

1 appropriately derived and selected the patients that  
2 had single-level disease with clinical manifestations,  
3 and patients with double-level disease with clinical  
4 manifestations, the alternate outcome would be the  
5 same. My only concern really relates on the  
6 biomechanical aspect to what Dr. Finnegan said  
7 earlier. That if we are fixating a level of the spine  
8 at one or two levels, we cannot consider that a  
9 meaningless undertaking because it does affect the  
10 biomechanical function of the entire spine, and there  
11 may be manifestations at other places or other sites  
12 that are directly related to the placement of these  
13 devices.

14 DR. YASZEMSKI: Thanks Dr. Diaz. Ms.  
15 Maher?

16 MS. MAHER: I don't have anything to ask  
17 anybody on this particular question.

18 DR. YASZEMSKI: Thank you. Dr. Doyle?

19 DR. DOYLE: Do we have any idea if we  
20 separated them out if it would make any difference?

21 DR. YASZEMSKI: Would you like someone  
22 from the sponsor to address that?

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1 DR. DOYLE: Yes.

2 DR. YASZEMSKI: Would someone address  
3 please, do you feel that -- Dr. Doyle's question is do  
4 you feel that if you separated out the data from one-  
5 and two-level, rather than pooling them, would your  
6 conclusions or results in your opinion be different or  
7 the same. Dr. White.

8 DR. WHITE: Yes. My name is Augustus  
9 White. And we do think that it's quite appropriate to  
10 pool these. It would not be different if we separated  
11 one- and two-level. I believe that what this  
12 represents is a spectrum of a broad degenerative  
13 process. And it's a matter of levels that are  
14 involved in the degenerative process, sometimes it's  
15 more longstanding, or the disease processes are  
16 slightly different, then it will be two. But the  
17 basic mechanisms and the basic considerations are  
18 quite the same.

19 DR. YASZEMSKI: Thank you Dr. White. Dr.  
20 Doyle, does that answer your question? Thank you.  
21 Dr. Kim.

22 DR. KIM: A comparison of the one-level

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1 versus the two-level results, correct me if I'm wrong.

2 The two-level patients did better, particularly in  
3 the physical function component, which is pretty  
4 dramatic, 73 percent success for the two-level and 46  
5 percent for the one-level. Is it possible that when  
6 you do a one-level treatment, that we're not getting  
7 that second level that is needed? And I guess my  
8 question is is there a way to look at adjacent levels  
9 again and determine if there is a threshold other than  
10 the 50 percent that you use for the criteria to do a  
11 two-level surgery instead of a one-level surgery?

12 DR. YASZEMSKI: Dr. Andersson.

13 DR. ANDERSSON: It's interesting how this  
14 discussion has moved from perhaps not doing two levels  
15 to perhaps doing two levels. It's possible that the  
16 better result with the two-level had to do with the  
17 fact that some patients who got one level X STOP  
18 should have had two-level X STOPS. We can look at  
19 that further. And I think it is a possibility. We  
20 don't know. At this point, it seems that the results  
21 are quite similar between one- and two-levels except  
22 for that one single aspect.

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1 DR. YASZEMSKI: Thank you Dr. Andersson.

2 DR. RUDICEL: I have just one comment to  
3 that, if that's okay.

4 DR. YASZEMSKI: Dr. Rudicel.

5 DR. RUDICEL: Did they actually do  
6 numerically better, or was just the increase better?  
7 I was not clear about that. So the level twos, their  
8 number might not have been as high but they had a  
9 better increase if they started out at a worse level?

10 DR. YASZEMSKI: Ms. Lysakowski.

11 MS. LYSAKOWSKI: Just to clarify, you are  
12 asking about the success rates --

13 DR. RUDICEL: Yes.

14 MS. LYSAKOWSKI: -- between the one-  
15 versus two-level? It's numerical, if you will. It's  
16 based on just the percentage of patients in each of  
17 those subgroups that met the criteria for success.

18 DR. RUDICEL: On the ZCQ, though, I was  
19 just -- their increment could have been greater, but  
20 their numerical score might not have been greater. I  
21 wasn't clear from the material I read.

