

1 Dr. Finnegan?

2 MEMBER FINNEGAN: Yes.

3 CHAIRPERSON YASZEMSKI: Dr. Finnegan, yes.

4 Dr. Kim?

5 MEMBER KIM: No.

6 CHAIRPERSON YASZEMSKI: Dr. Kim, no. Dr.

7 Naidu?

8 MEMBER NAIDU: Yes.

9 CHAIRPERSON YASZEMSKI: Yes. Dr. Mayor?

10 MEMBER MAYOR: No.

11 CHAIRPERSON YASZEMSKI: Dr. Larntz?

12 MEMBER LARNTZ: Yes.

13 CHAIRPERSON YASZEMSKI: Dr. Besser?

14 MEMBER BESSER: No.

15 CHAIRPERSON YASZEMSKI: We have a four to
16 four. So this is for a vote of class III. Now I want
17 to have a point of clarification since I am about to
18 vote. If my vote is for this motion, we will then
19 separate them out. If my vote is against this motion
20 that we do not make me them class III, is that also a
21 yes vote for a class II? And then we are going to
22 work on the supplemental data sheets. Clarification

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1 before I vote.

2 The point is that we have a motion for a
3 class III. And if this motion doesn't pass, the only
4 other choices are class II or class I.

5 MS. SHULMAN: Well, I think in that case
6 when we separate them out, you can go through the
7 sheets again and see if they end up in II or III.

8 CHAIRPERSON YASZEMSKI: Okay. I think
9 what we are going to do, then, just before I give my
10 vote, if my vote is going to be against this motion,
11 we still don't have a vote for something we are going
12 to pass. Then I am going to ask that we introduce a
13 motion for class II, for all of them together. We are
14 going to change the answer.

15 Basically, what effectively we are going
16 to do here is vote on the answer to number six. My
17 vote is going to be no against this motion. So no to
18 class III.

19 And I am going to suggest that from a
20 procedural perspective, the effect of that vote is
21 going to be to change the answer for number six from
22 no to yes. Then we are going to go through the rest

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1 of the sheet.

2 So I vote no. I will suggest that we have
3 now changed with that vote of no the answer for number
4 six from no to yes. And I would like to go through
5 the rest of the sheet. Everybody still gets to speak
6 with their vote on the next classification.

7 MEMBER BESSER: Mr. Chairman?

8 CHAIRPERSON YASZEMSKI: Yes, sir?

9 MEMBER BESSER: I'm Marc Besser speaking.

10 I disagree with your assumption that
11 voting this motion down just changes the answer to
12 question six. I think there are individuals at the
13 table who would like to split apart the total and the
14 unicompartmental mobile bearing knees. And that may
15 be what their expected outcome from a vote of no on
16 this proposal was, but perhaps I am wrong.

17 MEMBER FINNEGAN: I think there is total
18 confusion. I think some people voted yes and some
19 people voted no but they all wanted the same result.

20 CHAIRPERSON YASZEMSKI: Okay. Well, let's
21 do this.

22 MEMBER BESSER: Mike, can I suggest we

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1 vote for class III or for class II on both? That way
2 the yes and no doesn't confuse anyone.

3 CHAIRPERSON YASZEMSKI: Okay. Just a
4 moment. Before we do that, there seems to be
5 disagreement with what we have done. I think that in
6 going through the sheets from a procedural
7 perspective, I am okay with what I said. But I want
8 to have now a discussion of this as to how to proceed
9 next.

10 My opinion is that if we go through and
11 now make a motion for class II on both of them
12 together, people will be able to either approve or
13 disapprove the class II with their vote. And then we
14 can then go again to separating them out.

15 It is a little tricky, but I want to have
16 a little discussion of what you think about class III
17 and class II. I want to hear about what everybody
18 thinks about whether we should vote for them together
19 or apart. Let's just do that separate from the sheet.
20 And I think we can probably get through some of the
21 confusion that way.

22 So, John, Dr. Kirkpatrick, I want to start

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1 with you. Would you prefer that we vote for these
2 together or that we vote for these separately?

3 MEMBER KIRKPATRICK: Separately.

4 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

5 MEMBER MABREY: Together.

6 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

7 MEMBER FINNEGAN: Separately.

8 CHAIRPERSON YASZEMSKI: Dr. Kim?

9 MEMBER KIM: Separate.

10 CHAIRPERSON YASZEMSKI: Dr. Naidu?

11 MEMBER NAIDU: Together.

12 CHAIRPERSON YASZEMSKI: Dr. Mayor?

13 MEMBER MAYOR: Together.

14 CHAIRPERSON YASZEMSKI: Dr. Larntz?

15 MEMBER LARNTZ: Together.

16 CHAIRPERSON YASZEMSKI: Dr. Besser?

17 MEMBER BESSER: Together.

18 CHAIRPERSON YASZEMSKI: So we have five
19 people who want to vote for them together and five
20 people who want to vote for them separately. Excuse
21 me. Pardon me. Pardon me. Excuse me for my mistake.
22 We have five. I counted five to three.

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1 So I think that the panel generally wants
2 to consider them together. It's five to three for it
3 together. I think that is going to say, regardless of
4 how we get there, it is going to say that we are going
5 to vote, we are going to fill in this sheet as a yes
6 for number six.

7 Would everybody now agree that wanting to
8 consider them together is a yes for number six? We
9 have to get past number six. If we put --

10 MEMBER LARNTZ: I disagree with that.

11 CHAIRPERSON YASZEMSKI: Dr. Larntz, go
12 ahead.

13 MEMBER LARNTZ: I disagree with that. I
14 did not vote together to make a yes for number six.
15 That's what you just said I did, and I didn't do that.

16 I voted yes so we can consider them
17 together. And I would vote no for both devices.

18 MEMBER MABREY: Mr. Chairman?

19 CHAIRPERSON YASZEMSKI: Okay. So let's go
20 around again and talk about number six. We have to
21 get past number six. And the disagreement is hinging
22 on number six. So let's have some discussion. Dr.

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1 Mabrey?

2 MEMBER MABREY: Well, I think the problem
3 here is that once we get past number six, that
4 everybody on the panel is now voting for both at the
5 same time. I have the sense that there are
6 individuals on the panel who think that one device
7 should be class II and another device should be class
8 III.

9 If we continue to move along the lines of
10 voting for both at the same time, while their opinions
11 may be heard, then the outcome is still voting for
12 both at the same time. I mean, that is just my sense
13 of what has happened on the panel.

14 CHAIRPERSON YASZEMSKI: Now, let me
15 suggest, in response to your question, that what we
16 did initially was vote for both of them together. We
17 got to question number six and had a suggestion of
18 answering no. The instructions for answering no to
19 number six are to classify as class III. So the sheet
20 was complete at that moment.

21 If we vote for them together and answer no
22 to number six, the sheet is complete. We vote on it.

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1 And if that vote were for the sheet as filled out,
2 that would be a recommendation to keep them both
3 together in class III.

4 But that vote failed by a vote of five to
5 four. And so I am asking, where should we go now?
6 Dr. Kirkpatrick?

7 MEMBER KIRKPATRICK: I think we need to
8 clarify. There are two issues. One is apparently
9 there are some members who would vote no for either of
10 them being out of class III. And I think that issue
11 needs to be resolved because basically it is resolved
12 in the vote we just took.

13 Now we have to revise our poll to find out
14 the answer to actually question six because what we
15 asked was separate or apart. We didn't ask whether we
16 should approve both together now that we have not
17 separated them.

18 So basically what I am suggesting is we
19 have used the democratic method and determined that
20 separate is not going to work. So now we put them
21 together, and we redo the vote on six to determine
22 whether either of them or all of them can be approved

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1 to go to class II, as opposed to class III.

2 CHAIRPERSON YASZEMSKI: I am willing to do
3 that again, but I am going to submit to you that that
4 is what we already did. We put them both together.
5 With both together, we considered them as a no, which
6 would be a recommendation for class III.

7 We voted on that. And the vote was five
8 to four to not accept that. So that is how we started
9 out. My opinion is that we have already done that.

10 But I would like to hear more comment.

11 MEMBER KIRKPATRICK: The five to four vote
12 was confusing because, for example, I said yes to
13 class III. But the question says, "If yes, it's a
14 class II." So my vote may have been unclear.

15 Then you repolled the panel and found out
16 that your vote wasn't necessary. Remember? As I
17 understand the process.

18 DR. WITTEN: Mr. Chairman?

19 CHAIRPERSON YASZEMSKI: Dr. Witten?

20 DR. WITTEN: Yes. I realize it is the
21 panel's procedural prerogative here, but maybe you
22 should vote on this as filled out, which I think you

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1 did do, although maybe not everybody knew that is what
2 you were doing. So it might be good to do it again.

3 And then if that passes, we are done. And
4 then if it doesn't pass, then proceed like you were
5 going to do, which is change the X to a yes and then
6 see if that passes. And if it does, you're done. And
7 if it's not, then you have to fill out the sheet
8 again, you know, try splitting it up.

9 So maybe you could just vote on this,
10 saying that you're voting on whether to accept this
11 sheet or not. Just do that vote again if it's okay
12 for me to suggest that.

13 CHAIRPERSON YASZEMSKI: I'm going to say
14 okay to that, but first I want to hear commentary
15 before we vote so that when we vote on this, we are
16 done and we have no further discussion. So let's ask
17 Dr. Finnegan. Do you have a comment?

18 MEMBER FINNEGAN: I guess some
19 clarification. There is obviously significant
20 dissention among the panel. There are two separate
21 problems. I guess I don't understand why we are doing
22 them together because I think we probably could solve

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1 everything really quickly if we did them apart.

2 Could we take a vote on how many of the
3 panel members --

4 CHAIRPERSON YASZEMSKI: I would have to
5 ask. This is the discussion we want. So we have a
6 point raised in contradistinction to what Dr. Witten
7 suggested, that maybe our first attempt at this should
8 be to separate them.

9 Let's go around and talk about that. Dr.
10 Mayor, what do you think about that?

11 MEMBER MAYOR: My sense of the meeting is
12 that we are going to be stuck if we try to do them
13 together and that we can resolve the issues relatively
14 quickly if we separate them.

15 CHAIRPERSON YASZEMSKI: Okay. Let's
16 continue to go around. Dr. Larntz?

17 MEMBER LARNTZ: Even I agree with that.

18 (Laughter.)

19 CHAIRPERSON YASZEMSKI: Dr. Besser?

20 MEMBER BESSER: I agree.

21 CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick,
22 are you okay with that?

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1 MEMBER KIRKPATRICK: Separate them.

2 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

3 MEMBER MABREY: I support separation.

4 CHAIRPERSON YASZEMSKI: I know that Dr.
5 Finnegan does.

6 MEMBER FINNEGAN: Yes.

7 CHAIRPERSON YASZEMSKI: Dr. Kim?

8 MEMBER KIM: Separation.

9 CHAIRPERSON YASZEMSKI: Okay. Dr. Naidu?

10 MEMBER NAIDU: Okay. I'll go along.

11 CHAIRPERSON YASZEMSKI: Okay. So now
12 we're back, Ms. Shulman, to starting over. So let's
13 start over, and let's take that down. We're going to
14 do them all again. Let's do the total knees first and
15 not separate out the unicompartmentals that we'll
16 consider separately later.

17 So we are going to fill out the general
18 device classification questionnaire again this time
19 except that the generic type of device will be the
20 tricompartmental total knee and will not include the
21 unicompartmentals.

22 DR. WITTEN: Do you want new forms, the

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1 same forms, to start?

