flexion-extension radiographs, this patient had a considerable range of motion, so it's not interfering with motion. Next.

This is an HO Class of II, a little more, as you can see on the far left of the A/P, but based on flexion-extension this patient still had a very high degree of range of motion at the operative level. And again, this is 24 months post-operatively. Next.

And this just demonstrates the progression of HO in a single patient. So if you take a patient immediately post-op and follow them through two years post-op, this is what the HO, how it presents itself. And you can see it appearing at six months or six weeks post-operatively, and then you get some densification of the HO and by 24 months, it's very evidence on the A/P film. Next.

And this is just a CT scan demonstrating the location of the HO not within the disc space, but it tends to be in the peri-annular region adjacent to the disc and not in the psoas. This happens to be four years post-op. Next.

And this is the Visual Analog Scale, the

data of interest here. HO and non-HO cases pre-operatively, very similar based on VAS scores by 24 month post-operatively using the Wilcoxon Rank Sum. There was no statistical differences between the two groups in VAS. Next. And ODI, similar findings. Pre-op, nearly identical and at 24 months, no differences between the two groups. Next.

And this is the flexion-extension range of motion. Interestingly, if you were to group these out into HO and non-HO cases based on the pre-operative plain films, it's a little over 6 degrees of motion for both treatments. But then interestingly, at the 24 month post-operative period, the HO cases had more, a higher range of motion at the operative level, not statistical, but pretty close compared to the non-HO cases. So it doesn't appear to be -- actually, the range of motion is higher with the incidence of HO. Next. And that is pretty much what I have for that.

CHAIRPERSON YASZEMSKI: Thank you, Mr. Cunningham. Thank you, Dr. McAfee. Dr. Kim?

DR. KIM: Just going back to the question of why there is a proportion of people that don't get

better. A proportion of them probably is coming from the facet joint. If that's the case, if you looked at that, and should reconsider looking at the facet joint more closely prior to having somebody undergo this procedure. Can one of the sponsors comment on that?

DR. MCAFEE: I'll give it a shot after much deliberation. Paul McAfee. With any interbody fusion device, you tend to unload the facets. You're increasing the disc space height. The digitized results of all the series both at 045 and L5-S1 did show statistically that the increase in disc space height was better for the SB Charite group versus the BAK.

In addition, from the immediate six week visit film to two years, it turns out that the maintenance of the height was also better in the SB Charite group. In other words, there was slightly more subsidence with the BAKs. So we thought the main thing, the main purpose of the Charite, was to unload the facets and I can start with slide 247 if you would like. Looking at the baboons, I know it's only a six month follow-up, but the facet joints were normal at

sacrifice. Secondly, you know --

DR. KIM: Sorry to interrupt.

DR. MCAFEE: Yes.

DR. KIM: I guess what I was trying to get at is if you had the opportunity to sub-stratify those patients that persisted with back pain and compared them to the Charite group that did not have back pain and you just looked at the facet joint, would there be a difference that you know of?

DR. MCAFEE: We didn't look at that, but in a way we're selecting out patients that have problems with the facet joints pre-operatively. Remember in our workup, if the patient has some element of mechanical back pain, we would tend to get posterior facet joint blocks and if that facet joint is a pain indicator, then they are selected out of the study.

CHAIRPERSON YASZEMSKI: Thanks, Dr. McAfee. Dr. Kim, does that answer your question?

DR. KIM: It does.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Naidu?

DR. NAIDU: I agree with the rest of the group. Pain is a subjective measure. I think the only reason that the Charite group probably had more pain is probably the patient population itself was a more active group. From the data presented, the Charite group had a significantly lower body mass index and, in general, more active. So I mean, it is a subjective measure, but those are the only two reasons I can think of attributing it to.

CHAIRPERSON YASZEMSKI: All right. Thank you, Dr. Naidu. Dr. Witten, the Panel's discussion on Aim 3 is that pain being a subjective measure, there really are no concerns that the Charite group had this percentage of people who still had continued pain, and that this reflects the general treatment of low back pain be it by nonsurgical or surgical methods other than disc replacement.

Have we adequately answered this question to FDA's satisfaction?

DR. WITTEN: Yes, thank you.

CHAIRPERSON YASZEMSKI: Thank you. Let's move on to Question 4. Within the Charite group, the

mean range of motion and flexion-extension at the treated level at three, six, 12 and 24 months was 4.9, 6.0, 7.0 and 7.4 degrees, respectively. Lateral bending and axial rotation range of motion were not reported in this investigation. Please, comment on the sponsor's claim that the Charite permits "near physiological segment movement with up to 15 degrees bending and flexion-extension and a similar degree of lateral bending and axial rotation to the natural disc." Dr. Kim?

DR. KIM: I think the sponsor used very good preclinical data to show that the disc does achieve near physiologic motion at the time of implantation, but the results of the clinical study clearly show that the range of motion changes and is variable being as low as 0 and as high as 22 degrees.

There is a table that the FDA put together to try to make a correlation between outcome and that range of motion, and there really isn't a statistically significant correlation, although there is a trend toward better results if you have 5 to 9 degrees range of motion.

Given that, it's hard to decide whether or not this is significant. In addition, this range of motion question is going to require long-term follow-up, because one of the advantages is potentially decreasing adjacent segment disease and we may not see that for five to 10 years. So I don't think that this study has the ability to claim that it maintains physiologic motion and that that motion is the key to success.

Going onto the second question as to whether or not there is an equal amount of lateral bending and axial rotation, they show that clearly in the preclinical studies, but not in the clinical study, because they only looked at flexion-extension. The design is symmetric though and if something is moving 7 degrees in the flexion-extension plane, I have no problem assuming that in the lateral bending plane, in the actual rotation, we'll get similar degrees of motion.

So I'm not too worried about the comment on the lateral bending and axial rotation, but I think the difficulty lies in the significance of the range

in motion with clinical outcome.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Kim. Dr. Naidu?

DR. NAIDU: The normal range of motion cited in the literature in the PMA provided at the L5-S1 is about 9 degrees of flexion, 5 degrees of extension with a fairly large standard deviation of plus or minus 5 degrees, and I certainly think that the sponsor's claim that 4.9 degrees is physiologic in flexion-extension plane is valid, although this validity isn't confined to the flexion-extension plane only. Obviously, rotation is questionable, at best, at this point. That's it.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Naidu. Dr. Kirkpatrick?

DR. KIRKPATRICK: No additional comment.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Kirkpatrick. Dr. Blumenstein?

DR. BLUMENSTEIN: Could I ask George Chu a question here?

CHAIRPERSON YASZEMSKI: Yes.

DR. BLUMENSTEIN: In the, I think you

called it, addendum, I didn't understand the two tables that were presented, the difference between the two tables.

DR. CHU: Which two, the range of motion, the histogram?

DR. BLUMENSTEIN: Yes.

DR. CHU: Or the 2 by --

DR. BLUMENSTEIN: Yes, the 2 by 8 tables. I just want to make sure I understand. I mean, I see that one of them is repeated in the question that we're addressing at this point.

DR. CHU: The histogram is based on the available data for the randomized Charite patients. It's about 175.

DR. BLUMENSTEIN: Yes.

DR. CHU: So from the histogram, it looks like the range of motion at 24 months post-op is equally distributed about 10 percent among the different range. And for the table in the Panel draft, it's a 2 by 8 table, it basically just tries to see the general association between the range of motion and the outcome at 24 months. So the general

association test, the P-value is not significant.

DR. BLUMENSTEIN: Yes. But there was a second table in your addendum.

DR. CHU: Which table?

DR. BLUMENSTEIN: I received an addendum.

DR. CHU: Okay. I don't have that one. Can you show me that one? Yes, the second table is, basically, the assessed output for the statistical test.

DR. BLUMENSTEIN: May I ask, do we have that table in the FDA? That was part of your presentation, wasn't it, Dr. Chu?

DR. CHU: No.

DR. BLUMENSTEIN: Do we have that table on a slide, that everybody could see it?

DR. CHU: Yes, actually the main point here, just looking at the general association test between this success outcome and the range of motion.

DR. BLUMENSTEIN: I mean, the titles of the two tables seemed the same to me and not the second smaller table underneath the big one, but the second page of tables.

DR. CHU: The second table is just collapsed the last four column of the bigger table into just one column.

DR. BLUMENSTEIN: Oh, okay. I'm sorry, sorry to cause that. Then I have no comment.

CHAIRPERSON YASZEMSKI: Okay. Thank you. Dr. Besser?

DR. BESSER: While the ranges reported were slightly less than have been reported in the literature for physiological changes, they are well within the range of normal and I guess only time will tell whether, in fact, implanting a device that gives this extra range of motion prevents adjacent segments from needing fusing and future surgery, etcetera.

CHAIRPERSON YASZEMSKI: Okay.

DR. BESSER: No other comments.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Besser. Ms. Maher?

MS. MAHER: No comment.

CHAIRPERSON YASZEMSKI: Ms. Luckner?

MS. LUCKNER: No comment.

CHAIRPERSON YASZEMSKI: Thank you. Dr.

Diaz?

DR. DIAZ: No comment.

CHAIRPERSON YASZEMSKI: Okay. Dr. Mabrey?

DR. MABREY: I have no comment.

CHAIRPERSON YASZEMSKI: Dr. Finnegan?

DR. FINNEGAN: No comment.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Witten, we have talked about the ranges of motion. We generally feel that they are within the range of normal, that the flexion-extension numbers are in the physiologic range and less so for the other modes of motion. The range of motion link to clinical improvement shows a trend, but has not been met. In general, the Panel doesn't have any concerns on this issue.

And have we answered and discussed it adequately?

DR. WITTEN: Yes.

CHAIRPERSON YASZEMSKI: Thank you. Let's move on to number 5. Do clinical data provide reasonable assurance of safety? Dr. Finnegan?

DR. FINNEGAN: Well, I would have to say

that if this device was going to do its main purpose over a short-term, that is a two to three year period, and then would basically be physiologically non-functioning, then the data does suggest that this is probably safe. Unfortunately, this device is designed for a much longer period of time and I do not think that there is data present at the present time to say that it is, in fact -- there is reasonable assurance that it is safe for the lifetime that it is predicted to be necessary for.