22 MS. LYSAKOWSKI: Right. Well the criteria

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1 for success are based on a threshold level of  
2 improvement. So to be considered a success in any  
3 single domain, you would have to have a 0.5  
4 improvement for that domain. So they had to have  
5 either had -- they could have had more. They could  
6 have had --

7 DR. RUDICEL: But you don't know whether  
8 numerically they were higher or not? You just know  
9 that they had a --

10 MS. LYSAKOWSKI: I think perhaps you're  
11 asking if we looked at the mean change scores between  
12 the two subgroups?

13 DR. RUDICEL: Well, for example, the level  
14 twos might have been a 3.5, and the level ones might  
15 have been a 3.0.

16 MS. LYSAKOWSKI: Right. We did not  
17 compare mean change scores.

18 DR. RUDICEL: Okay.

19 DR. YASZEMSKI: Thank you. Dr. Naidu?

20 DR. NAIDU: I have nothing to add.

21 DR. YASZEMSKI: Thank you. Dr.  
22 Kirkpatrick?

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1 DR. KIRKPATRICK: Nothing to add.

2 DR. YASZEMSKI: Thank you. Dr. Li?

3 DR. LI: Just a question, and it may be in  
4 this packet and I missed it. Was using two levels  
5 something that was part of the original study? In  
6 other words, that the surgeon could decide whether or  
7 not one or two levels could be used? And if so, were  
8 the criteria the same for all the different centers?  
9 In other words, if you laid out who used two levels  
10 from the different centers, would the list of criteria  
11 be the same?

12 DR. YASZEMSKI: Dr. Andersson.

13 DR. ANDERSSON: Yes. Yes, it was part of  
14 the study design. And in fact, as you may remember,  
15 one of the inclusion criteria had to do with the size  
16 of the spinal canal.

17 DR. LI: And the second question about  
18 those that did two levels, were their criteria the  
19 same?

20 DR. ANDERSSON: Yes, they were.

21 DR. YASZEMSKI: Thanks Dr. Andersson. Dr.  
22 Ellenberg?

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1 DR. ELLENBERG: I have no further  
2 questions on this question.

3 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.  
4 Finnegan?

5 DR. FINNEGAN: A question and then a  
6 comment. The question is were the two levels done the  
7 same local, or were those ones that needed general  
8 anesthetic, and what was the time increase for the two  
9 levels?

10 The comment is that if you look at the x-  
11 rays that were provided, there certainly is more  
12 significant flexion in the two-level x-rays that were  
13 in our packet than in the single level, albeit the  
14 single level actually was an expulsion. And so one  
15 would have to assume that there are some biomechanical  
16 alterations that, again, we have not clarified. But  
17 the question were the two levels -- how much time did  
18 they take, and were they done under general or under  
19 local, with more sedation.

20 DR. YASZEMSKI: Dr. Hartjen.

21 DR. HARTJEN: Charles Hartjen, yes. As I  
22 understand it, none of the two-levels were done with

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1 general anesthesia. And adding an additional level,  
2 on average, added approximately 20 minutes to a  
3 procedure.

4 DR. FINNEGAN: And how long does a two-  
5 level laminotomy take in experienced hands, in the  
6 hands of your surgeons?

7 DR. HARTJEN: Well, there's a range from  
8 limited laminotomies and facetectomies to complete  
9 laminectomies that are done, but I would say typically  
10 a two-level decompression in most people's hands would  
11 be approximately two hours. Possibly two and a half.

12 DR. YASZEMSKI: Thank you Dr. Hartjen.  
13 Dr. Witten? Dr. White.

14 DR. WHITE: I don't think we addressed  
15 your biomechanical question about the two levels. I'd  
16 just like to comment, first of all, the very beautiful  
17 description that you described of the energy and the  
18 equation of how some change ought to exist. If you  
19 change the mechanics at one level, it has to affect  
20 other levels. And clearly on a theoretical basis that  
21 makes sense. However, in my opinion, in terms of  
22 practical clinical biomechanics, I think that the

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1 effect would tend to be minor. If we think in terms  
2 of a spinal fusion where there's a very rigid  
3 immobilization of one or two levels, this impacts  
4 understandably both clinically and experimentally the  
5 adjacent levels of the spine. However, this is not by  
6 any means a rigid immobilization that is anywhere in  
7 the range of a spine fusion or instrumentation. It  
8 actually continues motion, but it somewhat limits the  
9 motion. But this is in the realm of the partial  
10 immobilization, which I think will tend to have a  
11 minima biomechanical effect. This is speaking to some  
12 degree theoretical, but it is my honest opinion about  
13 the difference.

