate is?

1 CHAIRMAN BLANCO: Well, that is the addition of
2 the definition in the clinical matrix.

3 DR. EGLINTON: Add as defined by the clinical
4 matrix?

5 CHAIRMAN BLANCO: Right. So, that needs to be
6 added.

7 DR. EGLINTON: In the presence of a non-reassuring
8 fetal heart rate pattern as defined by the clinical matrix -

9 -

10 DR. O'SULLIVAN: Yes.

11 DR. EGLINTON: -- during labor and delivery?

12 DR. O'SULLIVAN: Yes.

13 CHAIRMAN BLANCO: Okay.

14 DR. ROY: But, Jorge, is that really defined
15 anywhere? It just states in the matrix that there is a non-
16 reassuring fetal heart rate pattern --

17 CHAIRMAN BLANCO: No, it describes it. It
18 describes what fits into the class two of what is a non-
19 reassuring fetal heart rate pattern.

20 DR. O'SULLIVAN: Can't that be included right
21 below the statement? Slide number 17.

22 DR. ALLEN: It is 2-61 in volume one.

23 CHAIRMAN BLANCO: Does anyone want to add anything
24 else, or are they satisfied with that?

25 DR. MITCHELL: Can I write this and then we come

1 back to it after I have it all written down exactly the way
2 you want to vote on it?

3 CHAIRMAN BLANCO: Please.

4 DR. MITCHELL: It will take me a minute.

5 DR. ALLEN: Are we adding the definition of non-
6 reassuring in the labeling?

7 DR. O'SULLIVAN: No -- yes.

8 CHAIRMAN BLANCO: Yes. Yes, that is part of the
9 inclusion of the clinical matrix, the definition as they
10 used it.

11 While you are writing it, Dr. Mitchell, the issue
12 that comes up is whether the committee would like the
13 statement, the safe continuation of labor, the reassuring
14 fetal oxygen saturation part put in there. I think that is
15 why the issue was brought up again. What is the pleasure of
16 the committee?

17 DR. DIAMOND: No.

18 CHAIRMAN BLANCO: Thank you, Dr. Diamond, for a
19 definitive statement. Anyone else want to make a definitive
20 statement? I have a feeling that is not going to be
21 included.

22 Why don't we go ahead, while she is writing, with
23 the physician labeling and then we will come back to the
24 indication the way it is written? One of the issues was you
25 have to know the presentation, the position. What was the

1 other one, Dr. Wolfson?

2 DR. WOLFSON: Well, didn't we talk about some
3 level of expertise with respect to intrauterine pressure and
4 scalp monitoring?

5 DR. O'SULLIVAN: Proficiency in the application of
6 scalp monitoring and intrauterine pressure catheters.

7 CHAIRMAN BLANCO: Thank you. Well put.

8 DR. WOLFSON: Then, thirdly, was the issue of
9 including a statement about the accuracy of the unit.

10 CHAIRMAN BLANCO: Also, didn't we mention a
11 disclaimer or warning about its inability, at this point at
12 least, to be correlated with fetal pO2? Didn't we say
13 something about that earlier on?

14 DR. WOLFSON: Yes, we did.

15 DR. IAMS: I thought that is what we used to
16 replace the accuracy statement. We were, I thought, kind of
17 unanimous in saying we didn't want to put in the physician
18 labeling the exact same accuracy data that we reviewed this
19 morning, but we responded to that concern this afternoon
20 with the second part of what you just said, which was a
21 statement that it doesn't necessarily reflect the actual
22 pO2.

23 CHAIRMAN BLANCO: Right, that is what we were
24 adding to the physician labeling. Should that be a warning
25 or a precaution? Remember the levels. You will figure it

1 out? Good. We will let you figure it out.