CHAIRPERSON YASZEMSKI: Okay. Thank you. I'm going to go around to Dr. Kim, but before I leave, based on that, Dr. Finnegan, I'm going to back to you with Question 7 and ask what you think. Dr. Kim?

DR. KIM: I would agree with that. I think the sponsors have done an excellent job in providing an honest assessment of their device, and it is absolutely clear that in the two year period that this device is safe, but, once again, I agree with Dr. Finnegan. This is a complex device. It's the first of its kind and designed to last for a long time, and we can't get at that question until we wait.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Kim. Dr. Naidu?

DR. NAIDU: I totally concur with Dr. Finnegan and Dr. Kim.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Naidu. Dr. Kirkpatrick?

DR. KIRKPATRICK: I concur and nothing further to add.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Kirkpatrick. Dr. Blumenstein?

DR. BLUMENSTEIN: I concur.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Besser?

DR. BESSER: I concur.

CHAIRPERSON YASZEMSKI: Thank you. Ms. Maher?

MS. MAHER: I would just urge the Panel to remember that we also have to look at least burdensome as we're figuring out how to evaluate the safety and effectiveness of this device.

CHAIRPERSON YASZEMSKI: Thank you, Ms. Maher. Ms. Luckner?

MS. LUCKNER: I concur with the earlier statements.

CHAIRPERSON YASZEMSKI: Thank you. As we come around to Dr. Diaz, Mr. Melkerson, if you have a comment, may I go to Dr. Diaz and then --

MR. MELKERSON: Actually, just a question.

CHAIRPERSON YASZEMSKI: Okay. Go ahead.

MR. MELKERSON: This is to the Chair himself. Being that Question 5 and 6 are related to safety and effectiveness, do you want to hear the other public speakers before you answer this question?

CHAIRPERSON YASZEMSKI: I think that we can probably hear them afterwards and then incorporate their thoughts when we get to voting if that would be okay. Dr. Witten, is that acceptable to you? Thank you. Thank you, Mr. Melkerson. Dr. Diaz?

DR. DIAZ: Nothing additional.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Mabrey?

DR. MABREY: Well, as has been pointed out by other Panel Members, I mean, this is a complex device. It's brand new and it's going to be

eventually implanted by a lot more than the original surgeons. So I think we're looking at two levels of safety. One is is it safe to implant, and I think over the first two years you have demonstrated that with your trained surgeons that it is safe to implant. And then the second question is is the device itself safe over a long period of time, and I don't think two years is long enough.

So I do have one question, and I would address this to Dr. Blumenthal or Dr. McAfee. At your training centers, the only analogous situation I can come up with is the experience with another company's foray into minimally invasive hip surgery and restricting access to that to those who have been trained at the company's facility.

One comment that I have heard from the trainers there is that there is a training of the trainers that goes on, and I guess my question is do the clinicians feel that with more experience, that your initial training of those people who will be implanting the device, does that become easier and have you learned to avoid some of the major problems

you encountered during the initial phase of this study?

DR. MCAFEE: I'll start, because one of the main concerns is neurologic problems, so there has been a great advance in instrumentation and, honestly, the key with any anterior interbody device is to keep it in the midline, so that newer instruments over the last two and half years happen to be called the centerline instruments, but they keep the implant in the midline and they prevent the surgeon from going into the lateral recess and causing a neurologic problem.

Secondly, if you can put up -- start with maybe slide 493. We did an analysis. We wanted to see what the effect of the training was. The training, you know, we had a perfect opportunity to do that, because we had a cohort of five cases from each group that were training cases, and we could compare how well the training patients did with the rest.

Well, the idea is whether there is a surgeon volume effect. Is the data good enough to show a surgeon volume effect, and this is from

Birkmeyer's New England Journal of Medicine and "JAMA," a lead article in December. And the key was there are 10 different operations that all show a surgeon volume effect, coronary artery bypass, grafts, aortic valve replacements, surgeons that did more and had a higher volume who had lower complications, but not a single spine procedure was in this group. Next slide, please.

So we looked at actually four areas. First, we looked at the 71 training cases versus the randomized cases. Then the next analysis was we looked at the four highest enrolling sites that all did more than 40 procedures versus the 11 remaining sites that didn't do as many cases. Now, the key is that all four groups fulfilled the FDA's success criterion of greater than 25 percent improvement in the Oswestry, as well as no neurologic progression, no return to the OR and no major complications. Next slide.

But there is a definite volume effect, and if you look at the training cases, which are on the left, the surgery time was larger in the person's

first five cases versus the enrolled. The length of stay was slightly longer for those patients, and the overall number of complications was higher as well. Next slide.

You know, we looked at all the parameters, but I'm just showing the ones that are significant. And then the high enrolling sites versus the low enrolling sites, the surgery time was much less for those sites that did more than 40 cases. The length of stay was less and the device failure incidence was lower. So in summary, surgeon volume really did have an effect. And then the last slide.

I think the key is to learn from the European experience, really almost memorize the IDE prospective randomized trial data. The key to avoiding complications are to identify a vascular access surgeon, go to company-sponsored courses to learn the specific instrumentation.

But what is even more important is what we haven't talked about and that is the model of the Scoliosis Research Society, which is something like the Spine Arthroplasty Society, what we'll hear from

the public comment period, is they are going to the forefront of continuous reassessment of results and having a surgeon group take some responsibility for setting the bench mark.

CHAIRPERSON YASZEMSKI: Thank you, Dr. McAfee. Dr. Witten, we have discussed the issue of safety and the consensus of the Panel is that over the study period in the short-term, this device is safe, and questions remain, of course, over the long period, because the data is not gathered yet and it's a new device without precedent.

Have we discussed this to the satisfaction of FDA?

DR. WITTEN: Yes, thanks.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Witten. We're going to move on to number 6. Do clinical data provide reasonable assurance of effectiveness? Dr. Diaz, can you lead off with this one?

DR. DIAZ: Yes. The question that we're being asked and I will read a little bit of the definition the FDA wants us to adhere to for

effectiveness. "A device is considered effective if, when used in a significant portion of a targeted population for the intended use and under the conditions of use, it provides significant results for that population."

To answer that question, I would look at the effect, clinical effect, on various aspects of the individual's life. When I operate on a patient, the question the patient asks me very frequently is will I get better? Will my pain get better? Will I be able to get back to work? And probably more important, will I be able to get back to play? Work in a back pain patient group is not always what they want to do, but play certainly is what they want to get back to do.

And as we have heard, the back problem, spine progressive degeneration is a dynamic problem. Coming from the Rust Belt in Detroit, when I talk to patients about spine surgery, I tell them that it is like dealing with rust. All patients in Detroit can understand rust. If you get it on the fender and you clean it, you patch it, you fix it, it will show up on

the door and a few years later, it will show up on the fender. So they can relate to the idea that perhaps this is not the only time that we'll see Dr. Diaz to take care of their problem.

So in regard to the effectiveness, does the device provide pain relief? Yes, it does. Perhaps not as well as it did for the BAK, but significantly equal. Does it restore function? We believe it does, based on the anatomical and on the mechanical presentations given. Does it allow patients to get back to their usual activities? The answer is yes. And to my personal liking, I was very pleased to see that patients could get back to very active function very quickly. Because within the week after surgery, they could be doing a lot of things that I keep my patients from doing when I fuse them.

If I fuse a patient, I really keep them sedentary for a long time. I don't like that. I like to be able to get people up and moving very quickly and I think this device provides for that opportunity. Do they return to work? Yes, perhaps they do. Maybe not as much as I would like them to see. But I don't

think we will ever be able to get back patients to get back to work as much as we would like them to do that.

And does it prevent adjacent level disease? I don't think that this single device will be the answer for preventing adjacent level disease, but I think it delays it, which I think is a very important achievement. So in my mind, I believe for the intended use that the device was proposed in the population as targeted with the possible applications as provided, it does fulfill the requirements of effectiveness under the FDA guidelines.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Diaz. Dr. Mabrey?

DR. MABREY: I fully concur with Dr. Diaz' comments.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Finnegan?

DR. FINNEGAN: I agree.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Kim?

DR. KIM: I agree as well.

CHAIRPERSON YASZEMSKI: Thank you. Dr.

Naidu?

DR. NAIDU: Same here.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Kirkpatrick?

DR. KIRKPATRICK: Well, we're not going to get a dissertation today. I think there are some concerns about effectiveness, but I think by the FDA's definition, I would agree with Dr. Diaz.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Blumenstein?

DR. BLUMENSTEIN: I believe the device has been shown to be not inferior to the standard control device that was used in the trial.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Besser?

DR. BESSER: I agree with almost everything Dr. Diaz said, other than I don't think we have any evidence to support that it will, in fact, delay adjacent segment disease. We hope, we'll see, nothing now.

CHAIRPERSON YASZEMSKI: Thank you. Ms. Maher?

MS. MAHER: Well, I would agree with Dr. Diaz. I would also remind the Panel that this product has been on the market since 1987 in Europe and there have been 7,000 cases or implantations. So when you talk about only having a two year follow-up, as we did on the previous question, I want you to remember that there actually is a much longer history outside the U.S. There is two years of good data from within the U.S.

CHAIRPERSON YASZEMSKI: Thank you. Ms. Luckner?

MS. LUCKNER: I concur with Dr. Diaz.

CHAIRPERSON YASZEMSKI: Thanks very much. Dr. Witten, the Panel feels that the device as presented is effective. Have we adequately discussed this?

DR. WITTEN: Yes.

CHAIRPERSON YASZEMSKI: Thank you. We're going to move on to number 7. Number 7, if you recommend approvability for this PMA, do you recommend a post-approval study? If so, please, discuss what types of end points would be useful for an updated

label and recommend the duration of such a study. Dr. Kirkpatrick, would you lead this one, please?

DR. KIRKPATRICK: I think he asked me because I already provided a list of suggestions. I would like to see mobility testing data for the complete reference, rather than just a two paragraph summary. And I did get a little bit more of it in the presentation today, but I would like to be able to review the data, and I think the FDA would like to be able to review that as well.