2 CHAIRPERSON YASZEMSKI: No. I think we
3 can probably do it like this.

4 Dr. Mayor, I am back to you. Is the
5 device life-sustaining or life-supporting, number one?

6 MEMBER MAYOR: No.

7 CHAIRPERSON YASZEMSKI: Any disagreements
8 with that?

9 (No response.)

10 CHAIRPERSON YASZEMSKI: Seeing none,
11 number two, is it for a use of which there is a
12 substantial importance in preventing impairment of
13 human health?

14 MEMBER MAYOR: Yes.

15 CHAIRPERSON YASZEMSKI: Any disagreement
16 with that?

17 (No response.)

18 CHAIRPERSON YASZEMSKI: Seeing none,
19 three, does the device present the potential
20 unreasonable risk of illness or injury?

21 MEMBER MAYOR: No.

22 CHAIRPERSON YASZEMSKI: Any disagreement

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1 with that?

2 (No response.)

3 CHAIRPERSON YASZEMSKI: Seeing none, we
4 did answer yes to one of the above three questions.
5 So the answer to number four is yes.

6 From number four, we go to number six.
7 Number six, is there sufficient information to
8 establish special controls in addition to general
9 controls?

10 MEMBER MAYOR: Yes.

11 CHAIRPERSON YASZEMSKI: Disagreement with
12 that?

13 MEMBER LARNTZ: I disagree.

14 MEMBER NAIDU: I disagree.

15 CHAIRPERSON YASZEMSKI: Okay. So now what
16 I would suggest that we do for a matter of order is
17 vote on number six. What we will do is vote on each
18 of these. You will have two chances to be heard.
19 What I will suggest is that the majority opinion on
20 each of these questions is what goes in as the answer
21 to the question. And then at the end, you get to
22 speak again with your vote on the sheet as a whole.

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1 So this is for number six. Yes or no?

2 And I am going to start with Dr. Mayor.

3 MEMBER MAYOR: Yes.

4 CHAIRPERSON YASZEMSKI: Dr. Larntz?

5 MEMBER LARNTZ: No.

6 CHAIRPERSON YASZEMSKI: Dr. Besser?

7 MEMBER BESSER: Yes.

8 CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

9 MEMBER KIRKPATRICK: Yes.

10 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

11 MEMBER MABREY: Yes.

12 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

13 MEMBER FINNEGAN: Yes.

14 CHAIRPERSON YASZEMSKI: Dr. Kim?

15 MEMBER KIM: Yes.

16 CHAIRPERSON YASZEMSKI: Dr. Naidu?

17 MEMBER NAIDU: No.

18 CHAIRPERSON YASZEMSKI: The vote is six

19 yes, two no. So the answer for purposes of this sheet

20 that we will put in on number six is yes. Again, the

21 persons who voted no get a chance to speak again when

22 we vote on the sheet.

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1 So now let's move down to number seven.
2 If there is sufficient information to establish
3 special controls to provide reasonable assurance of
4 safety and effectiveness, identify below the special
5 controls needed to provide such reasonable assurance
6 for class II.

7 Dr. Mayor, your suggestions as to which,
8 if any, and how many of these five boxes we should
9 check?

10 MEMBER MAYOR: Guidance document,
11 performance standard.

12 MEMBER MAHER: Excuse me. Can I clarify
13 on performance standards before you --

14 CHAIRPERSON YASZEMSKI: I will come to
15 you. Let's get to it first, and I will acknowledge
16 that we want comment from you.

17 Go ahead, Dr. Mayor. Either of the other
18 two? And if you have only those two, I am going to go
19 around. Others may suggest to add or subtract.

20 MEMBER MAYOR: Clinical studies.

21 CHAIRPERSON YASZEMSKI: Other clinical
22 studies.

1 MEMBER MAYOR: Device-specific training
2 called for in the labeling.

3 CHAIRPERSON YASZEMSKI: Dr. Larntz, did
4 you want to subtract any of those or do you want to
5 add any others?

6 MEMBER LARNTZ: I'm satisfied.

7 CHAIRPERSON YASZEMSKI: Okay. Dr. Besser,
8 do you want to subtract or add?

9 MEMBER BESSER: I need help. I need to
10 know the difference between performance standards and
11 guidelines.

12 CHAIRPERSON YASZEMSKI: A good point to
13 ask Ms. Maher to speak. Ms. Maher?

14 MEMBER MAHER: A performance standard is
15 something that goes through notice and comment
16 rulemaking; takes an exceedingly long time to get
17 through all of the systems; and is rarely, if ever,
18 used within the agency.

19 The agency has used, instead, guidance
20 documents. And in guidance documents, they outline
21 the types of things that the current state of the art
22 has them looking for, such as wear testing, et cetera.

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1 Performance testing, Dr. Witten, if you
2 could tell me how many times they've ever been used in
3 the past?

4 DR. WITTEN: Once.

5 MEMBER MAHER: Once. Okay. It's not the
6 way things are done, I know. It has to be on the
7 sheet because it is in the Food, Drug, and Cosmetic
8 Act, but it would not be appropriate in my mind.

9 CHAIRPERSON YASZEMSKI: Okay. Dr. Mayor,
10 would you be comfortable with including those
11 performance standards within the guidance document?

12 MEMBER MAYOR: Yes.

13 CHAIRPERSON YASZEMSKI: So we'll uncheck
14 performance standards. Dr. Kirkpatrick?

15 MEMBER KIRKPATRICK: I think there are
16 testing guidelines that are also included in what we
17 heard from the presenters. And I think that should be
18 included.

19 CHAIRPERSON YASZEMSKI: Okay. Thank you.
20 We will add testing guidelines.

21 Dr. Mabrey?

22 MEMBER MABREY: Guidance document, testing

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1 guidelines, device-specific training.

2 CHAIRPERSON YASZEMSKI: Thank you, Dr.
3 Mabrey.

4 Dr. Finnegan?

5 MEMBER FINNEGAN: Whatever we're now
6 calling device tracking, which is just that the
7 patient has identified the patient with lot number and
8 the surgeon has the same information.

9 CHAIRPERSON YASZEMSKI: Thank you.

10 Dr. Kim?

11 MEMBER KIM: I would agree with all of the
12 stipulations stated so far.

13 CHAIRPERSON YASZEMSKI: Thank you.

14 Dr. Naidu?

15 MEMBER NAIDU: Nothing more to add.

16 CHAIRPERSON YASZEMSKI: Thank you. So for
17 number seven --

18 MEMBER MAHER: Excuse me. Can I clarify
19 one thing?

20 CHAIRPERSON YASZEMSKI: Yes, Ms. Maher.
21 Go ahead.

22 MEMBER MAHER: Dr. Finnegan used the term

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1 "device tracking" and --

2 CHAIRPERSON YASZEMSKI: We are not going
3 to use those words.

4 MEMBER MAHER: Right. What we need to
5 just say is that she wants to have a patient card and
6 --

7 CHAIRPERSON YASZEMSKI: A patient card,
8 yes.

9 MEMBER FINNEGAN: Actually, can we
10 redefine that as a patient registry?

11 CHAIRPERSON YASZEMSKI: That's a bad word,
12 too. A card, a card that identifies the lot number,
13 the name of the device, and the fill-in for the
14 surgeon, hospital, the date of surgery. It wouldn't
15 be a registry. It would just be an identification
16 card, as discussed with FDA yesterday.

17 And I think, Dr. Witten, does FDA have an
18 understanding of what we mean by that term? Yes.

19 Any additional comments for number seven?

20 MEMBER BESSER: Can you reiterate what has
21 been decided on number seven?

22 CHAIRPERSON YASZEMSKI: That we would

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1 think that special controls would include a guidance
2 document, would include testing guidelines, the tests
3 that we have been discussing this morning but still
4 have to be developed. And this would be something
5 that the FDA would work with the sponsor to identify,
6 which they would be, the need under others for
7 potential clinical studies at the discretion of the
8 FDA and device-specific training and an identification
9 card.

10 Yes, Ms. Scudiero?

11 ACTING EXECUTIVE SECRETARY SCUDIERO:
12 Testing guidelines can be included in the guidance
13 document.

14 CHAIRPERSON YASZEMSKI: And FDA is getting
15 our message. Ms. Scudiero reminded me that testing
16 guidelines can be included in the guidance document.
17 And we will leave that to the discretion of FDA.

18 We will move now to number eight.

19 MEMBER BESSER: I'm sorry, Mike. Did you
20 add something after the device-specific training?

21 CHAIRPERSON YASZEMSKI: Yes, the
22 identification card that identifies the lot number of

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1 the device --

2 MEMBER BESSER: Thank you.

3 CHAIRPERSON YASZEMSKI: -- and the surgery
4 date and the hospital and the surgeon.

5 We did not check performance standards.
6 So we will skip number eight.

7 Number nine, for a device recommended for
8 reclassification into class II, should the recommended
9 -- number nine is also eight, isn't it? I'm sorry.
10 So we don't check nine?

11 MS. SHULMAN: And you can also skip ten.

12 CHAIRPERSON YASZEMSKI: And we skip ten.
13 Thanks, Ms. Shulman.

14 Number 11, identify needed restrictions
15 only upon the written or oral authorization of
16 practitioner licensed by law to administer or use the
17 device. Does anybody want to check that? Yes? I
18 heard a yes. Yes, Dr. Finnegan and Dr. Mabrey.

19 Used only by persons with specific
20 training or experience in its use. Is that a yes from
21 anybody? Dr. Mabrey is saying yes. Any others other
22 than those two? Dr. Kirkpatrick?

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1 MEMBER KIRKPATRICK: Just a question.
2 Specific training and experience in its use would be
3 determined by whom?

4 CHAIRPERSON YASZEMSKI: That's not for us
5 to say. Who might you suggest?

6 MEMBER KIRKPATRICK: Do we leave it up to
7 the FDA?

8 CHAIRPERSON YASZEMSKI: Yes, sir.

9 MEMBER KIRKPATRICK: Okay.

10 CHAIRPERSON YASZEMSKI: Now, let's review
11 the sheet as Ms. Shulman has it and ask if there are
12 any requests for changing any of them before we move
13 to the second sheet, the supplemental data sheet. Any
14 need to change the first sheet?

15 (No response.)

16 CHAIRPERSON YASZEMSKI: Let's move to the
17 supplemental data sheet. Number three is a device and
18 implant. I think we can say yes.

19 Number four is indications for use in the
20 device's labeling. Dr. Mayor, may I ask you as the
21 lead reviewer to make a suggestion for this? And then
22 while Dr. Mayor is talking, I am going to ask Dr.

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1 Finnegan to suggest number five.

2 MEMBER MAYOR: I think the indications for
3 use have been cited in some of the other documentation
4 we have, which include osteoarthritis, inflammatory
5 arthritis, posttraumatic arthropathy, avascular
6 necrosis, others that I've --

7 CHAIRPERSON YASZEMSKI: Would it be fair
8 to say as per OSMA's presentation?

9 MS. SHULMAN: Correct. You can say "as
10 presented."

11 MEMBER MAYOR: As presented.

12 CHAIRPERSON YASZEMSKI: Number five, Dr.
13 Finnegan?

14 MEMBER FINNEGAN: Well, I could cop out
15 and say as presented by everyone who presented, but I
16 think the significant risks are the implant-related
17 wear and instability.

18 CHAIRPERSON YASZEMSKI: Can we say as
19 discussed in the answers to the FDA's questions?

20 MEMBER FINNEGAN: That's fine with me,
21 yes.

22 CHAIRPERSON YASZEMSKI: Ms. Shulman, is

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1 that appropriate?