2 Are we ready?

3 DR. MITCHELL: For which one? The indications?

4 CHAIRMAN BLANCO: Yes, so this is what we
5 discussed, indications for use: Nellcor N-400 system
6 continuously monitors FSpO2 and is indicated for use as an
7 adjunct to fetal heart rate monitoring. When used in
8 conjunction with fetal heart rate monitoring under a
9 specified protocol. The system has been demonstrated to be
10 safe and effective.

11 Well, I think we can clean up the English, and I
12 would really make a reference, rather than under a specified
13 protocol, to the matrix and the definition itself, but maybe
14 that is overkill on my part. Okay?

15 DR. MITCHELL: So, you want the entire management
16 matrix --

17 CHAIRMAN BLANCO: Well, it is a reference to that.
18 I thought that was the desire of the committee.

19 DR. MITCHELL: Okay.

20 DR. SCHULTZ: Dr. Blanco, I think what I am
21 hearing is that you want reference made to the matrix, and
22 that when used according to the matrix the device would
23 allow for safely continuing to monitor patients who would
24 otherwise go to section. Is that okay with you? Something
25 to that effect?

1 CHAIRMAN BLANCO: Is that okay with the committee?

2 DR. IAMS: Well, not necessarily go to section.

3 Go to operative delivery might be a better word.

4 DR. SCHULTZ: Well, was that studied?

5 DR. IAMS: That was studied but it wasn't shown,
6 but that is the intent, I think.

7 CHAIRMAN BLANCO: Well, I think we need to go with
8 whatever was studied. So, I think section.

9 DR. IAMS: Okay.

10 MR. JARVIS: Do we also want to include the
11 statement in here, thereby reducing the C-section rate for
12 non-reassuring fetal status, in this indication because that
13 is one thing they did do?

14 DR. ALLEN: Well, yes, it is in there as part of
15 the indications that we specified that we wanted in. It is
16 not on the overhead.

17 CHAIRMAN BLANCO: Yes, the system has been
18 demonstrated to be safe effective in reducing cesarean
19 sections for non-reassuring fetal status. So, it is in
20 there.

21 Everybody read to vote on the indication?
22 Everybody is happy with the way it is? Any other
23 suggestions? All right, all those in favor, raise your
24 hand.

25 [Show of hands]

1 Those opposed? Okay, that is what we would like.
2 Now let's go to physician labeling. We have four things.
3 You should know the position.

4 MS. YOUNG: Excuse me, is that the position of the
5 fetus or the position of the mother?

6 CHAIRMAN BLANCO: No, the position of the fetus.

7 MS. YOUNG: Okay, because I didn't raise issues to
8 do with the maternal positioning.

9 CHAIRMAN BLANCO: Right, fetal position so that
10 you know how to apply the monitor to the cheek, where you
11 should go with it. Proficiency with insertion of IUPCs and
12 fetal scalp electrodes. Then, a warning on the accuracy of
13 the device and a disclaimer or warning, and we will leave it
14 up to FDA as to what level, that the reading doesn't
15 necessarily correlate directly with pAO2 in the fetus.

16 DR. CHATMAN: Should we say something about the
17 station?

18 CHAIRMAN BLANCO: It is in there. You mean, it
19 should really be below minus 2? In the labeling?

20 DR. O'SULLIVAN: It is in there.

21 CHAIRMAN BLANCO: We are reiterating that that is
22 important to us.

23 DR. CHATMAN: You are talking about physician
24 labeling, right?

25 CHAIRMAN BLANCO: Physician labeling, correct.

1 DR. CHATMAN: You are just creating it now?

2 CHAIRMAN BLANCO: Well, they have already made
3 some suggestions. These are things that we may want to
4 change or have them add, or subtract, or clarify.

5 Anything else that we want to put in with the
6 physician labeling?

7 DR. IAMS: Jorge, I just want to beat this dead
8 horse again, but I thought we were not going to put
9 something in there that was a warning to the doctors about
10 the accuracy. Rather, we were going to describe the fact
11 that it didn't necessarily produce the fetal arterial oxygen
12 saturation. I thought we wanted to avoid that warning about
13 the accuracy because that would be, we thought, misleading.
14 I thought that is all what we said yes to, but maybe I am
15 the one who is not understanding it.