14 DR. YASZEMSKI: Thank you Dr. White.  
15 Other comments? Dr. Witten, there seems to be good  
16 concordance of opinion on Number 2 that there is a  
17 clinical basis for pooling the outcomes of the one-  
18 and two-level patients. Dr. Rudicel began by  
19 questioning and getting the answer from the sponsors  
20 that the selections are done by clinical evaluation.  
21 And if the clinical evaluation points to one level or  
22 to two levels, and a one- or two-level procedure is

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1 subsequently done, the expectation would be the same  
2 for both of them, that the problem that exists be it  
3 one or two levels is completely addressed. And have  
4 we had adequate discussion from FDA's perspective on  
5 Question Number Two?

6 DR. WITTEN: Yes, thank you.

7 DR. YASZEMSKI: Thank you. Let's move on  
8 to Question Number 3. Dr. Holden?

9 DR. HOLDEN: The device labeling states  
10 that this device limits extension. In the pre-  
11 clinical cadaveric studies, ranges of flexion-  
12 extension were recorded under measured applied loads.  
13 The clinical radiographic measurements, however, were  
14 performed on static plain radiographs. Please discuss  
15 the interpretations of the measurements made on the  
16 clinical patients' radiographs as it relates to device  
17 effectiveness.

18 DR. YASZEMSKI: Thanks Dr. Holden. This  
19 time we're going to start with Dr. Kim, and we'll come  
20 clockwise around through Dr. Naidu.

21 DR. KIM: The importance of this question  
22 is related to the findings in the pre-clinical

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1 studies, that the only difference in canal and  
2 neuroforaminal parameters are found in extension. So  
3 we have to wonder why only static films, even though  
4 they're standing, were taken clinically since things  
5 like the neuroforaminal area, those differences we  
6 can't expect to find. Thus x-rays in this study looks  
7 for only device failures and hardware complications,  
8 and cannot really address the issues of neuroforaminal  
9 area, for example.

10 The second point I wanted to raise is that  
11 the sponsor contends that greater than 90 percent of  
12 the x-rays show maintenance of distraction.  
13 Unfortunately, the point was raised that the x-ray  
14 technique is likely unable to detect differences that  
15 are less than a few millimeters. There are  
16 differences in magnification, clarity, and even the  
17 angle of the tube that can affect that. So if this is  
18 an important question, I think the meaningful  
19 radiographic study would be to get either a CT or an  
20 MRI. I just want to ask the sponsors if they thought  
21 about this, and why they decided not to obtain that  
22 information.

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1           The second issue is whether or not to  
2 obtain flexion-extension views on the clinical visits,  
3 which is actually pretty common to do in clinical  
4 practice. Because one would want to look at a couple  
5 of things. One, over time with biologic remodeling  
6 there could be effects on the adjacent segments such  
7 as hypermobility, which may cause focal kyphosis, or  
8 other changes. And that would be worthwhile looking  
9 at.

10           And then finally, we have to wonder how  
11 the implant is behaving within that site. For  
12 example, is it hypermobile, is it rubbing against the  
13 bone, and is there a reaction to that implant that if  
14 we waited a few more years we'd notice that it would  
15 erode the bone or somehow cause it to fail.

16           And then finally, Dr. White already  
17 brought up, but I wanted him to expand a little bit  
18 further. You're doing two-level surgeries on the  
19 patients, but unfortunately two-level pre-clinical  
20 studies weren't done. And once again, all the points  
21 that I raised are even more important to look at when  
22 we do two-level surveys. So I hope I wasn't too

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1 lengthy, but if you could address those issues that  
2 would be great.

3 DR. YASZEMSKI: Maybe I'll ask as Dr.  
4 Andersson just repeat your first question so he can  
5 take them one at a time.

6 DR. KIM: The first question is do you  
7 think it's useful to get a CT or an MRI to look at the  
8 degree of distraction. You obviously didn't. If you  
9 could just give us the reason as to why you didn't  
10 think was important.

11 DR. ANDERSSON: Actually, no, it's very  
12 difficult to determine the degree of stenosis or  
13 changes within a motion segment using x-rays or even  
14 CTs. Measurements are so inaccurate that we  
15 essentially decided that it wasn't worth it in a study  
16 of this type. Instead, the x-rays were used to study  
17 effects of the implant itself, and the location of the  
18 implant, and whether or not the implant had any major  
19 effect on the spinous processes. So we did not use  
20 the x-rays to determine any stenotic aspect at all.