2 MS. SHULMAN: Yes.

3 CHAIRPERSON YASZEMSKI: Number six,
4 recommended advisory classification and priority.
5 This is for class II for the total mobile bearing
6 devices. And priority, please? Counsel us on that.

7 MS. SHULMAN: The priority is high,
8 medium, or low. There are no time frames associated
9 with the time for the reclassification. But it's how
10 far you want us to put it up in our workload.

11 CHAIRPERSON YASZEMSKI: And I'm going to
12 ask everybody to state, Dr. Kirkpatrick, high, medium,
13 or low.

14 MEMBER KIRKPATRICK: Medium.

15 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

16 MEMBER MABREY: Well done.

17 (Laughter.)

18 CHAIRPERSON YASZEMSKI: Dr. Mabrey, come
19 on. High, medium, or low.

20 MEMBER MABREY: High.

21 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

22 MEMBER FINNEGAN: Medium.

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1 CHAIRPERSON YASZEMSKI: Dr. Kim?

2 MEMBER KIM: Medium.

3 CHAIRPERSON YASZEMSKI: Dr. Naidu?

4 MEMBER NAIDU: Low.

5 CHAIRPERSON YASZEMSKI: Dr. Mayor?

6 MEMBER MAYOR: Medium.

7 CHAIRPERSON YASZEMSKI: Dr. Larntz?

8 MEMBER LARNTZ: Low.

9 CHAIRPERSON YASZEMSKI: Dr. Besser?

10 MEMBER BESSER: Low.

11 CHAIRPERSON YASZEMSKI: We have four for
12 medium, three for low, and one for high. Four takes
13 it. We will put in medium.

14 Number seven, devices and implant or as
15 life-sustaining. And it's categorized in any category
16 other than a class III. Explain fully the reasons for
17 the lower classification.

18 Might we include as discussed in the
19 answers to FDA's questions?

20 MS. SHULMAN: Yes, you can say that
21 general and special controls can handle the risk as
22 discussed.

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1 CHAIRPERSON YASZEMSKI: Number eight,
2 summary of information, including clinical experience
3 or judgment upon which classification recommended to
4 be based. It would be appropriate also to ask for the
5 discussion that occurred at the panel meeting today?

6 MS. SHULMAN: Yes.

7 CHAIRPERSON YASZEMSKI: Number nine,
8 identification of any needed restrictions in the use
9 of the device, special labeling, banning, prescription
10 use. Now, in filling out the other sheet, we did talk
11 about the identification label and device-specific
12 training.

13 Would it be appropriate from everybody's
14 perspective to include those in the answer to question
15 number nine?

16 MS. SHULMAN: Correct. We can refer to
17 question 11 of the general device questionnaire.

18 CHAIRPERSON YASZEMSKI: Thank you.

19 Question number ten. It is not a class
20 II. So I would say it is not applicable.

21 Question 11. It is class II. Recommend
22 whether FDA should exempt it from pre-market

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1 notification. Thoughts? Should it be not exempt?
2 Anybody disagree with not exempt?

3 (No response.)

4 CHAIRPERSON YASZEMSKI: Not exempt for
5 number 11.

6 Existing standards applicable to the
7 device, device subassemblies, or device materials. I
8 think perhaps as per the FDA and OSMA presentations,
9 I think they included those standards.

10 MS. SHULMAN: Yes.

11 CHAIRPERSON YASZEMSKI: Does anyone want
12 to add anything to either of these sheets before we
13 vote on them?

14 (No response.)

15 CHAIRPERSON YASZEMSKI: This will be a
16 vote for class II with the sheets as filled out. The
17 sheets will be our recommendation for the total mobile
18 bearing devices, not including the unicondylars. Any
19 questions before we vote?

20 (No response.)

21 CHAIRPERSON YASZEMSKI: Okay. We are
22 going to vote. Yes is for class II for the total

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1 mobile bearing knees, and no is to not accept class
2 II. Dr. Mayor?

3 MEMBER MAYOR: Yes.

4 CHAIRPERSON YASZEMSKI: Dr. Larntz?

5 MEMBER LARNTZ: No.

6 CHAIRPERSON YASZEMSKI: Dr. Besser?

7 MEMBER BESSER: Yes.

8 CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

9 MEMBER KIRKPATRICK: Yes.

10 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

11 MEMBER MABREY: Yes.

12 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

13 MEMBER FINNEGAN: Yes.

14 CHAIRPERSON YASZEMSKI: Dr. Kim?

15 MEMBER KIM: Yes.

16 CHAIRPERSON YASZEMSKI: Dr. Naidu?

17 MEMBER NAIDU: No.

18 CHAIRPERSON YASZEMSKI: The vote is six
19 yes, two no, and the motion passes for class II
20 recommendation to FDA.

21 Now, let's move on. New sheets to
22 consider, unicondylar. This will be the same sequence

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1 we just went through for the unicondylar mobile
2 bearing knees.

3 I will ask for a classification
4 recommendation after we get to number six. And I
5 think the answers for number one, if I may suggest,
6 are going to be the same as before.

7 Life-sustaining or supporting, no.
8 Substantial importance, yes for number two. Number
9 three, present a potential and reasonable risk, no
10 unless others disagree and want to make that a yes.
11 That makes number four a year.

12 And let's go to number six again here. Is
13 there sufficient information to establish special
14 controls in addition to general controls? Dr. Mayor?

15 MEMBER MAYOR: Yes.

16 CHAIRPERSON YASZEMSKI: What I want to do
17 around here now is just to go to everybody again. So
18 we are going to get everybody's opinion on number six.
19 Dr. Mayor is a yes. Dr. Larntz?

20 MEMBER LARNTZ: No for reasons I have
21 already given.

22 CHAIRPERSON YASZEMSKI: Great. Dr.

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1 Besser?

2 MEMBER BESSER: Yes.

3 CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

4 MEMBER KIRKPATRICK: No.

5 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

6 MEMBER MABREY: Yes.

7 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

8 MEMBER FINNEGAN: No.

9 CHAIRPERSON YASZEMSKI: Dr. Kim?

10 MEMBER KIM: Yes.

11 CHAIRPERSON YASZEMSKI: Dr. Naidu?

12 MEMBER NAIDU: No.

13 CHAIRPERSON YASZEMSKI: And I'm going to
14 vote yes. That makes it five/four. So you will all
15 get a chance to speak your conscience with your vote.

16 Now, we voted yes. So what this is going
17 to be, we are going to end up now voting on whether to
18 make the unicondylars a class II. And so although I
19 understand there is much disagreement on this, I would
20 like everybody to give their opinions as to what we
21 should put in the rest of these answers assuming it
22 gets to be a class II. Then we are going to vote on

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1 it.

2 Yes, ma'am?

3 MS. SHULMAN: Excuse me. As a matter of
4 clarification, you just voted for class II. That
5 classified it in recommendation four, too.

6 CHAIRPERSON YASZEMSKI: Right. That is
7 going to be the recommendation, but we still have to
8 vote on it after we fill the sheets out, correct?

9 MS. SHULMAN: Okay.

10 CHAIRPERSON YASZEMSKI: Okay. That's go
11 to number seven. Dr. Mayor, we have gone through
12 these. Maybe we can say again what we did before. We
13 had guidance document. We had testing guidelines to
14 be included in the guidance document and the others as
15 before. Would you want to change them for the
16 unicondylars or shall we include the same?

17 MEMBER MAYOR: I would include the same.

18 CHAIRPERSON YASZEMSKI: Would anybody like
19 to add or subtract anything from number seven to make
20 it different than it was before? Dr. Kim?

21 MEMBER KIM: I have a clarification point
22 first. For the total, one of the other categories was

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1 clinical data suggested. This unicondylar system has
2 less clinical data. So can we put it so that clinical
3 data is required?

4 CHAIRPERSON YASZEMSKI: FDA will listen to
5 the discussion. And you may let them know through
6 this discussion, as you are doing now, that you feel
7 more strongly that clinical data is necessary. But we
8 can still list it the same way.

9 Other comments?

10 MEMBER FINNEGAN: The PMA was just
11 recently approved. And I would like to see a time
12 period that those patients were followed out prior to
13 this being moved. I don't know if that is possible or
14 not but somehow to get the data from the patients who
15 have it.

16 CHAIRPERSON YASZEMSKI: We can suggest
17 that to FDA, and they will listen. So we will include
18 a suggestion for longer-term follow-up from the PMA
19 data by FDA.

20 DR. WITTEN: For what exactly?

21 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

22 DR. WITTEN: I mean, what are you

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1 suggesting that for? Before we take an action?

2 MEMBER FINNEGAN: Yes.

3 MEMBER MAHER: Can I have a point of
4 order, please?

5 CHAIRPERSON YASZEMSKI: Ms. Maher?

6 MEMBER MAHER: I'm not sure that that can
7 be done. I mean, that PMA is completed and closed
8 out. So I am not --

9 DR. WITTEN: Well, also that data, well,
10 the sponsor would have to provide it. It is not
11 automatically available to us to use for this purpose.

12 CHAIRPERSON YASZEMSKI: Dr. Finnegan,
13 would you be okay leaving it as a stronger feeling of
14 clinical data needed, as Dr. Kim did, so that FDA will
15 hear that without specifically requiring them to make
16 a follow-up on an existing PMA?

17 MEMBER FINNEGAN: What I would like to ask
18 is, was there a post-market surveillance required in
19 that PMA? There was? So, then, the data is available
20 to you.

21 DR. WITTEN: Well, that doesn't mean that
22 it is available for use with this petition, no. No.

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1 That is the sponsor's own data. We can use
2 information from published literature. But for that,
3 we would have to ask the sponsor if they wanted to
4 make that data available for the petition.

5 I'm not saying we couldn't do that. I'm
6 just explaining that.

7 DR. WITTEN: If the PMA had a post-market
8 surveillance requirement, then I would ask that that
9 surveillance be surveyed before this is approved.

10 CHAIRPERSON YASZEMSKI: And we can make
11 that recommendation to FDA.

12 Dr. Kirkpatrick?

13 MEMBER KIRKPATRICK: If I might suggest,
14 we are talking about unicondylars right now?

15 CHAIRPERSON YASZEMSKI: Yes, sir.

16 MEMBER KIRKPATRICK: Can we not state that
17 any unicondylar device that comes through on a 510k
18 will have post-market surveillance?

19 CHAIRPERSON YASZEMSKI: We can recommend
20 that as a --

21 MEMBER KIRKPATRICK: As a condition?

22 CHAIRPERSON YASZEMSKI: -- as a condition

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1 here.

2 MEMBER KIRKPATRICK: May I propose that?

3 CHAIRPERSON YASZEMSKI: We will add that
4 to other. Any others for number seven?

5 MEMBER MAHER: Can I again clarify?

6 CHAIRPERSON YASZEMSKI: Ms. Maher?

7 MEMBER MAHER: For the post-market
8 surveillance, that would, of course, be with the FDA's
9 discretion.

10 CHAIRPERSON YASZEMSKI: At the discretion
11 of the FDA. That is our recommendation to them. But
12 as we understand it, they have --

13 MEMBER KIRKPATRICK: I agree with that but
14 would urge the high acuity of looking for any
15 osteolysis in any polyethylene failures and any
16 implant dislodgement.

17 CHAIRPERSON YASZEMSKI: Thank you.

18 MEMBER KIRKPATRICK: Would be the high
19 acuity things to look for.

20 CHAIRPERSON YASZEMSKI: Thank you. We
21 will include that in our recommendation to them.

22 MEMBER FINNEGAN: Actually, could I add

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1 revision rate?