I think a little added study in the biomechanics lab of demonstrating that facet stresses or strains or some other element of a facet function is either unchanged or minimally changed after the insertion of the disc. I did not get that out of my read of the PMA and again, as I have repeatedly said, if you have that data and I missed it, please, tell me what page to find it on.

The third one is I still think that the wear data to 50 million cycles would be more appropriate. I did have concerns whether the curve on the wear data may have been accelerating over time.

Your curve on, I think it was, the weight of the specimen versus cycles was drawn as a curve going downward, which means it is accelerating as you get to the end of that 10 million cycles. I would like to know what it does in the next four decades of the 50 million cycle testing.

I think we need an acceptable rationale for not testing the response to submicron particles more extensively. Number 5 that is on the list, we can exclude, because I clarified that in my presentation and you clarified it in your presentation that the osteointegration studies are not relevant to the device you are presenting, so you can eliminate number five. However, I would like to know what the rationale is behind the long-term fixation of the device. Is it just the pegs or do you expect there to be some bone implant interface adherence?

6, I would like a clerical -- clarifying of the neurologic rating scale that you used, so I can understand how these statistics were applied to a qualitative physical exam. 7, I think that was handled by the FDA as far as stratifying the range of

motion, and it appears that outcome is not significantly different, although there were trends. So 7, I'll leave it up to the Panel whether we think we need to go further with that.

8, indication groups, especially the ones that did have known facet changes at the implantation. I would like to know if stratifying those out would make a difference in either your BAK group or your charity group. I would suggest again based upon the literature as well as my presentation that the concept is if we're preserving motion, we need to demonstrate that. And if people lose motion, I would like to know if that resulted in a difference in their other measures of effectiveness, such as the VAS, the ODI and that sort of thing.

So number 9 would say include those 0 to 5 degrees as failures and see if that correlates to clinical failure. And also, if you called them failures, what would happen to your statistics on the study success. 11 you can eliminate based upon the discussion of HO and the presentation you did in answer to one of our questions. I'm sorry, that's

number 10. Number 11 gets back to the facet issue. Can you do axial imaging at 24 months and look at the comparison between your pre-op and your axial imaging at 24 months and tell us whether there are facet changes.

Number 12, adjacent segment degeneration, I think, should be looked at. We obviously have the x-rays stored on computer data and that should be something that could be doable. And then 13 is perhaps the most difficult and that is, I think, the follow-up should be extended to five years to get to some semblance of a number of where we would see adjacent segment, so that we can back up the rationale that we are preserving the adjacent segment from the standpoint of the philosophy of the disc replacement. Thank you.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Kirkpatrick. May I ask before we move to Dr. Blumenstein, may I ask that among the suggestions you made there are some that seem to be answerable by relooking at the existing preclinical and clinical data and perhaps one or more that may require further

study data after approval. Would you care to comment on? It would seem to me that number 13 might, of course, require more study data clinically, and that maybe number 3 would require in-vitro data, but that the others perhaps could be answered by looking at the existing data. Would that be accurate?

DR. KIRKPATRICK: I agree that number 3 and 13 definitely would require additional work. I think the remaining things, as I recall, are either a discussion of their existing data or an expansion on analysis of their existing data.

CHAIRPERSON YASZEMSKI: Okay. Thank you. And then when we have the sponsor summary, I'll ask the sponsors to comment on these. Dr. Blumenstein?

DR. WITTEN: Can I just mention one thing?

CHAIRPERSON YASZEMSKI: Dr. Witten?

DR. WITTEN: Yes, I'll just mention one thing which is that when you get to the vote, you'll have to clarify for us for each of these recommendations whether or not these are things that you would expect to see pre-approval or post-approval, because if it is new data, for example, then that's

not a condition of approval recommendation. It's a recommendation to put the PMA in approvable form. So I just want a clarification of when you think we need this information.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Blumenstein?

DR. BLUMENSTEIN: My main concern is the long-term follow-up and I think that has been addressed.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Besser?

DR. BESSER: I concur.

CHAIRPERSON YASZEMSKI: Thank you. Ms. Maher?

MS. MAHER: I'm going to sound a little bit like a broken record like I always do and again remind everybody that we do have data back to 1987. We do have a significant patient population outside the United States, and so maybe a post-approval study following the other patients in the study now for longer would be appropriate, but some of the rest of the data may not be necessary.

CHAIRPERSON YASZEMSKI: Thank you, Ms. Maher. Ms. Luckner?

MS. LUCKNER: Nothing else to add.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Diaz?

DR. DIAZ: I would like to agree with Ms. Maher, because I think there is significant clinical data available in the world literature that indicates the longevity and the effectiveness of this device in the treatment of discogenic disease. The available literature does not answer all the questions that Dr. Kirkpatrick mentioned, but those could be answered on an ongoing type analysis, rather than trying to redesign a new study. I believe that there is sufficient information already available to answer many of these things. And going back to square one, I don't think is necessary.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Diaz. Dr. Mabrey?

DR. MABREY: Yes, I concur with the plan to go ahead with looking at those individuals that are currently under study and also perhaps extend some of

these investigations to those patients who are available in Europe. And particularly, I'm interesting in looking at the possibility of osteolysis at four and five years out. I think you have the potential to continue to look at radiographic data on the original 200 patients here and it's no additional great buren and it would be nice to see data from European studies indicating that there is no osteolysis.

CHAIRPERSON YASZEMSKI: Thank you.

MS. MAHER: Can I ask for a clarification for that? Were you talking about a post-approval type of look at it for that data?

DR. MABREY: Okay. This is my first Panel meeting and so we've been talking about post-approval.

CHAIRPERSON YASZEMSKI: And may I interrupt?

DR. MABREY: And PMAs and PDPs.

CHAIRPERSON YASZEMSKI: May I interrupt, Dr. Mabrey? What I'll suggest is all of these things that we recommend to FDA, we will need to recommend whether they are things that need to be done before

the approval, and thus defer the approval, vote that this is non-approvable or whether we would agree that this is an approvable application, and in addition as terms of the approval, we would like them to do further work and follow the patients.

DR. MABREY: Okay.

CHAIRPERSON YASZEMSKI: And we will just have to make that distinction when we come to voting.

DR. MABREY: Okay.

CHAIRPERSON YASZEMSKI: And thank you, Ms. Maher, for bringing that clarification up.

DR. MABREY: Okay.

CHAIRPERSON YASZEMSKI: Dr. Finnegan?

DR. FINNEGAN: Now, you've changed my train of thought. I was getting all my thoughts together. One of the problems with looking over the data here is that unfortunately of the 205 or so patients that had the Charite implants, a number of them have actually not reached two years yet. And I think that we have already all pretty much agreed that two years is probably not a safe length of time to follow these patients. So I do think that there needs

to be a long-term follow-up. I definitely agree with Dr. Kirkpatrick on that.

And I know that we are looking at the end plate with the spikes. If there is a change to a coated end plate, then that's obviously going to drastically change the biomechanics on the polyethylene and understanding that the company feels the polyethylene is cross-linked to some degree, it is obviously a random cross-linking. So I think all of those are things that need to be considered.

And as well, I do think that the company needs to be at least -- or the sponsor needs to be at least familiar with neurological response to chronic inflammation and be comfortable that that is not going to be a long-term problem. And I certainly agree with Dr. Kirkpatrick on adjacent segments. I think that some kind of study needs to be done on that.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Finnegan. Dr. Kim?

DR. KIM: I think if we only looked at the U.S. clinical trial data, I would be nervous with just two year results. But I agree with Ms. Maher that we

have the -- we are fortunate that we have a pretty extensive European experience of 7,000 patients. I think with the excellent U.S. clinical data of two years combined with the European data, it's a very promising device. And based on that, I feel like this device is safe and effective. But there are a lot of questions that remain and I think looking at the existing patients over the long-term, maybe over five or even 10 years, is a reasonable condition.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Kim. Dr. Naidu?

DR. NAIDU: You know, I would like to listen to the second open public hearings prior to commenting on this.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Naidu. Dr. Blumenstein?

DR. BLUMENSTEIN: I just get so enamored of the case series data that are likely to come out of Europe, other places like that. There's nothing more valuable than the data that have been invested into this clinical trial in a comparative way and the potential for that data to come out with an unbiased

comparison of the results as opposed to the uncontrolled convenient samples that are often published in the literature.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Blumenstein. Dr. Witten, as you've heard, we've had a more extensive discussion on this question. And I would like to review it and then to say that when we get around as a Panel to making a recommendation to vote on, we'll consider which of these suggestions might be conditions of approval and which we would want to be done after the approval vote.

We've talked about adding mobility testing data and in-vitro study of the facets, wear data to 50 million cycles, test response to submicron particles, to consider using data from the existing European studies and we have heard pros and cons about that from several Members of the Panel, osteolysis at four to five years. Many of the Panel Members thought that going out about five years for several of these end points would be appropriate. Dr. Finnegan mentioned the effects of inflammation on the neurologic tissues by chronic inflammation and Dr. Kirkpatrick about

adjacent segment.

Have we discussed this to your satisfaction?

DR. WITTEN: Yes, thank you.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Witten. That's going to conclude the discussion on the specific questions that the FDA has posed of us. We are going to move now to the second open public hearing. There are three people who wish to present to the Panel, at this point. These are Dr. Hochschuler, Dr. Van Ooij and Ms. Adams. Dr. Hochschuler will be first with a time of five minutes.

DR. HOCHSCHULER: I am Steve Hochschuler. I am a spine surgeon. I am Chairman of the Texas Back Institute, and today I am representing the Spine Arthroplasty Society in my presentation. First, I want to thank you for allowing me to come to the podium today. Secondly, despite having been a spine surgeon for about 28 years now, this is the first time I have been at an FDA Panel meeting. And I have to say as a citizen, I'm very impressed.

I have my own bias as to whether this

should be approved or not approved, but I must say it's almost like a TV show. I'm not sure how you are going to vote an I'm really intrigued. I think it's a wonderful process and I don't want to be supercilious, but I would like to compliment you and thank you.