21 DR. YASZEMSKI: Thanks Dr. Andersson. Dr.  
22 Kim, second question?

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1 DR. KIM: Can I ask a quick question about  
2 MRI. Is it possible to do an MRI with this implant,  
3 or is it considered a loose foreign body that would  
4 not be okay to MRI, just out of curiosity?

5 DR. ANDERSSON: Well, it's possible to do  
6 MRI with the implant. There is some disturbance, but  
7 it is possible to do MRI with the implant. And in  
8 fact, we are in the process of doing a study using  
9 standing MRI to look further into some of the aspects  
10 that we are scientifically interested in.

11 DR. KIM: And then finally, maybe this  
12 could be a combined question. What do you think is  
13 the effects -- I guess I want to ask why flexion-  
14 extension views weren't done, because I would be  
15 interested in looking at the effects on the adjacent  
16 segment. Even though in the pre-clinical studies  
17 there's no changes, as Dr. Finnegan brought up, over  
18 time the body will undergo a response, and that may  
19 eventually lead to hypermobility, for example, of the  
20 adjacent segments. And I would think that that would  
21 be more risk at two levels. So if you can just  
22 address why flexion-extension views you didn't think

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1 were that important.

2 DR. ANDERSSON: Well, we didn't do  
3 flexion-extension views again because we weren't  
4 trying to use x-rays for any other purpose than to  
5 evaluate the device. If we had been concerned with  
6 stability of say a fusion, obviously we would have  
7 done flexion-extension views. If we had been  
8 concerned about abnormal motion occurring, we would  
9 have done flexion-extension views. I don't think in a  
10 patient population that you do flexion-extension views  
11 as a routine unless the patient has complaints of back  
12 problems. And so those were the reasons why we  
13 didn't.

14 DR. YASZEMSKI: Thanks Dr. Andersson. Dr.  
15 Kim, had you said you wanted a question for Dr. White,  
16 did I hear you when you asked your question? Or has  
17 Dr. Andersson answered that?

18 DR. KIM: I don't have -- he answered it.  
19 I don't have any further questions.

20 DR. YASZEMSKI: Okay. Thank you. Dr.  
21 Naidu?

22 DR. NAIDU: My answer to Question Number 3

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1 is based on the current study, the PMA submitted,  
2 there is no x-ray basis for device effectiveness.

3 DR. YASZEMSKI: I'm sorry, say again?

4 DR. NAIDU: There is no x-ray basis.

5 DR. YASZEMSKI: Okay, thank you. Dr.  
6 Kirkpatrick?

7 DR. KIRKPATRICK: My comments are  
8 basically going to emphasize what has already been  
9 said, and also raise a question. If the sponsors felt  
10 the MRI does not give us accurate measurement ability,  
11 why did you use it in the pre-clinical study? I  
12 thought those were reliable numbers, and I trusted the  
13 improvement in the cadaver model based upon MRI data  
14 that you presented. And now you're telling me that in  
15 a clinical model it would not be effective in reliable  
16 measurements.

17 DR. ANDERSSON: No, I think what I was  
18 trying to say was that for purposes of determining  
19 spinal stenosis, MRI certainly can be very accurate,  
20 even in the process of an X STOP. But for routine  
21 study of the result of the X STOP in these patients,  
22 we decided not to use MRI because it added a

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1 significant complexity, and we know that there is no  
2 direct relationship between the change in the stenosis  
3 parameters and the patient symptoms. And so we  
4 thought the patient symptoms were the most important.

5 DR. YASZEMSKI: Thank you Dr. Andersson.  
6 Dr. Li?

7 DR. KIRKPATRICK: If I may finish --

8 DR. YASZEMSKI: Dr. Kirkpatrick, go ahead.

9 DR. KIRKPATRICK: To answer the question,  
10 I don't believe that the sponsor has provided in the  
11 clinical patients a demonstration that the philosophy  
12 of their device has been proven in that they have not  
13 provided us with any anatomic data, whether it's  
14 radiographs, CT, or MRI, which demonstrates that the  
15 foramen or the canal is prevented from getting  
16 narrower in the clinical population.

17 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
18 Dr. Li?