2 CHAIRPERSON YASZEMSKI: Yes, ma'am.
3 Eight, nine, and ten again are not to be filled out.
4 And number 11, I will suggest that we do just as we
5 did last time, by checking the first two boxes.

6 MS. SHULMAN: Correct.

7 CHAIRPERSON YASZEMSKI: Let's move to the
8 supplemental data sheet.

9 MEMBER KIRKPATRICK: Dislodgement or
10 motion of the implant from its original place and
11 polyethylene failure. You have already got revision
12 and osteolysis up there.

13 CHAIRPERSON YASZEMSKI: We're up to now
14 number three on the supplemental data sheet. Again,
15 it is an implant, yes. The indications for use,
16 should there be any differences in indication than
17 there were on the total? Shall we copy that?

18 MEMBER KIRKPATRICK: The sponsor's
19 presentation and the FDA discussion both had a
20 difference in the indications for unicondylar and
21 total. I would suggest that those be perpetuated.

22 CHAIRPERSON YASZEMSKI: Okay. We will say

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1 as per the FDA presentation.

2 MEMBER KIRKPATRICK: I can't remember the
3 slide in the FDA. I do remember that the sponsor did
4 have a difference in their indications. I would let
5 the FDA and the sponsor make sure that no extra
6 indications are added to what was presented.

7 MS. SHULMAN: That's fine.

8 CHAIRPERSON YASZEMSKI: Ms. Shulman, is
9 that appropriate to list it like that as per FDA
10 presentation?

11 MS. SHULMAN: That's fine.

12 CHAIRPERSON YASZEMSKI: Identification of
13 any risks to health. Again, ask for a panel
14 discussion, like last time.

15 MS. SHULMAN: Fine.

16 CHAIRPERSON YASZEMSKI: Recommended
17 classification, class II. Number seven.

18 MS. SHULMAN: For this one, you also need
19 a high, medium, or low for number six.

20 CHAIRPERSON YASZEMSKI: I'm sorry. High,
21 medium, and low. Let's go through it again. The
22 priority for making it a class II. Dr. Kirkpatrick,

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1 high, medium, or low?

2 MEMBER KIRKPATRICK: Low.

3 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

4 MEMBER MABREY: Medium.

5 CHAIRPERSON YASZEMSKI: Medium?

6 MEMBER MABREY: Medium.

7 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

8 MEMBER FINNEGAN: Low.

9 CHAIRPERSON YASZEMSKI: Dr. Kim?

10 MEMBER KIM: Low.

11 CHAIRPERSON YASZEMSKI: Dr. Naidu?

12 MEMBER NAIDU: Low.

13 CHAIRPERSON YASZEMSKI: Dr. Mayor?

14 MEMBER MAYOR: Low.

15 CHAIRPERSON YASZEMSKI: Dr. Larntz?

16 MEMBER LARNTZ: Low.

17 CHAIRPERSON YASZEMSKI: Dr. Besser?

18 MS. SHULMAN: He stepped out.

19 CHAIRPERSON YASZEMSKI: It's going to be
20 low because it is already six to one. So we will fill
21 that number out as low.

22 Number seven, supporting documentation as

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1 per the answers to the questions and the panel
2 discussion today. Same answer for number eight. No
3 needed restrictions for number nine. Number ten is
4 not applicable because it is class I.

5 Number 11, shall we? Any objections to
6 not exempt, as we did before?

7 (No response.)

8 CHAIRPERSON YASZEMSKI: And number 12,
9 existing standards as per presentation by FDA and OSMA
10 today.

11 Would anybody like to suggest any changes
12 to these sheets before we vote on this for the
13 unicondylar?

14 (No response.)

15 CHAIRPERSON YASZEMSKI: Okay. We are
16 going to go around the room and vote. I'll start this
17 time with Dr. Mayor. Dr. Mayor?

18 MEMBER MAYOR: In favor.

19 CHAIRPERSON YASZEMSKI: Yes. Dr. Larntz?

20 MEMBER LARNTZ: Against. The reason is
21 that there is no way to require clinical data without
22 making it class III.

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1 CHAIRPERSON YASZEMSKI: Thank you. We
2 will get Dr. Besser when he comes back in.

3 Dr. Kirkpatrick?

4 MEMBER KIRKPATRICK: Yes.

5 CHAIRPERSON YASZEMSKI: Dr. Mabrey?

6 MEMBER MABREY: Yes.

7 CHAIRPERSON YASZEMSKI: Dr. Finnegan?

8 MEMBER FINNEGAN: No. There is
9 insufficient clinical data.

10 CHAIRPERSON YASZEMSKI: Dr. Kim?

11 MEMBER KIM: Yes.

12 CHAIRPERSON YASZEMSKI: Dr. Naidu?

13 MEMBER NAIDU: No. There is insufficient
14 clinical data.

15 CHAIRPERSON YASZEMSKI: Dr. Besser, we
16 have come to you. We are voting on the petition to
17 classify unicondylars in class II with special
18 controls. And we will ask for your vote.

19 MEMBER BESSER: My vote would be yes to
20 reclassify to class II.

21 CHAIRPERSON YASZEMSKI: The vote is five
22 yes, three no. And the motion passes.

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1 I am now going to ask each panel voting
2 member the reason for her or his vote, starting with
3 Dr. Kirkpatrick. Then I will ask the consumer and
4 industry representatives for comments and finally Dr.
5 Witten for comments.

6 Dr. Kirkpatrick? And you may combine
7 them, the total and unicondylar, or you may separate
8 them at your discretion.

9 MEMBER KIRKPATRICK: I think the only
10 concerns I had were with the unicondylar as I don't
11 believe there is adequate clinical data. However, I
12 do recognize the effects of democracy and went with
13 the consensus opinion.

14 CHAIRPERSON YASZEMSKI: Thank you.

15 Dr. Mabrey?

16 MEMBER MABREY: I will consider them
17 together and believe there is enough clinical data for
18 the total mobile bearing knee. And there are adequate
19 controls within the FDA to ensure proper development
20 of components.

21 Also, with the unicondylar, I don't see
22 any deficiencies in the data. I would like to see

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1 more, but I think it is adequate for our purposes
2 today.

3 CHAIRPERSON YASZEMSKI: Thank you, Dr.
4 Mabrey.

5 Dr. Finnegan?

6 MEMBER FINNEGAN: I respectfully disagree
7 with my Texas colleague here. I think that the total
8 has reasonable assurance of safety and efficacy. I do
9 not believe the unicondylar has that.

10 CHAIRPERSON YASZEMSKI: Thank you, Dr.
11 Finnegan.

12 Dr. Kim?

13 MEMBER KIM: I believe the existing
14 devices have shown clinical safety and efficacy,
15 although the total knee replacement is better than the
16 unicondylar. And, therefore, I think this is approval
17 to go to class II as long as we have the conditions
18 that we stipulated.

19 CHAIRPERSON YASZEMSKI: Thanks, Dr. Kim?

20 Dr. Naidu?

21 MEMBER NAIDU: I will consider them both
22 together. I voted no mainly because I think they are

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1 inherently different devices. The current literature
2 indicates, most of the literature points to, the
3 rotating platform as the sole mobile bearing knee.
4 That has a good track record in the presentations.

5 I reach my conclusion that they are
6 inherently different devices and that clinical studies
7 are needed and that a PMA should be submitted. That
8 is why I voted no.

9 CHAIRPERSON YASZEMSKI: Right. Thanks,
10 Dr. Naidu.

11 Dr. Mayor?

12 MEMBER MAYOR: Well, the mobile bearing
13 devices are not identical with. I think they are
14 comparable to the fixed bearing devices that have been
15 in use for years.

16 I agree with the suggestion already
17 offered that clinical data is both appropriate and
18 necessary for new designs that might be promoted
19 subsequent to these deliberations.

20 CHAIRPERSON YASZEMSKI: Thanks, Dr. Mayor.

21 Dr. Larntz?

22 MEMBER LARNTZ: I voted no because I think

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1 the only way we can require clinical data is to be in
2 class III.

3 CHAIRPERSON YASZEMSKI: Thank you, Dr.
4 Larntz.

5 Dr. Besser?

6 MEMBER BESSER: I voted yes because I
7 think that the questions, the concerns can be handled
8 under class II, including the clinical data.

9 CHAIRPERSON YASZEMSKI: Thanks, Dr.
10 Besser.

11 Ms. Maher?

12 MEMBER MAHER: I think that both the panel
13 and all of the presenters have ensured that the FDA is
14 well-aware of where their concerns are and what needs
15 to be watched out as we are moving forward. I would
16 applaud everybody for a very good decision and working
17 well together.

18 CHAIRPERSON YASZEMSKI: Thanks, Ms. Maher.

19 Dr. Doyle?

20 MEMBER DOYLE: I agree with Dr. Larntz and
21 Dr. Naidu, who stated it much better than I can. I
22 was uncomfortable with the fact that we cannot control

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1 the need for clinical data. And while it isn't
2 perhaps appropriate here, if you consider
3 risk-benefit, I wasn't comfortable that these devices
4 offered sufficient benefit to balance any possible
5 risk, of which there seems to be some.

6 CHAIRPERSON YASZEMSKI: Thank you.

7 Dr. Witten, as you have seen, there has
8 been a lively discussion with a lot of feelings for
9 both directions. We have come to a vote. Any
10 comments from FDA that you would like further from us
11 or to make about the proceedings?

12 DR. WITTEN: No. I would like to thank
13 everyone for the discussion and the vote.

14 CHAIRPERSON YASZEMSKI: Thank you so much.

15 We are going to break for lunch. It is
16 now 12:25. We are going to start up again at 1:15,
17 1:15. Take about 45 minutes for lunch.

18 (Whereupon, at 12:24 p.m., the foregoing
19 matter was recessed for lunch, to
20 reconvene at 1:15 p.m. the same day.)

21

22

1 A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

2 (1:19 p.m.)

3 CHAIRPERSON YASZEMSKI: This afternoon we
4 are going to follow a similar agenda as for the
5 morning session for the draft guidance document. This
6 is the first industry group-prepared draft guidance
7 document. After the open public hearing,
8 representatives of OSMA will present as will FDA.

9 In the panel deliberations, Drs. Mabrey
10 and Larntz will provide their perspectives to start
11 the panel deliberations. There will be no panel vote
12 on this topic. Our response to the FDA questions will
13 constitute our consensus recommendations on the draft
14 guidance document.

15 I would like to remind the public again
16 that while this meeting is open for public
17 observation, public attendees may not participate
18 except at the specific request of the panel.

19 OPEN PUBLIC HEARING

20 CHAIRPERSON YASZEMSKI: We will now
21 proceed with the afternoon open public hearing portion
22 of the meeting for the proposed draft hip guidance

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1 document. Prior to the meeting, there were no
2 requests to speak in the open public hearing. Is
3 there anyone present who would like to speak as part
4 of the open public hearing

5 (No response.)

6 CHAIRPERSON YASZEMSKI: Seeing none, we
7 will proceed with the presentations. Is the first
8 OSMA presenter here yet? The first OSMA presenter
9 will be Mr. Joel Batts. Mr. Batts?

10 Thanks again. I will just comment while
11 it is powering up. You folks at the side table have
12 been really keeping us going all along, and we all
13 appreciate it. Thank you.