Having said that, I feel as a surgeon that it is our primary responsibility to care for the patient. And with that, I have been charged along with the rest of the Spine Arthroplasty Society to put together a position statement on some of the items you discussed earlier in terms of safety, how do we protect our patients, how do we get better outcomes. With this in mind, despite the fact I usually don't like to read directly, I would like to read this statement to you, since I've got limited time, and then go from there.

"Spinal Arthroplasty Society Educational Objectives." "The board of directors of the Spinal Arthroplasty Society has decided to take a unique step in establishing education and training goals for spine surgeons interested in new arthroplasty technologies.

The ultimate goals of this effort are to improve clinical outcomes and reduce technical complications in patients undergoing surgical treatment utilizing these new technologies by providing a strong educational core of knowledge for surgeons.

Traditionally, rigorous patient selection criteria have been required for inclusion in FDA trials. Additionally, investigators are specifically selected by the companies who design the studies based on their reputations and experience. However, when devices are approved for marketing to surgeons in the community, there has been no formal standardization for training these physicians in your use.

Training historically has run the gamut from a product introduction by a company representative sitting across the surgeon's desk to a brief course with a lecture in the morning followed by a crowded hands-on training using saw bones models to a comprehensive training program incorporating surgeon education for diagnostic workup, patient selection criteria, management of complications and ample time in a cadaver lab developing familiarity with the

instrumentation and surgical exposure.

Ideally, comprehensive formal training should be followed by proctorship at the training surgeon's hospital for its first case or cases by a teaching surgeon with a high level of expertise. This would serve to close the loop of the surgical proctoring process. Obviously, this level of training is expensive and time consuming, but it offers significant long-term advantages for patients, surgeons, industry and hospitals.

For patients, technical complications may be reduced and outcomes improved. For surgeons, their patients' clinical results may be more gratifying and litigation avoided. It is important for industry so that their devices can produce the best results possible. A product may be unjustly criticized for high complications and poor outcomes if surgeons have poor technical skills or employ too broad patient selection criteria.

Hospitals also have a vested interest in the training of surgeons. The hospital's mission like that of the surgeon is to ensure the maximum benefit

to the patient. While the technology of spinal surgery is steadily advancing, clinical safety and outcomes cannot be expected to improve unless the appropriate patient selection and optimal surgical techniques are taught. SAS is prepared to take a pro-active role in addressing surgeon education. A program of organized processes for training surgeons on new devices will incorporate didactic lectures, hands-on training and proctorships.

The role of the Society will be to develop guidelines for content of educational programs, identify training centers with adequate facilities and staffing for consistent quality training and organize access to specialists with experience with the specific devices to provide proctorships. Due to liability issues, certification can verify that the surgeon has completed training, but not that he or she has adequate skills. A document will be issued only to verify course attendance and subsequent proctorship.

The fact that training is provided through a Society and performed in an organized, standardized

format across the country and hopefully the world should enhance the overall quality of care for our patients. All parties concerned recognize the importance of having surgeons properly trained when introducing new technologies. With the rapid developments in spinal implants, SAS has an unprecedented and unique opportunity to play an important role in improving patient care, optimizing the application of new technologies and furthering the development of new implants by increasing the safety of new product introduction and adoption of these standardized training programs. Thank you.

CHAIRPERSON YASZEMSKI: Thank you very much, Dr. Hochschuler. Dr. Van Ooij? Dr. Van Ooij is scheduled for 10 minutes.

DR. VAN OOIJ: Thank you, Mr. Chairman. I am very honored to be here and to speak to you. I am an orthopedic surgeon, spine surgeon in Maastricht, the Netherlands for 24 years and I'm a member of the SRS, the Scoliosis Research Society and the European Spine Society. I will talk about the other side of the Charite disc prosthesis, so I talk about

complications that I see in a cohort of about 500 patients that were operated in a neighboring hospital, and another 500 has been operated by countrymen of me in Munich in Germany. So this is a cohort of about 50 patients. They are already a little bit more, but 49 were evaluated.

So if we could have the next slide? Where do I have to press? All right. Oh, yes. So in eight years, I saw 49 patients, 28 women, 28 men, and with a young age, of course, because that is in the indication and there were operations performed as early as in 1989. 20 in the period of the first five years. Then 24 in the second five years. And seven in the last four or five years. The next one. So most patients were operated in one level, of course, let me see, some in two levels. Two levels in 10 patients and three levels in two patients. There were a lot of previous operations done, but most had no operations before this.

Next one, please. So there were early complications, subluxation of a prosthesis and removal after a few days, some hematoma. In men, there is a

risk of retrograde ejaculation and erectile dysfunction. If you ask the male people, they sometimes have a dysfunction without retrograde ejaculation. There is one patient that had a urethra lesion with a large urinoma.

Next slide. This is the patient with a stint in place and here a large urinoma from a urethra lesion. This was punctured several times and there was pseudomonas involved and probably she has a low grade infect now in one of these prostheses, so this is really a problem. She is in a bed. All these patients have really terrible leg and back pain. They have VAS scores about 8 to 9 mostly.

Next patient -- sorry, next slide, please. The leg complications are migration. These mainly are prosthesis uncoated, so there were anterior migration, posterior migration, even the main cause of complaints after a year or a lot of them remainder complaints is disc degeneration at the other levels. In 13 patients it was -- this was not obvious before the operation on plain x-rays and discography, but there were the other ones had more or less degenerated disc, but without

pain on discography. Facet joint degeneration is a big problem, I think. In the late situation, we saw it 16 times.

Next, please. This is the patient with anterior migration. You can see that in 10 years this is 1991 and this is 2001, this was sliding anteriorly and pressed on the big vessels and we had to remove it and luckily we were successful in doing it without lesions of the vessels, but this has been reported and undoubtedly many times if you hear the conferences and there was a fusion done, and this is the only one of the re-operations that the patient is satisfied.

Next, please. There is a big issue, I think, in facet joints arthrosis because it's probably the biomechanical behavior of the prosthesis. I'm very worried about axial rotation that is increased in the prosthesis compared to the normal disc, so you get a big load, I think, on the facet joints. Probably also when it is more anterior located, you must put the prosthesis really posterior to get some kind of motion and these are the facet joints that are really very hypertrophic and are triadic.

Next, please. Subsidence is a big issue in this series. In 17 of these patients the prosthesis was obviously too small. There was some subluxation of the core. One big issue that was not spoken about today is breakage of the metal wire. If you look good at the x-rays, you can see the breakage and the flattening of the polyethylene core and probably also some wear debris. Hyperlordosis should be an issue if you distract the segments, you get easily in hyperlordosis and asymmetrical loading of your facet joints. And I think that the patient that Mr. McAfee demonstrated had, in my mind, really aware of the prosthesis.

Next case. So this is the patient, a patient with a subsidence that is seen many times and it can go all the way posteriorly or anteriorly or sideways and this was fused, but the patient keeps on complaining. Probably, I think, that the posterior stabilization and fusion is not the answer, because most people keep complaining because of micro motion in the prosthesis, despite the posterior fusion.

Next case. This is a patient that really

bothers me with degenerative scoliosis developing after seven years. Some patients have multiple degeneration above the discs in the Charite and they get degenerative scoliosis above or including the prosthesis. I think mainly from axial rotation problems or because of the forces that go through the spine that are blocked by the prosthesis. You can say that these are stones in the shoe. If you have a stone in the shoe, you get pain in all your leg and I doubt that this will mimic the natural motion so intimately that you prevent really motion degeneration.

Next. This is a case with a broken ring and a flattening of the core at the posterior side, but this is hard to see on this slide, but you should observe that and look very carefully at it. Next slide. And this is the patient with the wear, which has already been shown by Mr. McAfee, of one of my patients with holes in the bone and scoliosis and the flattening of the core. That is indicative of wear, I think.

Next, please. We did 21 or 21 additional

operations were done. We did 11 of them. 10 were already performed before. Most had posterior fusions, but most patients without much benefit, so I really would stress that it is not a good solution for the problem. Probably this prosthesis will be a pain source afterwards.

Next, please. Many patients in this series, I think, had back surgery, back placement and back sizing, but also in the boot placement and boot sizing that were problems and it seems from this very experienced surgeon that it's not really -- that it is really difficult to do good surgery like this disc prosthesis placement. And I think that it is not behaving as a normal disc. The center of rotation has been talked about. If you really put it posteriorly, it could be well, but then you have the risk of going over the edge and getting a rim fracture. Two patients in my series have a posterior placement. Nobody talks about shock absorption, but Lueck has shown that there is no shock absorption and that the normal forces that go down the disc are not going like normally when you have a disc prosthesis in.

Next, please. And the rotation, I already talked about. So a lot of problems will be seen, I think. Also, in the United States if you wait long enough, two years, in my mind, is far too short to see those problems. Wear will be a big issue in the future. I'm convinced of that, because the forces on the lower spine are very, very high. Revision is dangerous and sometimes impossible and I go to series from surgeons and they say that they couldn't reach the prosthesis, because the vessels were too adherent and the claim of preventing adjacent disc degeneration is not substantiated.

Next, please. So that was the end. I want to report an investigation that was presented yesterday in Porto, where I was yesterday, and it was from the Charite group. They sell from East Berlin of Berlin now where it was originated. They did a 17 year follow-up of 53 patients out of a group of 71 patients. And 60 percent of the segments were fused, really fused, didn't move anything and didn't move at all and most had already bone in it and were really fused. But they were the better one and the patients

that still fused still had some motion in it were the bed one, and I think you should look also to that series. That is the most, the longest experience to date, 17 years, and the conclusion of Mr. Brooks here was that there was no indication for a disc prosthesis in the disc disease. Thank you to showing it to you.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Van Ooij. May I ask before you leave, we have asked all the speakers to state for the transcriptionist for our record, the Conflict of Interest statement, the three questions and, please, your industry relations, any financial aspects that you might have and the source of funding for your trip here.