19 DR. LI: I only have just a short comment.  
20 I guess it appears that the FDA is circling this  
21 question around the device labeling issue about  
22 whether or not they can state the device limits

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1 extension. I think the only possible claim they could  
2 make on that would be from the laboratory testing of  
3 cadaver spines. There doesn't appear to be any  
4 clinical support for limiting extension.

5 DR. YASZEMSKI: Thanks Dr. Li. Dr.  
6 Ellenberg?

7 DR. ELLENBERG: No comments on this  
8 question.

9 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.  
10 Finnegan?

11 DR. FINNEGAN: I agree with what's been  
12 said.

13 DR. YASZEMSKI: Thank you. Dr. Rudicel?

14 DR. RUDICEL: No further comments.

15 DR. YASZEMSKI: Thank you. Dr. Diaz?

16 DR. DIAZ: I concur with Dr. Kirkpatrick's  
17 view. My basic concern with the presentation as it  
18 relates to this issue is that the anatomical  
19 confirmation that your device does what it's supposed  
20 to do was not given. So the fact that the patients  
21 got better does not mean that you changed the anatomy  
22 one bit.

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1 DR. YASZEMSKI: Thanks Dr. Diaz. Ms.  
2 Maher?

3 MS. MAHER: Nothing further.

4 DR. YASZEMSKI: Thank you Ms. Maher. Dr.  
5 Doyle?

6 DR. DOYLE: Nothing to add.

7 DR. YASZEMSKI: Thank you Dr. Doyle.  
8 Further comments? Dr. Witten, there seems to be a bit  
9 of a disparity of opinion on this. There has been a  
10 spectrum of opinions given from fully accepting  
11 clinical data as demonstration of effectiveness to the  
12 other extreme, that the effectiveness of the device in  
13 limiting extension has not been proved unless there is  
14 an extension film that shows that extension has in  
15 fact been limited, and this would need to be done  
16 post-operatively. Have we had adequate discussion  
17 from FDA's perspective?

18 DR. WITTEN: Yes, thank you.

19 DR. YASZEMSKI: Thank you. We're going to  
20 move on to Question 4(a).

21 DR. HOLDEN: Question 4 has two parts. The  
22 part that's common to both. Fewer than 50 percent in

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1 the X STOP treated group, and fewer than five percent  
2 in the control group achieved overall successful  
3 outcome. These results are considerably lower than  
4 what had been predicted at the outset of the study.  
5 In this study, an operative treatment was compared to  
6 a non-operative treatment in patients who had already  
7 failed conservative treatment, including epidural  
8 injections. A majority of patients had had symptom  
9 duration for more than two years prior to entering the  
10 study. Patients in both groups went on to have more  
11 than one epidural injection, and/or laminectomies. In  
12 10 to 15 percent of the X STOP treated patients who  
13 improved, symptoms returned during the course of the  
14 study. Moreover, there was a trend toward different  
15 results for use of this device at one versus two  
16 levels.

17 (a) Based on the data from this study,  
18 please discuss the appropriate population who might  
19 benefit from this device.

20 DR. YASZEMSKI: Thank you Dr. Holden. Dr.  
21 Kirkpatrick?

22 DR. KIRKPATRICK: With regard to (a),

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1 unfortunately I don't have enough information to  
2 discuss the appropriate population specifically who  
3 may benefit from this device. I think that the pool  
4 of patients with their clinical symptoms has enough  
5 variability that we cannot determine which within  
6 those we can pinpoint would benefit. Specifically,  
7 one question I would have is on the clinical symptom  
8 standpoint, the issue of one versus legs hurting. We  
9 heard from two patients who both described single leg  
10 pain. A lot of patients with stenosis also have  
11 bilateral leg pain. Many times the anatomic  
12 physiology causing one versus two leg pain may differ  
13 in that one foramen may be tighter than the other, or  
14 one subarticular region may be narrower than the  
15 other, much as was shown on the MRIs demonstrated in  
16 the presentation.

17 The second issue is related to the first,  
18 and that relates to the anatomic region which  
19 predominates in the stenosis. I am concerned that one  
20 particular type of stenosis predominating may actually  
21 show us a very successful intervention with the X STOP  
22 versus another one not having success at all. And the

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1 things that intuitively come to mind would be, again,  
2 a foraminal stenosis on one side versus a combined  
3 stenosis involving everything and a very large central  
4 stenosis. I would not expect to be as successful as  
5 the single foraminal stenosis with the use of this  
6 device. I have not heard the sponsor provide data  
7 that can help me discern these questions. If they do,  
8 I'm more than open to hear their comments. However,  
9 if they cannot, then I cannot state that I am  
10 comfortable defining the appropriate population for  
11 this device.