14 MR. BATTIS: Okay. Thank you.

15 INDUSTRY PRESENTATION

16 MR. BATTIS: My name is Joel Batts. I am
17 here on behalf of OSMA and employed by Corin Group, a
18 member company of OSMA. What I would like to do is
19 set up the presentations that will happen subsequent
20 to mine, Dr. Bernie Stulberg and Dr. Joshua Jacobs.
21 The way I would like to set this up is by giving you
22 a few definitions, which come out of the document

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1 itself. They will use these definitions throughout
2 their presentations. After this presentation, what we
3 will look at, for your information, against the
4 guidance document is to look at the process by which
5 the document was set up and then, secondly, the
6 implications the document would have for the clinician
7 in practice doing clinical trials.

8 So in the guidance document, there are two
9 terms. One is HRS. That is hip replacement systems.
10 We define that in this document as a hip replacement
11 prosthesis or a group of hip replacement prostheses
12 intended to replace one or both sides of the hip
13 joint. This includes FDA-cleared and non-cleared
14 prostheses. So obviously we are looking at more than
15 just investigational devices with this document.

16 The second term is what a clinical trial
17 is with this document. That is any investigation
18 carried out on an HRS due to clinician initiation,
19 interest, post-market surveillance, IDEs, or other
20 purposes.

21 So the HRS control groups to date,
22 typically the way that these studies have carried on,

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1 have made variation difficult for comparison. In
2 other words, the control groups have varied. The
3 designs have varied to such an extent that often you
4 get an apples and oranges comparison if you're trying
5 to look at prostheses against/across different
6 studies.

7 That is one element of control groups
8 today. The second is that there is an element of
9 burdensomeness for the clinician and industry to carry
10 out the studies with control groups to date. And,
11 thirdly, there are scientific limitations.

12 The purpose of the document is to move
13 towards benchmark development. And hopefully in doing
14 that, we eradicate or minimize some of the things we
15 just saw in that last slide with the scientific
16 limitations and the burdensome approach to studies.

17 The device form initiated this guidance
18 document with input from clinicians, scientists, FDA,
19 and industry. The guidance document covers a range of
20 study purposes, like I said in the first slide, it
21 covers a range all the way from IDEs to the clinician
22 who is interested in doing any kind of follow-up

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1 trial.

2 It comes out with a three-point composite
3 benchmark based on the literature and based on
4 clinician-scientist consensus. Dr. Stulberg will
5 comment on how that benchmark was arrived at based on
6 that consensus.

7 The short and long-term benefits of the
8 document are elucidated here. The short-term are that
9 it provides clinicians, industry, and FDA with a less
10 burdensome, more reliable method of conducting and
11 overseeing clinical trials.

12 It also provides patients with a clearer
13 understanding of the risks and benefits of study
14 participation. In the guidance document, you have got
15 a control group, which is a benchmark control group.
16 So you end up having a much easier time clearing up
17 the risks and benefits to a study participant. So it
18 does have some IRB implications there.

19 Thirdly, it improves confidence in the
20 conclusions from data analysis. With the various
21 control groups thus far in HRS studies, the
22 conclusions often are variable. Again, that helps us

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1 to compare.

2 Long term it permits a more apples to
3 apples comparison of study results. And the document
4 also provides a foundation for updating clinical and
5 scientific consensus as the body of knowledge grows.

6 So it's seen to be something which is
7 organic over time. And as the body of knowledge
8 grows, it would give us the foundation upon which we
9 could base future benchmarks as the body of knowledge
10 grows. It would give us a foundation, a starting
11 point for doing that.

12 Thank you.

13 CHAIRPERSON YASZEMSKI: Thanks very much,
14 Dr. Batts.

15 Dr. Stulberg?

16 DR. STULBERG: Dr. Yaszemski, ladies and
17 gentlemen of the panel. My name is Bernie Stulberg.
18 I am an orthopedic surgeon from Cleveland, Ohio. I
19 happen to be the Director of the Cleveland Center for
20 Joint Reconstruction, which is a private practice of
21 orthopedics.

22 I chair the Orthopedic Device Forum, which

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1 is a collaborative venture of scientists and
2 clinicians working in concert with its industry to
3 facilitate the introduction of safe and effective
4 devices to the American public when appropriate.

5 I would like to briefly review -- forgive
6 me. My disclosure is appropriate. I do serve as an
7 orthopedic consultant for Stryker Orthopedics and for
8 Zimmer.

9 My talk will briefly cover how we arrived
10 at the document before you, which was proposed as a
11 guidance document to begin to look at performance,
12 trying to develop performance criteria for implants
13 that have a long-established track record. We used
14 the benchmark approach to address this, these issues.

15 The device forum initiated this project
16 with OSMA in 2002 with the subcommittee directed by
17 Dr. Timothy Wright, who I am actually substituting for
18 today. Dr. Wright is the Ph.D. and head of
19 Bioengineering Lab at the Hospital for Special Surgery
20 in New York.

21 It was our feeling that an agreement on a
22 more standardized approach to control groups if it

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1 could be developed would ease the burden on all
2 parties involved in the clinical research that is
3 necessary to bring safe and effective devices to the
4 American public.

5 The mechanism that has worked for us in
6 the past has been to try to have our industry help
7 generate these documents with support from the
8 scientific and clinical community. And a task force
9 was assembled to pursue this approach.

10 We used the two-step approach to arrive at
11 a valid document. The first was to review the
12 literature and the second to approach our community or
13 orthopedists and orthopedic scientists to try to
14 develop a consensus and to determine whether there was
15 agreement in these two lines of information.

16 First was a PUBMED search carried out
17 using specific criteria, as we have outlined in
18 appendix 3, and resolve it in a series of articles
19 that we then categorized according to the level of
20 evidence, which we have provided for you in appendix
21 2, trying to identify the best source of information
22 possible to get at types and frequencies of problems

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1 encountered in hip replacement systems.

2 As a result of this search, we had 277
3 articles, which reviewed for type and frequency of
4 complications in a period of time less than two years,
5 which is the minimum period of time for IDE evaluation
6 in the PMA process.

7 In that literature review, we identified
8 a total number of almost 1,500 complications. They
9 were separated into four. You will see five on the
10 slide but actually four categories. These were
11 categories selected according to criteria used and
12 initially defined by the Biomedical Engineering
13 Committee of the American Academy of Orthopedic
14 Surgery, which identifies in any implanted device the
15 role of the device as part of a complication,
16 identifies the technical aspects of implanting that
17 device as well as unrelated but systemic complications
18 that are a result of the operative intervention.

19 We made these four categories: device
20 only, operative technique only, operative technique
21 plus device, and systemic and unrelated. That has
22 been characterized for you in appendix 4.

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1 We then took that series of articles and
2 review with the complications and submitted them to a
3 group of scientists associated with a group called the
4 Hip Society.

5 The Hip Society is a subspecialty society
6 as part of the American Academy of Orthopedic
7 Surgeons. It is made up of surgeons who have academic
8 interests and scientists related to that. Their focus
9 has been on the hip. It is a very small society of
10 about 100 surgeons. Of that group, 14 members
11 volunteered and were used in the process of evaluating
12 this document.

13 We used the literature review results. We
14 polled these colleagues to answer six questions as it
15 related to these findings. Those are outlined for you
16 in appendix 1. We then took their answers, went back
17 to the task force and tried to develop a composite
18 score that we could use to benchmark a hip implant.

19 We found good agreement between the
20 clinical opinions as they were expressed by these
21 colleagues and the results tabulated from the
22 literature review and, therefore, feel that they have

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1 been useful in establishing these benchmarks.

2 As a result, we believe that it is
3 appropriate to think about as an alternative approach
4 for regulatory evaluation the use of a benchmarking
5 approach, where we can define a successful hip
6 implant.

7 We have done this in two parts. There is
8 a specific composite score that is reflected for each
9 patient. That is, that patient who has had a device
10 implanted should have no device-related complications.

11 The patient should have a hip-specific
12 score, which we selected the Harris Hip Score, which
13 is the most widely used hip function and pain score
14 that is available. And a good or excellent result in
15 that scoring is greater than 80 points. So we defined
16 that as an appropriate endpoint. If a patient had had
17 revision surgery, that would then be considered a
18 failure.

19 So for a result to be successful, there
20 should be no device-related complications. They
21 should have a good or excellent clinical and pain
22 score on a disease-specific and joint-specific scoring

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1 composite score and had not had revision surgery.

2 Device-related was then defined as a
3 complication based on the literature review. Based on
4 that composite, a patient would either be successful
5 or not successful. And, therefore, a clinical trial
6 objective would be determined as it related to the
7 success or lack of that group of patients. The number
8 selected was 95 percent of that group would have
9 subject successful at the endpoint according to the
10 composition definition.

11 Now I am going to ask Dr. Jacobs to
12 explain the pros and cons of an approach of this
13 nature.

14 CHAIRPERSON YASZEMSKI: Thanks very much,
15 Dr. Stulberg.

16 Dr. Jacobs?

17 DR. JACOBS: Thanks very much, Bernie.
18 And I thank the panel for allowing me to speak. I am
19 Josh Jacobs. I am an orthopedic surgery. I work in
20 Chicago, Rush Medical College. I also chair the AOS
21 Council on Research and was a former member of the
22 device forum.

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1 I am not speaking on behalf of the AOS,
2 nor am I speaking on behalf of the council, but I am
3 happy to say that the leadership of the AOS does
4 support the activities of the device forum as over the
5 years, they have produced many successful initiatives
6 to improve and find a balance between patient safety
7 and innovation.

8 My conflicts are that I am a consultant
9 for Zimmer. I also have research funds from Zimmer
10 and Wright Medical. And I am on the board of
11 directors of ASTM International.

12 What I would like to do briefly is to talk
13 about the implications for the clinician of the HRS
14 document that we have been discussing. I am going to
15 discuss three key issues. One relates to scientific
16 aspects of the document; the second to the logistics
17 of studies; and, finally, to recruitment of patients
18 for these studies.

19 Now, the traditional approach requires the
20 use of control groups. They can be concurrent
21 controls that are either randomized or non-randomized.
22 This requires some sort of subjective determination of

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1 differences in treatment and effects, so-called delta.

2 In the past, these control groups,
3 typically these patients have had limited access to or
4 desire for information regarding surgical devices and
5 techniques. As I will mention shortly, this has
6 changed dramatically. This approach, previous
7 approach, required clinicians to use two or more
8 devices: the study device and one or more control
9 devices.

10 Also, it was possible in the traditional
11 approach to use historical control groups. This,
12 however, requires the data set from a comparable
13 device or from comparable patient demographics. It
14 requires a data set from comparable interoperative and
15 postoperative treatment protocols. And, as I will
16 discuss briefly shortly, this also has changed
17 dramatically.

18 Finally, in order to use historical
19 controls, you need access to complete original data
20 sets. That has to possess good integrity. That means
21 minimal attrition and minimal missing data points.

22 Now, there are some scientific limitations

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1 to the traditional approach. That is that bias is not
2 completely eliminated, even in randomized designs.
3 That is because, unlike drug studies for device
4 studies, the clinician knows which device is used in
5 the patient at the time of surgery and at the time of
6 follow-up. Hence, the data used to determine success
7 or nonsuccess are unavoidably collected under
8 unblinded conditions.

9 Secondly, the treatment effect or the
10 so-called delta is typically subjectively chosen and
11 is often based on a gut feel. So our scientific
12 foundation for these studies, as I mentioned, with
13 these two facts is somewhat compromised.

14 Thirdly, it is difficult to establish
15 homogeneity between groups, particularly when we are
16 talking about historical controls. The inclusion or
17 exclusion criteria set up to achieve homogeneity may
18 severely restrict enrollment. And often the data is
19 available from historical controls only in the summary
20 format but diminishing the statistical conclusions
21 that can be made.