DR. VAN OOIJ: Yes, thank you. I forgot to name that. I have no personal financial relationships with any industry. Medtronic Company brought me here, provided for the travel. And further, I have no relationship whatsoever.

CHAIRPERSON YASZEMSKI: All right. Thank you very much, sir. The third speaker will be Ms. Pam Adams from OSMA. And, Ms. Adams, you are scheduled for five minutes.

MS. ADAMS: Good afternoon. My name is Pamela Adams and I speak here today representing the Orthopedic Surgical Manufacturers Association or OSMA. OSMA, a trade association, with over 30 member companies welcomes this opportunity to provide general comments at today's Panel meeting. OSMA's comments should not be taken as an endorsement of the product being discussed today. We ask instead that our comments be considered during today's Panel deliberations. These comments represent the careful compilation of our member companies' views.

I would like, first, to provide a brief introduction and background. OSMA was formed over 45 years ago and has worked cooperatively with FDA and the American Academy of Orthopedic Surgeons, the American Society of Testing and Materials and other professional medical societies and standards development bodies. This collaboration has helped to ensure that orthopedic medical products are safe, of uniform high quality and supplied in quantities sufficient to meet national needs.

OSMA membership currently includes

companies who produce over 85 percent of all orthopedic implants intended for clinical use in the United States. OSMA has a strong and vested interest in ensuring the ongoing availability of safe and effective medical devices. The deliberations of the Panel today and the Panel's recommendations to the FDA will have a direct bearing on the availability of new products.

We make these comments to remind the Panel of the regulatory burden that must be met today. We urge the Panel to focus its deliberations on the product safety and effectiveness based on the data provided. As regards reasonable assurance of safety and effectiveness, the FDA is responsible for protecting the American public from drugs, devices, food and cosmetics that are either adulterated or are unsafe or ineffective. However, FDA has another role to foster innovation.

The Orthopedic Devices Branch is fortunate to have available a staff of qualified reviewers, including a Board certified orthopedic surgeon to evaluate the types of applications brought before this

Panel. The role of this Panel is also very important to the analysis of the data in the manufacturer's application and to determine the availability of new and innovative products in the U.S. marketplace.

Those of you on the Panel have been selected based on your expertise and training. You also bring the view of practicing clinicians who treat patients with commercially available products. OSMA is aware that you have received training from FDA on the law and the regulation and I do not intend to repeat that information today. We do, however, want to emphasize two points that may have a bearing on today's deliberations.

Firstly, reasonable assurance of safety and effectiveness and secondly valid scientific evidence. As regards the first point, there is a reasonable assurance that a device is safe when it can be determined that the probable benefits outweigh the probable risks. Some important caveats associated with this over simplified statement include valid scientific evidence and proper labeling and that safety data may be generated in the lab, in animals or

in humans.

There is a reasonable assurance that a device is effective when it provides a clinically significant result. Again, labeling and valid scientific evidence play important roles in this determination. The regulation and the law clearly state that the standard to be met is a reasonable assurance of safety and effectiveness. Reasonable is defined as moderate, fair and inexpensive.

As regards the second point, valid scientific evidence, the regulation states that well-controlled investigations shall be the principal means to generate the data used in the effectiveness determination. The following principles are cited in the regulation as being recognized by the scientific community as essentials in a well-controlled investigation, a study protocol, a method of selecting subjects, a method of observation and recording results and comparison of results with a control.

In conclusion, the Panel has an important job today. You must listen to the data presented by the sponsor, evaluate the FDA presentations and make

a recommendation about the approvability of the sponsor's application. We speak for many applicants when we ask for your careful consideration. Please, keep in mind that the standard is a reasonable assurance balancing the benefits with the risks. The regulatory standard is not proof beyond a shadow of a doubt.

When considering making recommendations for further studies, remember that FDA takes these recommendations seriously, often as a consensus of the Panel of a whole and such recommendations may delay the introduction of a useful product or result in burdensome and expensive additional data collection. Therefore, you play an important role in reducing the burden of bringing new products, products that you and your colleagues use in treating patients to the market.

Please, be thoughtful in weighing the evidence. Remember that the standard is a reasonable assurance of safety and effectiveness and that there is a legally broad range of valid scientific evidence to support that determination. On behalf of OSMA, I

would like to thank the FDA and the Panel for the opportunity to speak today. Our association trusts that its comments are taken in the spirit offered, which is to help the FDA decide whether to make a new product available for use in the U.S. marketplace. Thank you.

CHAIRPERSON YASZEMSKI: Thanks very much, Ms. Adams. We're going to break now and then proceed with the summation from both the FDA and the sponsors. It's about 3:51. Let's come back and start at 10 minutes past 4, 4:10.

(Whereupon, at 3:52 p.m. a recess until 4:14 p.m.)

CHAIRPERSON YASZEMSKI: Can I ask everybody to take your seats, please? We're going to get started. We're going to ask, at this time, for the FDA and sponsor summations and then we're going to proceed to the voting. And I will first ask FDA. Dr. Witten, would FDA like to add anything, and I would specifically like to ask you to comment on the rules regarding conditions and their effect on the vote?

DR. WITTEN: I'm sorry. You're asking me

to clarify the rules on post-approval commissions and the vote?

CHAIRPERSON YASZEMSKI: Yes.

DR. WITTEN: Yes. Okay. Thank you for asking me. I will just amplify what I said before the break, which is that if there is a condition that is asking for new data or a new analysis, if the request is for that new data or new analysis to be provided to us after approval to answer some focused, specific question or a series of questions then that, you know, would be what we would consider a condition of approval.

If what you are requesting or what the Panel recommends is a condition where you're asking for new data or a new analysis, that you want it provided to us for our review prior to approval, then what that is to us in terms of the vote and the recommendation is a non-approvable recommendation, and what you're providing us with are the recommendations of how to put the application in approvable form.

So that's why I had said prior to the break when Dr. Kirkpatrick was going through his list

that we need to understand whether, for each of these that you may agree on, the Panel is recommending that we have the data in hand to review prior to approval, which would mean you're really making a non-approvable recommendation with a recommendation of how to put it in approvable form versus telling us you would like us to look at a specific, focused question and get some data around those questions after approval, which would be a post-approval condition.

And let me just clarify one additional thing, in case the question should come up, which is, you know, under what would we take such an application back to Panel and it would be our option of whether or not we felt that we had, you know, additional issues we wanted to ask the Panel about.

CHAIRPERSON YASZEMSKI: Okay. Thank you, Dr. Witten. I would like to ask if the sponsor has any summation comments to make, Mr. Christianson?

MR. CHRISTIANSON: Thank you, Dr. Yaszemski. Jack, could I have the first slide, please? We heard some discussion today that several of the Panel Members expressed concerns that we don't

know what the long-term safety profile of the Charite Artificial Disc is, and I would just like to remind the Panel that we did conduct a 24 month randomized prospective study per the FDA guidance document on spinal devices, and that has been used for all previous spinal devices and, indeed, all previous orthopedic devices have been approved based on a two year follow-up study.

In addition, several people did remind the Panel during the course of the discussion that there are, indeed, long-term follow-up data from Europe. There is a very good case series from Dr. LeMaire and a six year case series from Dr. David, and case series do meet the FDA definition of valid scientific evidence, so the Panel can, indeed, take those series into consideration that are available in the literature.

And we also heard some discussion about a post-approval study. Indeed, that's the place that's appropriate and accepted to develop the longer term data in a post-approval study after the device has been approved and the company certainly is amenable to

conducting a five year follow-up study as Dr. Kirkpatrick recommended in his document. Next slide, please.

Sorry, Dr. Kirkpatrick, we didn't know what to title this slide when we put it together, but reviewing your list of recommendations that you passed around, we agree that most of the recommendations on your list are reasonable and we will certainly discuss them with FDA and put the answers together that we can with our existing data.

However, I must comment on your recommendation for 50 million cycle testing. The company believes that that is an excessive requirement for testing. For example, for metal on a polyethylene device, that will take at least 15 weeks to conduct, probably longer, and that would potentially delay the approval of the device for a significant period of time.

The testing that we have submitted, the 10 million cycle testing that is already in our PMA, does represent 80 years of significant bends while listing a 20 kilogram weight, so we do think that we provided

adequate long-term mechanical test data. And so if that's an issue that we'll need to negotiate with FDA, I wanted to get that statement on the record. Last slide, please, Jack.

And I'll close with the same statements that I made when we closed our Panel presentation. We're presenting a device to you that's got a long clinical history of use in Europe, fully biomechanically characterized, robust, valid, scientific evidence that the device is safe and effective and we, again, ask the Panel to recommend that this device be approved for use in patients in the U.S.

CHAIRPERSON YASZEMSKI: Thank you, Mr. Christianson. Ms. Scudiero will now read the three possible Panel recommendation options for pre-market approval applications. Ms. Scudiero?

MS. SCUDIERO: These were in the meeting handouts. They are entitled "Panel Recommendation Options for Pre-Market Approval Applications." The medical device amendments to the Federal Food, Drug and Cosmetic Act, as amended by the State Medical

Devices Act of 1999, allows the Food and Drug Administration to obtain a recommendation from an expert Advisory Panel on designated medical device pre-market approval applications that are filed with the Agency.

The PMA must stand on its own merits and your recommendation must be supported by the safety and effectiveness data in the application or by applicable publicly available information. Safety is defined in the Act as "Reasonable assurance based on valid, scientific evidence that the probable benefits of health under the conditions on intended use outweigh any probable risk." Effectiveness is defined as "A reasonable assurance that in a significant portion of the population, the use of the device for its intended uses and conditions of use, when labeled, will provide clinically significant results."

Your recommendation options for the vote are as follows: (1) Approval, if there are no conditions attached. (2) Approvable with conditions. The Panel may recommend that the PMA be found approvable subject to specified conditions, such as

physician or patient education, labeling changes or further analysis of existing data. Prior to voting, all the conditions should be discussed by the Panel. (3) Non-approvable. The Panel may recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or if a reasonable assurance has not been given that the device is effective under the conditions of use prescribed, recommended or suggested in the proposed labeling.