12 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
13 If anyone from the sponsor would like to comment, we  
14 can do it now or after we've gone around the room. If  
15 someone wants to specifically address Dr.  
16 Kirkpatrick's question and would like to do it now,  
17 please to do so. Dr. White?

18 DR. WHITE: This is obviously an important  
19 point that you raise. I think that the pathology of  
20 lumbar spinal stenosis is a cumulative obliteration of  
21 space available in the canal. I think if you can take  
22 a functional spinal unit, whether it's unilateral

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1 disease primarily or circumferential disease  
2 primarily, if you can do a separation, and reach that  
3 threshold which alleviates and provides, again, enough  
4 space to avoid all of the pathologic mechanisms that  
5 you so nicely described, that you will in fact cure  
6 the disease, whether it's unilateral or whether it's  
7 bilateral. The important thing is to open up and  
8 provide enough incremental space to reach that unknown  
9 threshold of tightness so that you get from a too-  
10 tight canal, for whatever reason in whatever region,  
11 to a not-too-tight canal, and then that alleviates the  
12 leg pain and improves the symptoms. So I think while  
13 your point is very good, I don't think it matters  
14 really whether it's unilateral or bilateral disease,  
15 just so long as you separate the vertebrae.

16 DR. YASZEMSKI: Thank you Dr. White. Dr.  
17 Li?

18 DR. LI: I agree with everything Dr.  
19 Kirkpatrick said. And I think choosing the  
20 appropriate patient population is difficult, not only  
21 for what he said, but we still have this lingering  
22 issue of this variation between center to center of

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1 success rates from 13 to 85 percent.

2 And perhaps a follow-up question to Dr.  
3 White. You know, in the best of cases the numbers  
4 worked out about a little less than 50 percent are  
5 reporting a success rate. Maybe down to 33 percent if  
6 you take out the St. Mary's group. So does that mean  
7 in the patients that are unsuccessful, the device did  
8 not perform its function of providing you enough  
9 separation?

10 DR. YASZEMSKI: Dr. White.

11 DR. WHITE: I don't think we know in every  
12 case why a given patient is not successful. I think  
13 that we know that we have altered the mechanics in a  
14 way to give the patient the possible benefit of being  
15 successful. But I don't think we can know why it  
16 might not be a successful outcome.

17 DR. LI: So you don't believe that some of  
18 the features, for instance, that appeared to tend to  
19 give you a successful result, like having a younger  
20 patient, or things like that, you don't believe those  
21 are actual patient indications that would narrow the  
22 indications for the device?

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1 DR. WHITE: No, I didn't say that. No, I  
2 don't mean to say that.

3 DR. LI: So do you think, knowing what you  
4 know now, would you think that the patient indication  
5 is now narrowed to perhaps a younger population, or  
6 somebody with a certain amount of stenosis, or  
7 anything like that?

8 DR. WHITE: Well, I think the criteria as  
9 has been suggested and has been recommended, given  
10 currently available knowledge is the best set of  
11 indications, and the best set of criteria to determine  
12 whether or not to offer the procedure. That may  
13 change with increased additional clinical experience,  
14 but right now I think this is a very good first  
15 approximation.

16 DR. LI: Thank you. So my short answer is  
17 I agree with Dr. Kirkpatrick. I don't know how you  
18 would determine the appropriate patient population.

19 DR. YASZEMSKI: Thanks Dr. Li. Thank you  
20 Dr. White. Dr. Ellenberg?

21 DR. ELLENBERG: In the beginning of my  
22 presentation I showed a graphic that appeared to

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1 indicate that the patients that had the increased  
2 severity at baseline tended to do better with the X  
3 STOP procedure. And my sense would be that while we  
4 as a panel do not have the data now to look at a  
5 possible stratification by initial severity, FDA could  
6 look at that post panel and perhaps make that  
7 determination on their own. So my sense is, from the  
8 data I've seen that is available in the dataset now,  
9 initial severity might be a way to look at  
10 compartmentalizing the groups that would most benefit  
11 from this procedure.