22 A final scientific point I want to make is

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1 typically the time line to detect clinically
2 significant and important differences in, for example,
3 randomized controlled studies or controlled studies is
4 not necessarily in accord with the regulatory time
5 frame.

6 What about study logistics? The clinical
7 studies need to integrate within the clinician's
8 practice. And there are many changes in practice that
9 have occurred over the last several years that make
10 this increasingly challenging.

11 There are many considerations, including
12 the burdens of data collection. Anyone who has
13 conducted these studies knows that this places a
14 tremendous burden on the staff to do the study
15 appropriately. IRBs are getting more and more
16 difficult to deal with. The amount of paperwork to
17 get a study through the IRB is increasing daily.

18 Patient recruitment can be challenging, as
19 I will discuss. And also we are dealing with a whole
20 new set of regulations, the hip regulations for
21 patient privacy that really have put up a barrier to
22 clinical research.

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1 We have a more and more mobile and
2 transient patient population. We are dealing with
3 problems with continued follow-up for managed care
4 organizations. And in an era of declining
5 reimbursement, there is pressure on clinicians to have
6 greater and greater throughput.

7 Randomized and non-randomized concurrent
8 studies require a significant number of patients,
9 typically greater than 100 in each group depending
10 upon your treatment effect chosen. So there is
11 greatly increased work load. And as the number of
12 patients increase, the likelihood of attrition
13 increases.

14 What about recruitment? We have a totally
15 different set of patients out there. In this era of
16 direct to consumer advertising and also aggressive
17 marketing by certain orthopedic surgeons, patients are
18 increasingly requesting specific devices, operative
19 techniques, et cetera, and will enroll in studies only
20 if that specific technique is to be used. Thus, it is
21 harder and harder to get control groups.

22 Furthermore, from the clinician, they may

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1 have a preference about the device that they would
2 prefer to use. Some clinicians are not comfortable
3 implanting certain devices, regardless of the
4 regulatory status. And if a clinician was required to
5 use such a control, the consent process could be
6 compromised.

7 So, in summary, the scientific nature of
8 the previous studies is compromised in the sense that
9 randomization does not eliminate bias. Traditional
10 control groups create overly burdensome conditions for
11 overworked staff, particularly when we are dealing
12 with hip replacement systems, where we have a
13 tremendous amount of literature and benchmarking
14 information is available. There is an increasing
15 involvement of an educated patient, which serves as a
16 barrier to recruitment of control groups.

17 And this study guidance takes seriously
18 the limitations mentioned above by enlisting clinician
19 consensus based on extensive literature and clinical
20 experience. It allows for a more standardized method
21 of study design and regulatory review, making protocol
22 writing submissions and data collections more

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1 accessible to more clinicians. Finally, it creates a
2 reference point from which future benchmarks may be
3 set as the body of knowledge grows.

4 Thank you very much for your attention.

5 CHAIRPERSON YASZEMSKI: Thanks very much,
6 Dr. Jacobs.

7 We will ask Dr. Buch to come up now and
8 give her presentation. While she is setting up, if
9 there are any questions any of the panel wants to ask
10 Dr. Jacobs, Dr. Stulberg, or Mr. Batts, we can maybe
11 get one question in while Dr. Buch is setting up. Dr.
12 Mabrey?

13 MEMBER MABREY: Could I get a comment from
14 the sponsors regarding the actual length of follow-up
15 for the studies, the endpoint?

16 MR. BATTIS: Insofar as what was in the
17 document itself? Did you want to know what the
18 endpoint was on the document?

19 MEMBER MABREY: As to why that was chosen.

20 MR. BATTIS: That was chosen because there
21 was a feeling amongst clinicians that -- there was
22 some discussion within the Hip Society clinician group

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1 about that, but at the end of the day, it was felt
2 that the majority of the opinion -- and this was even
3 the opinion of those who had said that a two-year
4 follow-up is what we would like to see. It was their
5 opinion that there is not necessarily a difference
6 between one and two-year complication rates or
7 different complications but that that has been
8 something ingrained in our heads from journals and
9 that there is a two-year minimum before a journal will
10 accept the data.

11 So, again, going back to the scientific
12 limitations of these things, we didn't feel that there
13 was a scientific reason for requiring the two-year
14 endpoint, that when the clinicians came down and said,
15 "two years," there was no reason other than that is
16 what the journals tell us: two. So one year was --

17 CHAIRPERSON YASZEMSKI: Dr. Stulberg?

18 DR. STULBERG: If I could just add one
19 comment? Mr. Batts is correct. The actual polling
20 and consensus varied substantially from six months to
21 as long as five years.

22 I think the general sense of the group was

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1 two years was reasonable, but it might be possible
2 after reviewing the data to actually shorten that a
3 little bit. So the general feeling of the consensus
4 group was about 24 months.

5 CHAIRPERSON YASZEMSKI: Thanks, Dr.
6 Stulberg.

7 While we are going, if there is another
8 question? Dr. Kim?

9 MEMBER KIM: Can I ask a question from the
10 sponsors? One of the criteria was that device-related
11 failure would be one of the success criteria. But in
12 your presentation, another factor is device and
13 technique-related failures. How good can we
14 distinguish between device only and device and
15 technique-only complications? Why did you leave out
16 device and technique?

17 CHAIRPERSON YASZEMSKI: Dr. Stulberg, I
18 can ask you to use the table. There is another mike
19 over there.

20 DR. STULBERG: Sorry.

21 CHAIRPERSON YASZEMSKI: Thanks. Dr. Buch,
22 do you need help before Dr. Stulberg answers from our

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1 colleagues at the side? It has to reboot. Okay. I'm
2 sorry. Dr. Stulberg, please go ahead.

3 DR. STULBERG: In the document, I believe
4 we have indicated that we would ask for or suggest
5 that manufacturers provide probable and possible
6 relationships.

7 There are times you simply can't
8 differentiate technical abnormality or misalignment
9 that overloads the device and then leads to device
10 failure. You need to list those, but it is difficult
11 to sort out the technical features from the device in
12 certain situations. We believe they ought to be
13 reported, not necessarily in the sense that they
14 punish the manufacturer if it happens to be an
15 implantation problem.

16 So it should be in there that both should
17 be listed possible. If you look at appendix 4, where
18 we have listed all of the complications, we list them
19 as category 2 and category 3 with category 2 being
20 device implant only and 3 operative technique and
21 implant, where we simply couldn't sort it out.

22 CHAIRPERSON YASZEMSKI: Thank you, Dr.

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1 Stulberg.

2 While Dr. Buch is getting ready, the first
3 FDA presenter is Dr. Barbara Buch. She is an
4 orthopedic surgeon and a medical officer in the
5 Orthopedic Devices Branch at FDA. As soon as your
6 computer is ready, we will look forward to hearing
7 from you.

8 Any other questions while we are waiting
9 for boot-up? Dr. Mabrey, it looked like you had.

10 MEMBER MABREY: You should have bought a
11 Dell.

12 (Laughter.)

13 FDA PRESENTATION

14 DR. BUCH: I can start. I'm going to be
15 speaking about this document from a different point of
16 view today. Our three previous presenters did a good
17 job of presenting the content of the document and the
18 rationale behind it. So I will not repeat that for
19 you.

20 What I will do is show you our side of the
21 picture. And if it looks like I am giving you two
22 sides of the coin, I am because these are things that

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1 FDA has to consider when looking at a document such as
2 this. So I ask your indulgence for another second
3 here.

4 I will introduce some of the regulatory
5 considerations that go along with this document. We
6 are going to charge the panel to consider what is
7 proposed in the guidance document and to identify any
8 additional information that should be used and
9 included in a future guidance on the topic of hip
10 replacement systems.

11 I am going to hopefully get a slide. I am
12 going to touch on some necessary elements that would
13 go into a guidance document and discuss what was
14 presented in the document, what we would need in
15 addition to that. And then Mrs. Phyllis Silverman
16 will continue with the discussion of the statistical
17 nature of the document you see before you.

18 And then at the end, we are going to ask
19 the panel to answer some specific questions. I
20 emphasize "specific" because I would appreciate some
21 specific answers to those questions.

22 So what is a guidance document submission?

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1 Dr. Stulberg touched on this, but, actually, FDA
2 publishes in the Federal Register and on the internet
3 a list of possible topics for future guidance document
4 development or revision in the coming year. This is
5 in accordance to an actual regulation, 21 CFR
6 IB-10.115(5). The submission we are discussing today
7 is a result of this request and OSMA's response to
8 this request along with discussions between industry,
9 professional societies through the orthopedic device
10 forum.

11 In accordance with another regulation, 21
12 CFR IB-10.115(3), anyone can submit drafts of proposed
13 guidance documents for the FDA to consider. These
14 documents are termed "guidance document submissions"
15 and are submitted to the Dockets Management Branch of
16 FDA.

17 It should be emphasized that this is not
18 a petition for the reclassification of hip replacement
19 systems. Any hip systems included that are currently
20 class III would remain class III and any that are
21 currently class II would remain class II after today's
22 discussion.

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1 It is also important to realize that this
2 is not a guidance document that FDA will accept or
3 reject. From now on in my discussion, I will refer to
4 the submission as the GDS to avoid confusion with the
5 term "guidance document," which is generated by FDA.

6 What is the subject of the GDS? We know
7 it's a clinical design for studies for evaluating hip
8 joint replacements, which is an all-encompassing term,
9 to include both conventional hip arthroplasty,
10 cemented and non-cemented, and modern technological
11 improvements on the conventional designs. As was
12 discussed, it contains three objective performance
13 criteria as a composite endpoint and a performance
14 benchmark for study success.

15 Since this is ODE's first guidance
16 document submission, we will ask the panel to consider
17 what is proposed and provide input as to the adequacy
18 of the elements proposed to discuss acceptable
19 specific endpoint criteria and acceptable endpoints at
20 a specific point in time and to identify additional
21 information that should be included for a future FDA
22 clinical guidance on the topic of hip replacement

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1 systems. I want to emphasize that FDA will not ask
2 the panel to approve or disapprove this guidance
3 document submission.

4 How can we use this guidance document
5 submission? In keeping with FDA's objective, which is
6 to ultimately develop a clinical guidance for studying
7 new hip systems to assure their safety and
8 effectiveness, I would now like to discuss how we can
9 use this GDS and how the notion of objective
10 performance criteria may be incorporated, what the
11 essential elements would be for a clinical guidance
12 and highlighting potential additional topics that are
13 not presented in the GDS. The panel's discussion and
14 input are constructive in moving towards that goal.

15 A guidance by definition represents FDA's
16 current thinking on a topic. Therefore, FDA can use
17 this document as a comment and update of industry's
18 and orthopedic professionals' current thinking about
19 ways to study new hip systems and the expectation for
20 patient safety and effectiveness outcomes.

21 FDA can also use this as an innovative
22 concept for developing a model for a potentially less

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1 burdensome method of studying hip systems while
2 assuring safety and effectiveness and as a way to meet
3 FDA and industry goals of getting certain hip systems
4 and devices to patients faster.

5 It is important to note that devices with
6 a novel design, new materials, or indications for use
7 may or may not be included in any guidance eventually
8 developed from this meeting.

9 Since the previous three speakers have
10 clearly presented the content of this GDS, the process
11 by which it was created, the justification for its
12 concept, and the method by which it was composed, I
13 would like to highlight the endpoints and outcome
14 measures. And Mrs. Silverman will highlight the
15 statistical issues of the document.

16 The comprehensive guidance document we
17 believe would necessarily contain all of these
18 essential elements. I would like to look at each of
19 these briefly and point out what was provided in the
20 GDS and what other issues would be needed in order to
21 compose a comprehensive guidance.