Following the voting, the Chair will ask each Panel Member to present a brief statement outlining the reasons for their vote, and this became effective June 14, 1999.

CHAIRPERSON YASZEMSKI: Thanks, Ms. Scudiero. I would like to make a few comments before we ask for a motion. First, with respect to voting, the eight Panel Members will vote. Our consumer representative, our patient representative, that is, and our industry representative will not vote. I will only vote in the event of a tie.

Regarding the motion, the sequence that

can happen is we have a motion, a second for the motion, discussion and a vote. If that sequence occurs and the vote is for the motion, then we're finished. If the vote is either against the motion or if there is not a second for the motion, then we'll ask for another motion.

With that in mind, the lead reviewer for this was Dr. Kirkpatrick and I'm going to ask him to make a motion. Dr. Kirkpatrick?

DR. KIRKPATRICK: To borrow from Dr. Hochschuler, I felt a little bit like Simon at the beginning of my discussion and I hope that we can understand each other as far as where we're coming from.

A recent editorial in the NAS Journal indicated that I am part of an increasing or a decreasing majority of spine surgeons. The editorial was discussing the fact that there is a number of spine surgeons who will do things on patients that they would never consider for themselves. This reminds me of what the FDA's purpose is and that is, first, protecting the public. As such, some of my

comments and my motion will be directed towards that.

The second rationale I have for my motion is being a bone setter from Alabama means I have adopted certain habits and customs. One of those customs happens to be watching NASCAR. As many of you know, NASCAR is a race around a track that generally runs between 250 and 500 miles or sometimes, on one occasion a year, 600 miles in length. The design of the tires is specific for the track and the type of racing done and is not expected to exceed the length of time that the gas tank is full. In other words, when you run out of gas, your tires are going to need to be replaced.

I think we need to think of the same design rationale as far as a disc replacement. We need to make sure that we are assured of both the safety and effectiveness for the intended length of use. Now, I know that's an onerous thing if we're talking 50 years, and I don't propose that at all. However, I do think that a two year follow-up, in all due respect to Mr. Christianson and his colleagues as far as discussion of precedent, this is an

unprecedented device and I don't think two years is adequate.

As such, I would recommend or, excuse me, I move that we call this PMA not approvable and that would be my motion.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Kirkpatrick. Do we have a second for that motion? Dr. Finnegan?

DR. FINNEGAN: Yes.

CHAIRPERSON YASZEMSKI: We have a second. Discussion?

MS. MAHER: Well, can I lead off the discussion?

CHAIRPERSON YASZEMSKI: Ms. Maher?

MS. MAHER: As a non-voting member, I can lead this off pretty well. I have to take exception, Dr. Kirkpatrick, to what you're saying, because spinal cages were approved initially with two years follow-up and they also, at the time they came on board, were a first of their kind. And if I actually recall correctly, they even had much less animal data and other data than we have on this product, which, again,

as Mr. Christianson put up on the slide, we do have data since 1987 showing that it has been used safely and effectively in Europe for many years.

So I have some deep concerns that if you tell a company they can't launch something for five years after they have started developing it, we're going to put a stop to new product innovation in the medical device or the orthopedic world. And I'm wondering why you feel that that's more appropriate than having a post-market approval study, a post-approval study where you can follow the devices and look at what's happening.

You have got a cohort of patients that already has two years. You can have three more years and you will have the five year data, in which case you'll have the other patients. It will be available for sale. It will be being sold and being used, but I think they have provided adequate evidence that it would be safe and effective, so I have to disagree with you.

CHAIRPERSON YASZEMSKI: Thank you, Ms. Maher. Dr. Diaz?

DR. DIAZ: I also would like to disagree with Dr. Kirkpatrick's statement, because I think we are making a statement that flies against a very large body of evidence. There has been 17 years of use of these devices throughout the world. We are the only country in the industrialized world that does not approve its use yet.

To expect to compare a mechanical device like a tire that is running on a NASCAR track to the function of the human body is counter-intuitive. If the good Lord had designed our gas tank to allow our functioning parts to last the exact same time, we would die in perfect physical condition and that is not a reality. We run out of gas at about the same time when all our parts have fallen apart.

So I think that the motion is not what I would endorse. I disagree entirely that there is not sufficient evidence to indicate its use. It can be done, I believe, with some continuing monitoring and perhaps longitudinal studies to answer some of the questions, but I believe the experience in France and Germany have already shown the various things that

will happen.

And if we were to say that ultimately, all the device does is delay the occurrence of a natural fusion, as was presented already in a relatively small comment made at the end of the presentation of Dr. Ooij, I believe is his name, from the Netherlands, Ooij, Dr. Ooij. Even if we gain 10 years of extension on the function of a disc, I think we have provided a sufficient opportunity for the individual not to have a fusion that perhaps would occur spontaneously or that may be induced by the introduction of mechanical devices, which we have already approved. So I think that the decision not to allow it is incorrect.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Diaz. Dr. Mabrey?

DR. MABREY: Well, having trained in North Carolina at the same time that Dr. Kirkpatrick did at Duke, I can certainly share his observations of NASCAR as a NASCAR dad, but I do see an opportunity here to provide additional information after approval. The developers of the device and the clinicians have demonstrated that they have a very good cohort of

patients. They have gone out of their way to document every complication that has occurred, and I think we have the opportunity to follow that data after approval and look at that data both at four and five years out.

John, I agree. I think, you know, maybe 50 million cycles isn't an unreasonable number of cycles to go through, but, again, that type of data could be ongoing rather than pre-approval. So I would argue for approval with certain conditions.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Mabrey. Dr. Finnegan, you were the seconder.

DR. FINNEGAN: Yes, I'm not sure that some of the Panel Members and maybe Ms. Maher will understand that just because we say not approval doesn't mean this is going into the closet. Not approval means that, at the present time, the Panel is not comfortable with all of the data. It does not mean it has to come back to Panel. It just means that certain things have to be done before the FDA makes a decision and that it's quite possible, given the discussion today, that it will not need to come back

to Panel. But if there are some things that we really feel strongly need to be done before the FDA gives it approval, then by regulation we cannot approve it.

Now, one of the biggest concerns is that of those two year follow-up patients, they haven't all reached two year follow-up and, in fact, if I read the numbers correctly, in fact, the latest patient to get this is probably less than 10 months ago. So if you take all of those patients out to two years, you're actually going to have some three and a half or four year data, which will be much more helpful than doing it now when some of the patients haven't reached their two year mark.

CHAIRPERSON YASZEMSKI: Thanks, Dr. Finnegan. Dr. Kim?

DR. KIM: This is such a difficult topic to vote on because of the complexity of the disease and the fact that this is a brand new product, but I was reading the FDA Modernization Act of 1997 and what that Act basically entails is the spirit of trying to promote innovation, and I think by requiring much longer follow-up, it will deter companies from being

able to produce these innovative materials and I think the burden will be too onerous.

So I think that the two year clinical data, which is excellent, combined with the long-term follow-up of the European literature, which, as Ms. Maher pointed out, is data that we can use as an FDA Panel to make decisions, are compelling and I would lean toward approval with specific conditions that addresses some of the concerns that we have.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Kim. Dr. Naidu?

DR. NAIDU: You know, after listening to the presentation from the Netherlands, the physician from the Netherlands as far as device complications, it appears as if device related complications including anterior/posterior migration is less than 1 percent. In addition, the sponsor has conducted an excellent study where they have shown a significant improvement in objective outcomes, including the ODI and the VAS.

They have also shown that it's non-inferior to BAK, that's the fusion device, and they

have also shown that it's at least equivalent and it's not inferior, and I'm not sure as to why we are debating as to approvability of this device. I think it's approvable without any conditions.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Naidu. Dr. Blumenstein?

DR. BLUMENSTEIN: I can't go along with disapproval. I have to think that there are some conditions that we could put on with an approval with conditions that would satisfy the long-term follow-up requirement.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Besser?

DR. BESSER: I would also look for approval with conditions. I think we can resolve the issues here post-approval.

CHAIRPERSON YASZEMSKI: Thank you, Dr. Besser. Would anybody else like to add commentary? Hearing none, what we're going to do now is vote on this motion, which is for non-approval. I will go around the room and ask everybody to say yes or no for non-approval. If you vote yes, that means you agree

and you would like this to be not approved.

If this motion passes, then we're finished and our recommendation is non-approval and we'll discuss after that conditions that need to be met to make it approvable. If the motion does not pass, then we will ask Dr. Kirkpatrick if he might entertain a new motion.

Let's start, Dr. Diaz, with you.

DR. DIAZ: I disagree with the motion.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Mabrey?

DR. MABREY: Disagree.

CHAIRPERSON YASZEMSKI: Dr. Finnegan?

DR. FINNEGAN: I agree.

CHAIRPERSON YASZEMSKI: Dr. Kim?

DR. KIM: I disagree.

CHAIRPERSON YASZEMSKI: Dr. Naidu?

DR. NAIDU: I disagree.

CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

DR. KIRKPATRICK: I agree.

CHAIRPERSON YASZEMSKI: Dr. Blumenstein?

DR. BLUMENSTEIN: Disagree.

CHAIRPERSON YASZEMSKI: Dr. Besser?

DR. BESSER: Disagree.

CHAIRPERSON YASZEMSKI: The motion does not pass. Our two remaining options are approval or approval with conditions and I will ask, at this time, Dr. Kirkpatrick, would you entertain another motion?

DR. KIRKPATRICK: I would be glad to. I would also like to take a moment to recognize the beauty of democracy and the fact that we can agree to disagree, and that we have the freedom to do so at the expense of a number of our countrymen right now.

I would suggest, I would like to make the motion that it is approvable with conditions and if that passes, I would like to itemize conditions and take them individually if that's okay with the Chair.

CHAIRPERSON YASZEMSKI: Yes, the way that we're going to do it is we're going to go around. If you make a motion for approval with conditions, what we now do is consider the conditions first. I'm sorry, a point of order. Ms. Scudiero just reminded me that I did not ask for a second.

Dr. Kirkpatrick has made a motion for

approval with conditions. Do I have a second? Dr. Besser has seconded the motion. Thank you, Ms. Scudiero.