16 CHAIRMAN BLANCO: Okay, you have to put it
17 somewhere in the physician labeling so it is either
18 contraindication, a warning or a precaution saying that the
19 reading of the machine does not necessarily correlate with
20 the pAO2 of the fetus. That is what you want said. At what
21 level do you want that included?

22 DR. O'SULLIVAN: Do you want to say it that way or
23 do you want to say that that information is not yet
24 available?

25 CHAIRMAN BLANCO: Well, it is up to the committee

1 to recommend how it should be put. So, how would you like
2 it?

3 DR. O'SULLIVAN: Well, the point I am trying to
4 make is that it was not clear to me that they actually
5 proved that it did correlate and, therefore, we don't have
6 any information that it doesn't correlate.

7 CHAIRMAN BLANCO: So, how would you word it?

8 DR. O'SULLIVAN: Well, the information we have is
9 that there is a wide margin there.

10 DR. ALLEN: We may be able to say something --

11 DR. ROY: I think all we really have is
12 information at a pO2 of 40 percent, that the standard
13 deviation is 4.7. We have no data as to its accuracy at 30
14 percent.

15 CHAIRMAN BLANCO: Let me make a suggestion and see
16 how you buy this, a precaution that says there is
17 insufficient data to be able to correlate the reading from
18 the monitor with the arterial O2 of the fetus. Therefore,
19 this monitor should not be used to predict pAO2's in the
20 fetus. Something to that effect, and they can clean up the
21 English.

22 DR. ALLEN: Actually, I would like to step back
23 from that because I think there is a degree of accuracy. It
24 is not 100 percent precise, but I think it is acceptable
25 within the community for the intents that we have outlined

1 in the indication for use. I think Dr. Iams brought up
2 before that it was sufficiently confusing to us here, as a
3 panel, and that it would be even more confusing to the
4 community physician. And, I would be quite comfortable to
5 leave it out unless we just put in this margin of error or
6 standard deviation. But I think it is just too hard to
7 understand when you talk about what Dr. Iams was talking
8 about before, you know, if it is 30 percent for 20 minutes
9 there is less deviation or variability than if it is 30
10 percent for a second. It is just too complicated I think to
11 put in the labeling.

12 CHAIRMAN BLANCO: But that was kind of the whole
13 reason why I thought Dr. Iams had come up with the issue
14 about just making it as a general statement. It is the
15 pleasure of the committee. Let's just make it formal. Do I
16 hear a motion that we include some warning about not
17 utilizing this as an estimation of pAO2?

18 DR. DIAMOND: Yes, so moved.

19 CHAIRMAN BLANCO: A precaution? Okay. Is there a
20 second?

21 DR. WOLFSON: Second.

22 CHAIRMAN BLANCO: Any more discussion? How many
23 would vote in favor, raise your hand.

24 DR. CHATMAN: What is it again?

25 CHAIRMAN BLANCO: The motion is that we include a

1 precaution that there is insufficient data to utilize the
2 FSpO2 level to correlate to the fetal pAO2, some sort of
3 wording like that which FDA can do better than I can.

4 All those in favor?

5 [Show of hands]

6 Opposed?

7 The next issue is we are going to put that
8 statement in and we are not going to put in any numbers in
9 terms of the accuracy of the 4.7 percent, 0.6 percent, etc.
10 Is that agreeable to the committee? A lot of shaking heads,
11 yes.

12 Now, back to the other things we had done here in
13 the physician labeling, any other issues that we need to add
14 or are we ready for a vote? It looks like we are ready for
15 a vote. All those in favor of those three issues up there,
16 please signify by raising your arm.

17 [Show of hands]

18 All those opposed? It carries.

19 All right, anything else that we would like to
20 consider as conditions? Not hearing any other conditions,
21 then let's review the motion. The motion is for approval
22 with the various conditions that we have already outlined,
23 and it was voted. All those in favor of the motion for
24 approval with the conditions that were presented, please
25 raise your hand.