22 The first question on everybody's minds is

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1 the consideration of the duration of the study, which
2 in the GDS is one year. The Orthopedic and
3 Rehabilitation Devices Advisory Panel has repeatedly
4 promoted a minimum of two-year studies for new
5 devices. This is consistently required as well by
6 peer-reviewed journals for publication of outcomes.

7 The proposed evaluation intervals are
8 baseline 6-week, 6-month, and 12-month postoperative
9 evaluations. When queried in the past, the panel has
10 previously recommended that even two-year data is an
11 inadequate surrogate for long-term performance. FDA
12 has always recommended for prosthetic devices that
13 data be collected at a minimum of two years and to
14 collect data until the last enrolled patient has had
15 its 24-month evaluation, as this allows for the
16 collection of some data beyond 2 years.

17 As it is written, the GDS did not provide
18 an adequate rationale or data to support the proposed
19 objective performance criteria at one year. At the
20 end of this presentation, we will be asking the panel
21 for recommendations regarding the combination of the
22 proposed objective performance criteria and the

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1 proposed time of last evaluation.

2 The main object of the GDS is that it
3 contains objective performance criteria as a control
4 in a composite patient success criterion, and as a
5 performance benchmark for study success for future hip
6 replacement studies.

7 How can we consider such a benchmark for
8 outcomes? We have all been trained that the ideal and
9 preferred vehicle for establishing safety and
10 effectiveness for any device is the randomized
11 prospective controlled clinical trial. However, there
12 are other sources of valid scientific evidence to show
13 safety and effectiveness that can be considered in an
14 effort to provide a least burdensome approach to
15 pre-market applications, as was outlined in this
16 guidance document submission.

17 This approach would be a singular
18 allowance in the orthopedic devices forum, not the
19 orthopedic device forum, the orthopedic devices forum,
20 due to the long history of consistent device
21 performance, as has been previously mentioned,
22 reported in peer-reviewed literature and by

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1 professional experience dating from before 1960. This
2 allows comprehensive review and understanding by
3 industry, physicians, patients, and FDA.

4 Over the past two decades, total hip
5 arthroplasty has become a standard of care for end
6 stage arthritic and other medical conditions affecting
7 the weight-bearing surfaces of the hip joint.

8 We have come to know that improved quality
9 of life through the reduction of pain and return to
10 function are well-accepted outcomes in the
11 professional, scientific, and patient communities.
12 This experience is supplemented by some well-developed
13 bench preclinical and clinical performance evaluations
14 in standard use that characterizes devices well.

15 All of this combined historical knowledge
16 and experience along with standards information would
17 allow the FDA to consider the development of benchmark
18 criteria by which to measure new emerging
19 technologies.

20 Currently at FDA there exist some
21 examples, both preclinically and clinically, for
22 acceptable endpoint criteria based on a meta analysis

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1 of medical literature are used as a control against
2 which safety and effectiveness emerging technologies
3 are measured.

4 Examples of clinical objective performance
5 criteria in use today include cardiac heart valve
6 devices, cardiac ablation catheters, and intraocular
7 ophthalmic lens devices. Of course, there are two
8 sides to every story. So I am going to give them to
9 you.

10 The benefits of using historical controls
11 or target benchmarks are that this method can become
12 a least burdensome approach. We can develop a
13 standard approach that is considered valid scientific
14 evidence, and there is potential to facilitate the
15 review of any clinical data.

16 The drawbacks, on the other hand, include
17 resulting studies that can become one-armed
18 observational studies. And since there is no
19 randomization, any comparative statistical inference
20 is compromised.

21 The use of historical controls and a study
22 of the past assume that the knowledge gathered can

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1 answer new clinical questions. The assumption is that
2 a review of the literature allows complete and
3 adequately detailed records for review, which we all
4 know is not the case. A meta analysis based on
5 published reports may be subject to publication bias
6 as negative clinical studies are less likely to be
7 published.

8 With vast historical experience based on
9 patients and medical thinking of the past, there is a
10 strong possibility of temporal bias. Baseline
11 conditions of a population will change over time. And
12 what naturally follows is a question of the capacity
13 and soundness of a comparison between historical
14 controls and future patients to be treated.

15 The concern associated with these factors
16 that has changed since the time of historical review
17 is whether historical data applied to new devices may
18 or may not discern whether the device is inferior to
19 current treatments.

20 In contrast, a known advantage of
21 randomized trial design is that confounding factors,
22 such as selection, demographic, or covariate biases,

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1 are counteracted because of the randomization. If
2 there is no randomization, there is a greater need to
3 check for and avoid potential confounding factors that
4 lead to bias in a trial. Thus, there need to be tools
5 in place to mitigate the biases that exist inherently
6 with historical controls. All of these issues
7 regarding the clinical trial control are what we are
8 asking the panel to discuss.

9 Primary and secondary endpoints as
10 surrogate outcomes to predict device safety and
11 effectiveness are essential for clinical trial design.
12 The primary endpoints for the study as proposed in
13 this document include pain and function as evaluated
14 by the Harris Hip Score, the revision rate over time,
15 and adverse events. Other primary endpoints may
16 include radiographic endpoints, but these are not
17 clearly defined in the document.

18 Quality of life secondary endpoints are
19 suggested, but a return to work or activities of daily
20 living may be more appropriate measures of quality of
21 life. The questions that arise are whether these
22 evaluation tools or endpoints used historically are

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1 still appropriate for populations to be treated by
2 emerging technology and whether the development and
3 testing of new technology in advancement of hip
4 arthritis treatments includes the development of more
5 appropriate surrogate outcome measures to predict
6 patient and device safety and effectiveness.

7 Evaluation tools proposed in this document
8 have been used for several decades, but are they still
9 appropriate for 2004 and the future? Are there other
10 pain and function outcome scales that would be more
11 appropriate?

12 And if we decide that the Harris Hip Score
13 is still appropriate, is there a minimal acceptable
14 change from baseline on the Harris Hip Score or other
15 scales that would serve as a surrogate for successful
16 patient outcomes?

17 What radiographic criteria are surrogates
18 for predicting implant or patient failure? What
19 measures should be performed? And what are the
20 minimally allowable or acceptable quantities of those
21 measures? Are there other evaluation tools that also
22 should be considered? These are all questions that

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1 need to be considered in the development of a
2 comprehensive guidance document.

3 It is notable that traditionally studies
4 have not employed patient subjective evaluations for
5 pain and function when evaluating hip replacement
6 systems, but these have been used in the evaluation of
7 other types of orthopedic devices. This begs the
8 question, do patient subjective evaluations also have
9 a place in evaluating hip replacement systems? This
10 is, admittedly, a controversial debate.

11 Specific inclusion and exclusion criteria
12 for patient selection is an important element of the
13 design of a study. But general criteria were not
14 included as a part of the GDS. Of interest to us is
15 how confounding factors that affect patient outcomes
16 can be avoided, such as those that are listed here.

17 Most importantly, we are concerned about
18 the safety of devices and the consideration of adverse
19 events. A list of commonly reported events associated
20 with hip replacement systems and the incidences based
21 on the meta analysis are captured in appendix 4 of the
22 GDS.

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1 I would like to note, in contrast to that
2 proposed in the GDS, FDA includes adverse events
3 attributable to surgical technique as part of
4 device-related events since the surgical technique is
5 considered labeling for the device. But does the
6 analysis provided capture all of the adverse events?

7 Again, several questions arise based on
8 the analysis provided. Are all of the events
9 applicable to all current and future materials,
10 bearing couples and designs? Are there enough
11 published studies for newer bearing surfaces to
12 include all possible events? And are the types of
13 devices that were included in the analysis and the
14 type of study the data came from inclusive of what is
15 applicable to current technology? Again, these are
16 issues the FDA is asking the panel to consider during
17 their discussion of panel questions.

18 The criteria proposed in the document is
19 interdependent on the sample size that the
20 statisticians will discuss shortly. But are the
21 benchmarks consistent with what we see in larger
22 studies of conventional hip replacement studies?

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1 Since most studies show that patients
2 achieve a Harris Hip Score of good to excellent, I
3 would like to present three large study examples for
4 you to consider in comparing these criteria proposed
5 in the GDS at one year as they appear on this slide.
6 I am going to focus on implant survival and revision
7 rates.

8 The most recent results of the Swedish Hip
9 Register were published in 2002. Implant survival is
10 high at one and two years. Revision rates are lower
11 at ten years than those proposed for success at one
12 year in the GDS. Nine to ten-year implant survival as
13 reported was 93 to 98.3 percent.

14 With the use of modern cementing
15 techniques, a 94.8 percent 10-year implant survival
16 rate was noted for total hip replacement for
17 osteoarthritis with loosening as an endpoint. When
18 all other causes for revision are included, the
19 overall implant survival was reduced by one to two
20 percent.

21 Cementless implants when looked at
22 separately have a lower implant survival than

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1 cemented. In the cohort review starting in 1991, the
2 revision rates for cemented implants were 2.5 percent
3 over 10 years.

4 The graph on the right shows implant
5 survival by age and type of fixation from the period
6 of 1992 to 2000. Note for the patients younger or
7 older than 55 years, at 2 years implant survival is 99
8 to 100 percent.

9 All groups had survival of the implant of
10 about 95 percent up to 10 years. I would like to
11 point out that this data comes from all hip
12 replacements at rural, central, and university
13 hospitals, not just under controlled and monitored
14 conditions with experienced surgeons performing the
15 procedures in selected patients.

16 In this graph, patients aged 55 or more
17 show a survival rate of 96.6 at 9 years. The blue
18 line is the patient cohort who is older than 55 years
19 of age for comparison to the other three for patients
20 55 years or younger who received cemented implants
21 depicted in the red line, uncemented in the green, and
22 hybrid implants in the yellow. The black vertical

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1 line transects the graph at two years.

2 Next, the NIH consensus meeting in 1994
3 looked at 30 years of follow-up data on patients who
4 had conventional total hip arthroplasty, mostly metal
5 on polyethylene, as a couple.

6 The results showed that greater than 90
7 percent of all hips were never revised. Revision
8 rates for cemented femoral components were less than
9 five percent at ten years. And revision rates for
10 uncemented acetabular components was approximately two
11 percent at five years. And the most common adverse
12 events leading to revision are listed here.

13 Finally, the Dartmouth Atlas of
14 Musculoskeletal Health Care Investigators explored the
15 most common musculoskeletal diseases and injuries in
16 the Medicare population. The in-depth clinical focus
17 includes an analysis of variations in the care of
18 degenerative joint disease, conditions of the spine,
19 and treatment of fractures. Specific procedures
20 addressed included total hip joint replacement.

21 In 2000, for patients in the Medicare
22 population, over 65, the primary hip revision is

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1 reported to be under three percent within two years.
2 The FDA will ask the panel to consider benchmark
3 criteria in light of these examples from the
4 literature, both European and U.S. populations.

5 The GDS discussed several statistical
6 issues relating to sample size delta and confidence
7 intervals related to patient and study success. A
8 guidance would need to include other statistical
9 issues, including the treatment and analysis of
10 patients requiring bilateral treatment, patients who
11 are lost to follow-up, how covariates would be
12 considered, and justification of target values based
13 on the control populations for the investigational
14 population. These are not dealt with in this
15 document.

16 Next I would like to ask Mrs. Phyllis
17 Silverman to come up and provide a statistical comment
18 on the GDS.

19 CHAIRPERSON YASZEMSKI: Thank you, Dr.
20 Buch.

21 Ms. Silverman?

22 MS. SILVERMAN: Good afternoon. I'm

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1 Phyllis Silverman, and my job is to explain to you the
2 statistical theory behind this guidance document so
3 that you can make an informed recommendation.