What we'll do prior to voting is have a discussion and ask for conditions. And if someone brings a condition up, we'll discuss that condition and then vote on that condition, and that condition will then either be included or not included. If persons have disagreements with the conditions that get voted in, then they can exercise their disagreement by voting no for the motion when it comes to a vote.

So I would like to entertain now if there is a motion for a condition from anybody. Yes, Dr. Kirkpatrick?

DR. KIRKPATRICK: In a follow-up to my concern about the length of follow-up, I would suggest that a condition would be that all of the currently enrolled patients, including the -- I can't remember what you termed it, but basically the patients that aren't in the IDE, but the ones that have continued to be done.

UNIDENTIFIED SPEAKER: The continued access.

DR. KIRKPATRICK: The continued access group be followed to the last of the continued access group being a minimum of two years follow-up. That should give us close to five years on most of the IDE patients if I'm remembering correctly on your block of time.

CHAIRPERSON YASZEMSKI: Yes. Thank you.

DR. KIRKPATRICK: That would be the first of several conditions I would propose.

CHAIRPERSON YASZEMSKI: We have a motion for a condition to include all the continued access patients until they have completed two year follow-up. Is there a second for this motion?

DR. DIAZ: Second.

CHAIRPERSON YASZEMSKI: Dr. Diaz and Dr. Finnegan, we have seconds. But is there discussion on this motion? Dr. Besser?

DR. BESSER: I'm questioning as to whether two years is long enough. I'm not sure how many of the people will be out to five years at that two years

after the last patient. If, in fact, we're looking for data out to five years, I would like to see the last patient at five years and that would give us even longer data and better data for the rest.

CHAIRPERSON YASZEMSKI: Mr. Christianson, could I ask you or a member of your company to comment on this question from Dr. Besser?

MR. CHRISTIANSON: Yes, the first patient was enrolled in 2000 and the last continued access patient was enrolled last week. So if we follow that patient through five years, the patient from 2000, someone do the math for me quick, is going to be extensive.

UNIDENTIFIED SPEAKER: Nine years out.

MR. CHRISTIANSON: So I believe that the entire randomized cohort will be at or beyond five years if we followed the last continued access patient through two years.

CHAIRPERSON YASZEMSKI: Okay. Thank you, Mr. Christianson. Dr. Besser, does that answer your question?

DR. BESSER: It answers my question, but

I'm not sure I'm convinced to shorten that. I would still like -- you know, nine years of data would be great.

CHAIRPERSON YASZEMSKI: Okay. Thank you. Others?

DR. KIRKPATRICK: May I amend my --

CHAIRPERSON YASZEMSKI: No, we have a second already.

DR. KIRKPATRICK: Okay.

CHAIRPERSON YASZEMSKI: We'll have to vote on it first. Any other discussion on this point?

DR. BESSER: I believe you can withdraw a motion.

DR. KIRKPATRICK: I don't want to withdraw it.

CHAIRPERSON YASZEMSKI: Let's have discussion.

DR. KIRKPATRICK: I want to include yours.

CHAIRPERSON YASZEMSKI: No, we can make another one. More discussion? Seeing none, Dr. Diaz, you're in the number one position here. I'm going to keep asking you first.

Let's vote, vote on this condition. The condition is to include all the continued access patients until they have completed two years of follow-up. This would be a condition to a motion for approval with conditions. This is the first condition.

DR. KIRKPATRICK: That would be a report on all patients once the last of the continued access reaches two years.

CHAIRPERSON YASZEMSKI: Yes, that's assumed.

DR. KIRKPATRICK: I just wanted to clarify that.

CHAIRPERSON YASZEMSKI: That's assumed. Yes, sir, Dr. Diaz?

DR. DIAZ: I agree.

CHAIRPERSON YASZEMSKI: Dr. Mabrey?

DR. MABREY: I agree.

CHAIRPERSON YASZEMSKI: Dr. Finnegan?

DR. FINNEGAN: I agree.

CHAIRPERSON YASZEMSKI: Dr. Kim?

DR. KIM: I hate to do this, but wouldn't

it be better to follow the IDE patients that are randomized for a total of five years?

CHAIRPERSON YASZEMSKI: We can do that as a separate motion. I think we need to finish voting here.

DR. KIM: So based on that, I would disagree.

CHAIRPERSON YASZEMSKI: Okay. Thank you. Dr. Naidu?

DR. NAIDU: I agree.

CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

DR. KIRKPATRICK: Agree.

CHAIRPERSON YASZEMSKI: Dr. Blumenstein?

DR. BLUMENSTEIN: Disagree.

CHAIRPERSON YASZEMSKI: Dr. Besser?

DR. BESSER: Disagree.

CHAIRPERSON YASZEMSKI: And this motion passes 5 to 3 and so one condition for Dr. Kirkpatrick's motion for approval with conditions is that the currently enrolled patients in the continued access category and all other enrolled patients in the IDE study have follow-up at the time that the

continued access patients reach two years follow-up.

Now, would anybody like to introduce a second condition? Dr. Finnegan?

DR. FINNEGAN: It seems to me that this is the ultimate device for device tracking and I would, therefore, like to introduce the condition that this device be tracked.

CHAIRPERSON YASZEMSKI: We have a motion to include a condition for device tracking. I would like to ask Dr. Witten to comment on the device tracking condition.

DR. WITTEN: Well, I just would like -- that term is always really confusion, and so I would like clarification as to what exactly that means, whether it's that we want to be able to track the device to the patients or there are specific data elements we want when it gets implanted. Is this all patients and, for example, maybe I could start with asking what the objective would be and then we could better understand what it is.

DR. FINNEGAN: See, the objective would be as this is put in, one of the unfortunate problems at

present is when a device is put in and five years later significant complications are known and probably, what am I thinking about, the -- what's the hip that got -- anyway, we have reason to -- yes, the Saltzer Hip, that we have had recent experience that patients are panicking, lawyers are calling everybody to find out if they have got the device in them or not and no one has the answer, which maybe the sponsor thinks would be a good idea.

But anyway, what we're looking for is a way that a patient would know what device was in them. The physician would know what patients they had implanted the device in. The sponsor would know that the device was in Patient X, so that when, long-term, something came up, you would know where to go.

DR. WITTEN: Okay. So it's to identify the patients and the physicians, and that's for anybody who receives the implant. It's not a data collection mechanism?

DR. FINNEGAN: That is correct.

DR. WITTEN: Okay.

CHAIRPERSON YASZEMSKI: Thank you. We

have a motion for device tracking. Is there a second? Dr. Mabrey. Discussion? Dr. Diaz?

DR. DIAZ: I would like to just make sure that we call it device ID follow-up rather than tracking, because tracking to me implies something very different. To me that means a responsibility on the corporation to follow every single device that's implanted wherever it happens to end, and I think that's an onerous condition of its approval. I think it is important for the patient and the surgeon to know what device was implanted in whom when and where and leave it at that.

CHAIRPERSON YASZEMSKI: Okay. Thanks, Dr. Diaz. May I go out of the order first and I would like commentary from Ms. Maher on this.

MS. MAHER: Yes, I would support what Dr. Diaz just said. Device tracking, when you go to the degree as to what that term actually means, is exceedingly burdensome to the industry and in the days of HIPAA is almost going to be impossible to do. It's not one of those things that patients want to be followed and want to be tracked. You know, they move.

They don't tell you they have moved. Keeping track of where they are is virtually impossible.

The device tracking requirements were originally put into place for products where if they were to fail, such as the heart valves, it would be catastrophic to the patient immediately and I don't see that this product necessarily fits that definition of being catastrophic immediately.

I like what Dr. Diaz suggested, that we actually train people more and have the labeling require more, that the patient is supposed to know that you have gotten a DePuy Charite Disc. I know many people who have gotten joint replacements and have no idea what joint they had placed in them, which I also find bizarre.

But I think that if you go to this N^{th} degree, you're adding a burden that is almost impossible to meet and I'm not sure I see the benefit of it, especially given what that regulation and law was originally intended for.

CHAIRPERSON YASZEMSKI: Thanks. And, Dr. Diaz, may I ask for a clarification on your use of the

term follow-up? Would it be similar to what Ms. Maher has just said? What would you suggest the follow-up be?

DR. DIAZ: I think it should be limited only to providing the patient with a name of the device, perhaps an ID number that all of these devices have. The patient would have the name of the surgeon, the place where the surgery was done and the date and leave it at that.

CHAIRPERSON YASZEMSKI: Thank you. Now, I haven't yet asked for a second and I would like to--

UNIDENTIFIED SPEAKER: You have a second.

CHAIRPERSON YASZEMSKI: I have a second? I'm sorry. I did so.

DR. DIAZ: This is just a friendly editorial amendment.

CHAIRPERSON YASZEMSKI: Yes. May I come first to Dr. Mabrey and then we're going to come to Ms. Luckner?

MS. LUCKNER: From the patient's perspective, I think you are asking for patient identification to know what device was implanted and

to know the number. That is totally reasonable from a patient perspective. I do not wish to reveal totally in this room, but I have two knee replacements. I carry in my wallet that I have a knee replacement, so that I have no difficulty with going through airport security systems.

Now, I will tell you it does not say on it the manufacturer and I am one of those people that, over here my colleague said, I have no idea what knee replacement I have. Listening to this conversation, you can believe when I return to Toledo, Ohio, I will find out exactly what is in my knees.

CHAIRPERSON YASZEMSKI: Thanks, Ms. Luckner. Dr. Mabrey?

DR. MABREY: Yes, I agree with Ms. Maher's comments that a tracking type of program would be somewhat onerous and my chief concern is trying to keep in line with all the HIPAA regulations. I think that becomes a quagmire, if I can borrow from another era.

However, every one of my total joint patients get a card and they know exactly what implant

they have in them and I make sure they have it, but then again, not everybody puts in total joints. I think it's reasonable to provide the patient not only with a card that identifies what implant they have and the date it was implanted, but also a serial number much along the lines of the pacemakers.