1 [Show of hands]

2 Seven. All right, all those opposed, please raise
3 your hand.

4 [Show of hands]

5 And those abstaining? I don't think you voted
6 either way, Mike.

7 DR. NEUMAN: I am not part of the panel.

8 CHAIRMAN BLANCO: Dr. Schultz, will you please be
9 part of the panel? Thank you. We have to come around and
10 have everyone justify their vote. At this point it is 7-1,
11 and whether you approve with conditions for or against.

12 DR. NEUMAN: I would vote for approval with
13 conditions.

14 CHAIRMAN BLANCO: Somebody else abstained -- we
15 still have 11 people and I got 9 votes. Let's do that
16 again. All those in favor of approval with the conditions,
17 please raise your hand.

18 [Show of hands]

19 Ten -- I just can't count. Thank you. Then one.
20 The motion carries 10-1.

21 Having voted, that marks the end of the need for
22 this panel meeting. I would like to thank all the panel
23 members -- oh, I forgot, sorry. We have to poll everyone as
24 to why they voted the way they did. Dr. Roy, let's start
25 from your end. Ms. Young is not a voting member, sorry.

1 Well, do you have any comments, Diony?

2 MS. YOUNG: Well, yes, I would like to make a
3 statement, brief. Twenty years ago I wrote a booklet, co-
4 authored with Dr. Charles Meehan, in Florida, Unnecessary
5 Cesareans: Ways to Avoid. That was twenty years ago and
6 during that time I have always been very concerned about the
7 rising cesarean section rate, and very concerned about
8 looking at ways to reduce that rate.

9 By the same token, in 1985 I was at a conference
10 in New York City and I heard Dr. Emmanuel Friedman and Dr.
11 Edward Hahn talk about misuse and abuse of the electronic
12 fetal monitor. So, my concern with this particular device,
13 and it has been reiterated many times by other panel
14 members, is that it be used appropriately and within the
15 parameters of the matrix, and any other parameters that are
16 the result of any further surveillance that is done so that
17 it will be used accordingly with a population of women for
18 whom it is appropriate.

19 CHAIRMAN BLANCO: Thank you. Mr. Jarvis, would
20 you like to make a comment?

21 MR. JARVIS: I have no comments.

22 CHAIRMAN BLANCO: Thank you. Back to you, Subir.

23 DR. ROY: Well, I voted for approval with
24 conditions because I think the sponsor proved their primary
25 objective, which is not to say that everything is perfect

1 with it and I think the panel discussion illustrates that we
2 would all like to obtain more information as has been
3 characterized. I am particularly mindful of the need to try
4 to refine exactly what the branch point is, and to the
5 extent that additional studies can be done with the purview
6 of what we have recommended or independently, that would
7 simply help everyone, including the sponsor, in having this
8 tool used appropriately.

9 CHAIRMAN BLANCO: Thank you.

10 DR. SHARTS-HOPKO: I agree with Dr. Roy's
11 rationale and I would also like to add that this was a very
12 paradoxical discussion for me. I abhor the medicalization
13 of birth. So, to add one more gadget to the array gives me
14 some distress, but it is because of the promise that it
15 shows to reverse that trend that I would like to give this a
16 really good chance.

17 DR. DIAMOND: I voted against the motion as it was
18 stated. I thought that while the data showed that the rate
19 of cesarean sections for abnormal heart rates did in fact
20 decrease, the overall study population did not have a
21 difference in their cesarean section rate. Unfortunately,
22 this may be because of the increase in dystocia, and with
23 that unexpected finding the data did not exist for
24 intrauterine pressure catheters to know whether labor was
25 adequate to be able to more accurately and closely define

1 that and try to explain the observations that they had.