4 Our lesson in statistics will focus on
5 objective performance criteria and the factors that
6 affect sample size. Although I will refer to certain
7 elements of the guidance document, it is by no means
8 in final form. And my review of it was included in
9 your panel pack.

10 If we could sample everyone in the world
11 who would receive a certain medical device, there
12 would be no need for statistics. We would know the
13 truth. And there would be no variability to deal
14 with.

15 Since this is not possible, statistics
16 allows us to make an inference about a population
17 parameter, such as the success rate, based on
18 information that we collect in a sample.

19 Our specific task is to estimate the true
20 success rate at a given point in time for all of the
21 people in the world who might receive a particular
22 hip. This time point might be 12 months or 24 months,

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1 for example. We want to conduct a clinical study to
2 do this.

3 If we conducted a second study from the
4 same patient population, we would obviously get a
5 slightly different success rate. Statistics allows us
6 to account for this variability.

7 We want to compare our study success rate
8 to a fixed constant; for example, 95 percent. This
9 can also be called a target value and objective
10 performance criteria or OPC or a fixed historical
11 control.

12 You are familiar with concurrently
13 controlled studies, where there is variability in each
14 treatment arm. This guidance is proposing a one-arm
15 study using a target value so that there is only one
16 source of variability, that from the test device
17 population. This target value cannot be chosen
18 arbitrarily. It must be objectively defined from
19 public data sources or literature studies on
20 comparable patient populations.

21 Each patient is labeled a success or
22 failure based on clinically defined criteria. The

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1 success criteria in this guidance document relate to
2 Harris Hip Score and the absence of complications and
3 revisions.

4 Then the proportion of study successes is
5 statistically compared to the target value. This can
6 be done using a confidence interval where it's the
7 lower bound that is of interest to us -- and I will
8 show you a picture of this in a minute -- or you can
9 do a test of one proportion against an alternative
10 value and actually get a *p*-value.

11 Speaking of confidence intervals, the
12 literal definition of a confidence interval is if you
13 repeated the trial many times with the same sample
14 size, each time calculating the observed success rate
15 and confidence interval, 95 percent of your computed
16 intervals would contain the true population parameter.

17 Again, the population parameter in our
18 case is the success rate. However, since generally we
19 just do trials once, the working interpretation of
20 this would be that you are 95 percent confident that
21 your interval contains the true population parameter.

22 So if you are trying to show superiority

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1 -- well, I am going to show you both the superiority
2 and the non-inferiority scenario here so that you can
3 see the difference. So for superiority, the
4 confidence interval would have to lie entirely above
5 the target value, which in this example is 95 percent.

6 Please don't confuse the 95 percent shown
7 on the axis with our degree of confidence. It's just
8 a coincidence that the target value and the degree of
9 the confidence are the same here.

10 The red dot would be the observed success
11 rate from your particular study, which would have to
12 be greater than 95 percent, perhaps 97 or 98 percent
13 depending on your sample size. And the red
14 parentheses show the bounds of the confidence limits.

15 For non-inferiority, the study success
16 rate could be a little below the target value or maybe
17 even a little above, but the lower bound of the
18 confidence interval must be within delta of the target
19 value.

20 Think of delta as the margin of
21 non-inferiority or the clinically insignificant
22 amount. So if delta equals four percent, as this

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1 guidance document proposes, the lower bound must lie
2 above 91 percent. We could then infer that the true
3 success rate is within 4 percent of 95 percent or no
4 worse than 91 percent.

5 When designing a study such as proposed by
6 this guidance, you pick a target value and delta, set
7 the type 1 error and the power, and then compute a
8 sample size. Alternatively, you can fix the sample
9 size and the detail and then see what observed study
10 success you must meet and what your power is to do so.

11 The next slide will show you how sample
12 size, delta, power, and observed study success all
13 interrelate. So if you have a target of 95 percent
14 and you want to be within 4 percent of that, which is
15 the current proposal from the guidance document
16 submission, you would need 266 patients and you would
17 need to observe a success rate in your study of 94
18 percent in order to be guaranteed by that confidence
19 interval that you are at least 91 percent.

20 Now, if you go down to the fourth row,
21 I've put in the sample size that the guidance document
22 proposes, which is 235 with a 4 percent delta. You

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1 would need to observe a study success of 94.5. So you
2 would actually have to be a little closer to your
3 target value of 95 because you have fewer patients,
4 but the guarantee is the same. If you make that 94.5
5 percent, your guarantee is that you are at least 91
6 percent, which is within the 4 percent of the 95
7 percent.

8 Now, I have shown some examples for larger
9 deltas of six and eight percent. These are probably
10 more than would be considered clinically acceptable,
11 but I just want to point out that, no matter what you
12 choose, the target value minus the delta equals your
13 minimum guarantee.

14 So here are the things to consider when
15 setting any guidelines. Sample size increases as
16 target value decreases. This is because there is less
17 variability with almost certain success. Things are
18 most variable at 50 percent, when it could go either
19 way. Therefore, more patients are needed for lower
20 target values. Sample size increases as delta
21 decreases. Subtle differences are more difficult to
22 see than larger ones. So, hence, you need more

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1 patients. And sample size increases as power
2 increases. To increase power, one must decrease
3 variability. More patients will do this.

4 Dr. Buch will now go over the questions
5 for which you will be asked to make recommendations.
6 But, first, are there any questions on the statistics?

7 (No response.)

8 CHAIRPERSON YASZEMSKI: Dr. Larntz is just
9 waiting, but he'll enter later. Thanks so much, Ms.
10 Silverman.

11 Dr. Buch?

12 DR. WITTEN: Do you want me to go through
13 them or do you want me to ask for them after the panel
14 discussion?

15 CHAIRPERSON YASZEMSKI: We can do it
16 after. That would be fine.

17 DR. WITTEN: What's that?

18 CHAIRPERSON YASZEMSKI: As you desire.
19 Either way is fine.

20 DR. BUCH: The questions that we're going
21 to ask you involve the topics of the objective
22 performance criteria, the statistical plan, study

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1 duration, patient selection, outcome measures,
2 post-market study necessity, and what hip systems need
3 to be included or excluded.

4 Please discuss each of the following
5 proposed in this GDS: the adequacy of the composite
6 endpoint criteria and each individual component at the
7 defined time point, the necessity of other endpoints
8 to be included in the endpoints and outcome targets
9 for the devices proposed, the adequacy of the sample
10 size, success rate, delta, and confidence intervals
11 for the observed success rates that are based on the
12 proposed objective performance criteria at the defined
13 time point.

14 Do you want me to keep going?

15 CHAIRPERSON YASZEMSKI: Perhaps what we
16 could do, Dr. Buch, if you would just read them now so
17 everybody kind of gets an idea what they are? Then I
18 am going to ask Dr. Mabrey to give his presentation,
19 if we could, and get the presentations done by both
20 Dr. Mabrey and Larntz. Then we will have a break in
21 the discussion.

22 DR. BUCH: If any of the above-mentioned

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1 are not adequate, please discuss what options would be
2 reasonable in terms of endpoint, sample size, success
3 rate, and any other parameters.

4 Based on previous discussions about
5 orthopedic implants, the Orthopaedic and
6 Rehabilitation Devices Panel has indicated that
7 long-term follow-up is preferred for orthopaedic
8 implants. The benchmarks for success proposed in this
9 document suggest achieving these at a one-year point
10 of reference.

11 Based on the facts presented in the NIH
12 consensus document and summaries provided by the
13 Swedish Hip Registry and the Dartmouth Atlas of
14 Musculoskeletal Health Care, the outcomes for hip
15 replacement vary according to the length of follow-up.

16 Please comment on the duration of patient
17 follow-up in the context of the proposed composite
18 objective performance criteria for patient and study
19 success presented in this document.

20 We would like you to include a discussion
21 of the time patients should be followed after
22 treatment in order to establish durability of effect

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1 and safety for permanent hip implants.

2 The success of any device is based on
3 proper patient selection. Please discuss any
4 inclusion and exclusion criteria that would be
5 important to incorporate into a guidance.

6 Include in this discussion the diagnoses,
7 the recreational activities, work level, anatomical
8 factors, medical or psychological co-morbidities, and
9 any other confounding factors that would affect the
10 outcome of the patients receiving hip joint
11 replacement.

12 Also comment in your discussion any entry
13 criteria related to endpoint assessment scales in
14 terms of disability, pain, and radiographic criteria,
15 or quality of life. For example patients to be
16 enrolled would have to have a maximum of 70 on the HHS
17 score for entry into the study for treatment.

18 There may be some disagreement in the
19 orthopedic scientific community over what constitutes
20 a successful outcome, leaving nebulous definitions of
21 endpoints which would correlate with prosthetic
22 failure or success.

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1 Despite common acceptance, outcome
2 assessment has been limited by the use of various
3 outcome assessment tools that rely on the surgeon's
4 assessment of pain and function.

5 Many of these measures have not been
6 adequately characterized in terms of validity,
7 reliability, and responsiveness to change.
8 Conventionally used outcome measurements have not
9 included any standard patient-oriented evaluations of
10 function, satisfaction, or a global outcome measure.

11 Please propose and discuss any new ideas
12 for appropriate alternative outcome measures and/or
13 surrogate endpoints to predict success in patients who
14 may be younger, healthier, heavier, and more active
15 than those in the historical literature reviewed.

16 Long-term outcomes studies are not always
17 possible. However, with a reduction in economic
18 burden facilitated by a guidance, such as that
19 proposed in the guidance document submission,
20 post-market surveillance studies may be appropriate to
21 evaluate specific clinical questions.

22 Please comment on the following: the

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1 types of questions a post-market study may be
2 appropriate to address; if necessary, the duration of
3 follow-up that would necessary to address the
4 questions asked; and the amount and type of data that
5 should be collected to answer the posed questions
6 after device clearance or approval.

7 And, finally, in the introductory remarks
8 of the guidance itself, the sponsor has included
9 several different classifications of hip systems to be
10 considered. These systems are general categories of
11 systems which have been in use for several decades.

12 We would like to ask you, based on your
13 experience and the experience in the published
14 literature to comment on the types or classifications
15 of hip systems that would be amenable to the use of
16 objective performance criteria and which would not.
17 And that's it.

18 CHAIRPERSON YASZEMSKI: Thanks very much,
19 Dr. Buch and Ms. Silverman.

20 We will now begin the panel discussion.
21 Dr. Mabrey and Dr. Larntz will open this part of the
22 meeting with their remarks. Then the panel will have

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1 general discussion, after which the panel will focus
2 their deliberations on the six FDA questions that Dr.
3 Buch just presented. The panel's responses to those
4 FDA questions will constitute its recommendation to
5 the FDA on the proposed guidance document submission.

6 Dr. Mabrey?

7 PANEL DELIBERATION

8 MEMBER MABREY: Mr. Chairman, members of
9 the panel, thank you for giving me the opportunity to
10 make this presentation this afternoon.

11 My discussion may seem somewhat repetitive
12 based on the fact that I am the sixth speaker to stand
13 up here, but my goal here was to set up a basis for
14 discussion with the panel to provide some suggestions
15 but not to definitively answer the FDA's questions in
16 this particular presentation.

17 Just briefly in case you missed it in the
18 last five presentations, the petition is looking for
19 a standardized method that is the least burdensome and
20 also provides for safety and effectiveness and
21 consistency in study design.

22 Their clinical trial design looks at

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