I believe most pacemaker implants have a serial number associated with them. The manufacturer will be keeping at least a registry of those serial numbers and should there ever be a problem with that group, it seems like it would be a simple matter for the patient then to take the initiative and contact the physician or the company to follow-up on that serial number.

It's certainly also helpful. I would love to have every total hip patient and total knee patient in the country carrying around their serial numbers, so that I could call up that company and find out exactly what size implant I'm going to revise, and I don't see that as being too onerous on industry or too onerous on the patients and, certainly, you know, would put everyone's mind at ease.

CHAIRPERSON YASZEMSKI: Along the lines of what you have just discussed, would it be reasonable to consider having a card come with every prosthesis that has that identification number and then which the surgeon just fills out his or her name, the patient's name, date and hospital?

DR. MABREY: Well, I don't put these devices in, but it looks like there's three parts to it and they all come in three separate boxes. But there are peel-off stickers that could go with that. I would only caution you that if they go into your wallet, then after a couple of years the numbers will probably wear off. So I'm not sure how we would handle that.

CHAIRPERSON YASZEMSKI: All right. Thanks, Dr. Mabrey. Dr. Blumenstein?

DR. BLUMENSTEIN: Well, as a concerned father of teenagers, perhaps we could put the tattoo parlors to work and have them --

CHAIRPERSON YASZEMSKI: Thank you, Dr. Blumenstein. Dr. Kirkpatrick?

UNIDENTIFIED SPEAKER: They would be too

busy to work on your kids.

CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

DR. KIRKPATRICK: May I suggest that implied in this condition would be that the FDA would work with the manufacturer in order to make sure that there is a legal way to do this, because the Joint Registry is already significantly alone working on those problems. FDA is aware of those issues and if it can be done, it can, but if it can't be done, that the Panel would accept that, but we would encourage it to be done. Is that implicit in the motion?

DR. FINNEGAN: It is implicit in the motion, but I think, Jay, I don't want to give people sort of a cop-out, because I think Jay is right. I think if you put the serial number on and the patient has the access to the serial number, that doesn't have to have a lot of data and then you can do the same thing that, you know, Mercedes does when their brakes don't work. They say if your car, you know, has this serial number or was between this and this date, then you need to call the company. Here is the 1-800 number. I mean, that's a pretty straightforward thing

to do.

DR. KIRKPATRICK: I agree that it's straightforward, but, believe it or not, that minimal of a data set is significantly complicated in trying to get through other federal agencies as far as whether it's HIPAA compliant.

DR. FINNEGAN: But if the patient signs the consent, I don't think it is.

DR. KIRKPATRICK: Exactly.

DR. FINNEGAN: So if the patient signs, it says that they are quite happy to have the serial number and to have the company know what serial number they have, then I don't think that's --

CHAIRPERSON YASZEMSKI: Okay. Thanks. Dr. Mabrey?

DR. MABREY: Well, if I could just clarify. I don't even think that we're asking that the company know which patient has it, but just that the company know what implants are out there and have been implanted, and we're placing part of the -- yes, we're putting part of the responsibility on the patient now to look at the serial number and then get

in contact with industry. I think this then keeps us out of all the problems with HIPAA. Carrying around a serial number that only you know you have and industry having that same serial number, but having no idea who you are, I think that's reasonable, and I think it may be reasonable to at least keep track of which physician put it in.

And I know the way industry does the total joints, they certainly know what region it goes into and I know that our distributor keeps track of just about every implant I have put in anyway. I will have to check and see what HIPAA rules we're violating on that when I get back though.

CHAIRPERSON YASZEMSKI: All right. Thanks very much. Dr. Finnegan, do you have additional comments? Otherwise, I'll go to Dr. Kim.

DR. FINNEGAN: I have no other comments.

CHAIRPERSON YASZEMSKI: Okay. Dr. Kim?

DR. KIM: I would agree with what Dr. Mabrey said.

CHAIRPERSON YASZEMSKI: Thanks. Dr. Naidu?

DR. NAIDU: Same here.

CHAIRPERSON YASZEMSKI: Thanks. Dr. Kirkpatrick, additional comments?

DR. KIRKPATRICK: No.

CHAIRPERSON YASZEMSKI: Dr. Blumenstein?

DR. BLUMENSTEIN: No comments.

CHAIRPERSON YASZEMSKI: Dr. Besser?

DR. BESSER: No comments.

CHAIRPERSON YASZEMSKI: Thanks. Ms. Maher?

MS. MAHER: I would just like a little clarification. We're probably talking about lot numbers here, not serial numbers, and I would recommend that we actually, since the FDA now knows from this details conversation that what we really want is for patients to know what device they have had implanted and what lot numbers it was, that we leave it to the FDA and the sponsor to work out the best way to obtain that information.

DR. MABREY: I think lot numbers are --

CHAIRPERSON YASZEMSKI: Okay. All right. Thank you. Now, before we vote, I want to ask Dr.

Finnegan, because you made the motion and you did start with the words device tracking, but in light of the discussion, would you be okay if the motion did not include those specific words, which impose a certain level of --

DR. FINNEGAN: All I want --

CHAIRPERSON YASZEMSKI: -- responsibility on the company, but to go along with what we discussed.

DR. FINNEGAN: All I want is the patient to be able to know if the implant they have has a problem.

CHAIRPERSON YASZEMSKI: Okay. Thank you. I will state the motion then in the form it is after discussion. The motion is that the patients be supplied with the name and lot number of the device, the doctor and hospital and date that it was put in, that the company know only that the device was implanted and that if problems do arise, the company can send out a notice and it would be the patient's responsibility to recognize that they have one of the implants in them that was in the notice.

We're going to vote on this now. Dr. Diaz?

DR. DIAZ: I agree.

CHAIRPERSON YASZEMSKI: Dr. Mabrey?

DR. MABREY: I agree.

CHAIRPERSON YASZEMSKI: Dr. Finnegan?

DR. FINNEGAN: I better agree.

CHAIRPERSON YASZEMSKI: Dr. Kim?

DR. KIM: I agree.

CHAIRPERSON YASZEMSKI: Dr. Naidu?

DR. NAIDU: I agree.

CHAIRPERSON YASZEMSKI: Dr. Kirkpatrick?

DR. KIRKPATRICK: Agree.

CHAIRPERSON YASZEMSKI: Dr. Blumenstein?

DR. BLUMENSTEIN: Agree.

CHAIRPERSON YASZEMSKI: Dr. Besser?

DR. BESSER: I agree.

CHAIRPERSON YASZEMSKI: This motion passes as the second condition of the motion for approval with conditions.

We will now move on and ask if there are other conditions that people would like to raise and

include in the motion for approval with conditions. Dr. Kirkpatrick?

DR. KIRKPATRICK: I need a clarification before I make my motion. When Mr. Christianson said that it would be 15 weeks, there was a lot of mumbling in the background and I assume that means it's longer than that.

CHAIRPERSON YASZEMSKI: Mr. Christianson, would you care to comment?

DR. KIRKPATRICK: That's on the 50 million cycle tests.

MR. CHRISTIANSON: Yes. Thank you for asking that question. When I got back, I was told. I meant to say 15 months. It's not 15 weeks.

CHAIRPERSON YASZEMSKI: Thank you. So 50 million cycles, 15 months.

DR. KIRKPATRICK: In the spirit of that, I would like to suggest a post-approval study that takes the wear data out to 50 million cycles as discussed in my presentation. I would also like to ask if they could do a study looking at the other coupled motion, meaning flexion and extension coupled

with lateral bending, and provide a rationale for the length of that testing that is reasonable. I don't know.

I don't think that needs to be taken to 50 million necessarily, because I think what is going to happen is we need to see what happens after somewhere intermediate range, you know, maybe 5 to 7 million and then change directions and see if that makes more wear debris come off or, if you want to, you can do the coupled motion all the time to make sure such as like a figure 8 motion doesn't make a different wear debris pattern. Is that clear enough?

CHAIRPERSON YASZEMSKI: I'll --

DR. KIRKPATRICK: First, to summarize it, it's, basically, number one is extending data post-approval for 50 million cycles and studying the effect of coupled motion of flexion-extension with lateral bending, as opposed to axial rotation.

CHAIRPERSON YASZEMSKI: Okay. I will ask for a second for this motion.

DR. MABREY: Second.

CHAIRPERSON YASZEMSKI: Dr. Mabrey has

seconded. Discussion? Dr. Diaz?

DR. DIAZ: I don't have any comment.

CHAIRPERSON YASZEMSKI: No comments? Dr. Mabrey?

DR. MABREY: No comments.

CHAIRPERSON YASZEMSKI: Dr. Finnegan? Dr. Kim?

DR. KIM: It seems so excessive to have to test the device for 15 months, so I would question the need to do that, but I do agree with testing the other motions, but for a reasonable period of time.

CHAIRPERSON YASZEMSKI: Okay. What would you consider a reasonable period of time?

DR. KIM: The 10 million cycles, which represents 80 years if, in fact, that is correct seems very reasonable to me.

CHAIRPERSON YASZEMSKI: Thank you. Thank you, Dr. Kim. Dr. Naidu?

DR. NAIDU: I concur with Dr. Kim. It appears as if 50 million cycles will be excessive.

CHAIRPERSON YASZEMSKI: Thank you. Dr. Blumenstein?

DR. BLUMENSTEIN: Let me see if I can understand this. This is not done inside the body, but is done outside the body? It seems excessive to me.

CHAIRPERSON YASZEMSKI: Dr. Besser?

DR. BESSER: As the testimony we have heard today, they referred to failed prostheses and the failed procedures, none of them in my memory were because of device problems with particulate matter. There were other reasons why it failed. I also would think that the 50 million cycles is probably excessive and the 10 million cycle data that has already been presented is adequate.

I would, however, like to see the multiple modes. I'm wondering whether we can separate this motion into two.

CHAIRPERSON YASZEMSKI: What we'll do is vote on this and if it passes, they will both occur and if it doesn't pass, we can entertain another motion for one or the other of them. Ms. Maher?

MS. MAHER: Yes, I would just like to take this opportunity again. It seems excessive to me. I