2 Other things that I thought were missing was the
3 lack of reproducibility of monitoring the FSpO2 at the 30
4 percent cut-off to be utilized in clinical use; the lack of
5 data on how often the FSpO2 became less than 30 and then
6 corrected, and to what degree it would correct, how long it
7 would stay corrected, and how long it then took to intervene
8 for clinical care.

9 Also, in situations where scalp pH was evaluated
10 at the time when the FSpO2 was low, it was not known by the
11 sponsors at this time if this influenced the clinical care
12 and the outcome measures that were evaluated.

13 At this point in time, as it would go into
14 clinical use, based on this pivotal trial, there is not a
15 single defined protocol for what to do if the FSpO2 is low
16 in as much as each clinician was using their own paradigms
17 and, therefore, we don't have any consistent clinical
18 guidelines to offer to practitioners.

19 I would have preferred to see a study addressing
20 these issues prior to approval because it is my concern that
21 if it is approved and in use, it is going to be like water
22 that is over the dam. It is going to be out there and the
23 concerns that have been raised around the table about
24 inappropriate use in the future or use in other indications
25 will be things that will be very hard to control. So, my

1 preference would have been to require other studies to be
2 done prior to the approval of product and its distribution
3 for general use.

4 DR. ALLEN: I voted for approval. I found it
5 significant that the cesarean sections for non-reassuring
6 fetal heart rate tracings were, in fact, decreased as had
7 been proposed in the study design.

8 I did have concern about the overall increased
9 section rate in the study in general above the baseline
10 study. I think it is crucial that data be collected
11 prospectively from hereon out to discern what was the
12 underlying basis for that and how that falls out so that the
13 cesarean sections that are done with this monitor in place -
14 - is it truly done for dystocia or, in fact, will it
15 actually, as the power gets larger, show that there is no
16 real significant increase in cesarean sections.

17 DR. IAMS: I voted for approval with the
18 stipulations or conditions attached because although I share
19 Dr. Diamond's concern about the failure to show a decline in
20 cesarean section, I think the only arena in which that
21 really can be tested is the real world. I think further
22 studies before that point will simply delay something that
23 has a fair bit of promise. So, my approval vote is
24 literally conditioned on the expressed willingness of the
25 FDA to track cesarean section rates, and expect them to go

1 down, and expect there to be some noise if they don't go
2 down when this device is widely used.

3 DR. EGLINTON: As Jorge said, I have been coming
4 to these meetings now for eleven years either as a panel
5 member or a consultant, and I am gratified to see that the
6 quality of the studies, the design, the implementation and
7 reporting has improved steadily during that time. I voted
8 for approval because I think this is the best one I have
9 seen in this forum.

10 I share the concern that everybody else has about
11 the increased cesarean section rate seen between the
12 baseline and the RCT and I am eagerly awaiting the results
13 of some sort of surveillance post-market.

14 DR. O'SULLIVAN: I voted for approval with the
15 conditions applied and I really can't add anything to what
16 everybody else has said, other than to reiterate it so I
17 will not do that.

18 DR. WOLFSON: I voted for approval as well with
19 conditions. I chose to do so because in, my experience, I
20 believe that the invocation of cesarean delivery for non-
21 reassuring fetal heart rate is prevalent. I believe it is
22 also particularly a challenge in rural areas of the United
23 States, and that is true in my community and to the area
24 south. And, I believe that this modality is going to help
25 physicians reduce the cesarean rate for that specific

1 indication, though it may be broader than what was
2 specifically studied.

3 I also voted for approval because I too felt that
4 the study was well designed, well executed, and I had no
5 question about its specific efficacy based on that. And, I
6 look forward, as I think other panel members, to learning
7 some of the other details, particularly about dystocia,
8 infection rate and acceptability to the patient population.

9 DR. D'AGOSTINO: I voted for approval, again
10 subject to conditions. I think the trial that was presented
11 fits fairly nicely into the notion of large simple trials
12 where you don't have necessarily a strong, detailed list of
13 conditions for administering treatments or a particular
14 decision-making but, rather, leave it somewhat in an actual
15 use mode.

16 It leaves us in a quandary in terms of
17 interpretation, but I think the results are quite striking
18 in terms of the positiveness, as has been mentioned over and
19 over again, about the overall rates. But I think the
20 primary objective has been shown quite clearly, and I think
21 the outline that we give for data collection activities
22 will, in fact, give us the data that we are very much
23 concerned about seeing. So, I am quite comfortable with the
24 decision I made and the committee made.

25 DR. CHATMAN: I voted for approval with conditions

1 as well. I don't think less is more. I think the more
2 information we have about the fetus in utero the better off
3 we are going to be. Obviously, EFM has been misused. If we
4 have information about the oxygenation of the fetus inside
5 the uterus, then we have the potential for improving
6 perinatal outcome, and I think that what all obstetricians
7 are basically about.

8 I did have some concerns about the 30 percent. As
9 I read these volumes at home, prior to coming here, I
10 wondered why we didn't just raise the bar a little bit in
11 order to be more safe, but the study was obviously well
12 designed. I am not sure if it was consistently well
13 executed, but that is another story altogether.

14 The one concern that I have has to do with the
15 infection rate. I know what the numbers stated but in
16 looking at the RCT group, the group on which the instrument
17 was used had I think 99, thereabout, infection or maternal
18 fever indications or results. I am not sure exactly what
19 that meant. Some were stated as mucous membrane problems.
20 Some were outright fever. Some were endometritis,
21 postpartum and intrapartum. And I wondered what the
22 infection rate is going to wash out to be, but if we get
23 some information about the fetus in utero, the oxygenation
24 of the fetus in utero, we can't be worse off; we can only be
25 better off. So, for that reason, I thought this is a good

1 thing for the FDA to approve.

2 DR. NEUMAN: I voted for approval with conditions
3 for reasons that have already been mentioned.

4 CHAIRMAN BLANCO: All right, a few finishing
5 items. De. Eglinton has a couple of words he would like to
6 direct to us.

7 DR. EGLINTON: There are some support groups made
8 up of women who have had cesarean, and at least some of
9 these groups prefer to expunge the term cesarean section
10 from our jargon in obstetrics. So, I would argue in their
11 favor for using cesarean or cesarean delivery rather than
12 cesarean section, which implies something that is being done
13 to a woman rather than for her.

14 CHAIRMAN BLANCO: Dr. Schultz, any comments?

15 DR. SCHULTZ: Well, I would just like to thank the
16 panel. I would like to sort of provide a corollary to what
17 Dr. Eglinton said. I think that the discussion by the panel
18 today, the level with which the panel delved into what was
19 obviously a very complex data set, and the thoughtfulness of
20 the discussion and the conclusions that were reached I think
21 is a tribute to the chair and to the rest of the panel
22 members, and we do appreciate it. And, we understand that
23 you have provided us with a mandate and the company with a
24 mandate to move on from here and make sure that this device,
25 in going to market, goes to market in a way that will best

1 serve the women of America, and we intend to do that. Thank
2 you.

3 CHAIRMAN BLANCO: Dr. Harvey?

4 DR. HARVEY: Two relatively mundane matters. One
5 is that the panel materials you have you can leave behind
6 here and they will be taken up, if you prefer that.

7 For panel members who are here this evening, you
8 can come and see Colin and me about dinner plans.

9 CHAIRMAN BLANCO: Thank you. I would like to
10 thank everyone, the audience, the sponsor and FDA for a
11 wonderful day. I would like to thank the panel members for
12 their input and their presence here. And, with that, we
13 will adjourn.

14 [Whereupon, at 5:43 p.m., the proceedings were
15 recessed, to be resumed at 8:00 a.m., Tuesday, January 25,
16 2000]

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C E R T I F I C A T E

I, **THOMAS C. BITSKO**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.



THOMAS C. BITSKO