12 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.  
13 Finnegan?

14 DR. FINNEGAN: Well actually, in deference  
15 to Dr. Kirkpatrick, I think there are a couple of  
16 parameters that have been defined. They did not  
17 appear to have any problems doing this under local  
18 anesthetic, either patient problems or implant  
19 problems. So obviously those patients who could not  
20 tolerate a general anesthetic or a prolonged surgical  
21 procedure, this might in fact be an implant for them.

22 As well, certainly, those patients who are

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1 not going to because of their comorbidities have much  
2 activity post implant might be patients that are also  
3 candidates for this. And given the limited longevity  
4 we have on the implant, perhaps those patients who  
5 have limited longevity. So I would say a patient  
6 population, and I agree with Dr. Ellenberg, because  
7 these are probably the patients that have increased  
8 symptomology, are not good candidates for a surgical  
9 procedure, and are probably not going to put high  
10 demand on it. The data that we have to date I think  
11 would support that.

12 DR. YASZEMSKI: Thank you Dr. Finnegan.  
13 Dr. Rudicel?

14 DR. RUDICEL: I have nothing more to add.

15 DR. YASZEMSKI: Thank you. Dr. Diaz?

16 DR. DIAZ: I generally agree with Dr.  
17 Finnegan, but on this one I don't think I can agree.  
18 Because the population is so non-homogenous. Spinal  
19 stenosis is one of those animals that is a big  
20 wastebasket of people. There is a huge variety of  
21 patients that have stenosis caused by either bony  
22 hypertrophy, facet hypertrophy, synovial enlargement,

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1 hypertrophy of the ligamentum flavum, spondylitic  
2 changes, and not all of them are the same thing. To  
3 provide a one bullet treatment for all of them I  
4 think, in my opinion, is not the right approach.

5           Furthermore, the longevity of these  
6 patients is really one of those things that we need to  
7 be concerned with. There is many of us sitting in  
8 this room right now who have active severe spinal  
9 stenosis and who are asymptomatic. How do we know  
10 that those patients are going to be for one strange  
11 reason or another not going to have a CT scan or MRI  
12 scan of the spine in which they find stenosis, and for  
13 which we provide this X STOP treatment? I am not  
14 comfortable with the definition of the population as  
15 presented, and I don't think we can select the people  
16 based on the criteria given.

17           DR. YASZEMSKI: Thank you Dr. Diaz. Ms.  
18 Maher?

19           MS. MAHER: Well, I don't have anything to  
20 really answer on the (a) section. I would like to  
21 remind the panel that as a whole, this was a clinical  
22 study, and the control group was developed in

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1 conjunction with the FDA. So the decision to use  
2 conservative care of course was a joint decision with  
3 the FDA, and the sponsor going forward.

4 I'd also like the sponsor to elaborate a  
5 little bit on how they came up with the predicted  
6 outcomes. I mean, if we all had a crystal ball and  
7 could predict the outcomes in advance, then none of us  
8 would need jobs. So if they could explain where the  
9 predicted outcomes came from. And I know in their  
10 presentation they went through and showed how things,  
11 you know, if you went back to what was in the  
12 literature and used those criteria things changed a  
13 little bit. If they could just give a brief summary  
14 of that I'd appreciate it.

15 DR. YASZEMSKI: Someone from the sponsor  
16 want to comment on that? How did you come up with the  
17 expected outcome numbers from which the study began?  
18 Dr. Andersson.

19 DR. ANDERSSON: Those numbers were based  
20 on the literature. And in reality, we realized after  
21 we finished the study that they were not appropriate  
22 when you use the stringent criteria that we used. If

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1 we had used different criteria, they would have been  
2 appropriate, and we would have been much closer. As  
3 it turns out, the difference in result actually  
4 increased, and the sample size could actually have  
5 been smaller.

6 DR. YASZEMSKI: Thank you Dr. Andersson.  
7 Dr. Doyle?

8 DR. DOYLE: Nothing to add.

9 DR. YASZEMSKI: Thank you Dr. Doyle. Dr.  
10 Kim?

11 DR. KIM: Nothing to add.

12 DR. YASZEMSKI: Thank you Dr. Kim. Dr.  
13 Naidu?

14 DR. NAIDU: Nothing to add.

15 DR. YASZEMSKI: Thank you. We're going to  
16 go around and answer Question 4(b). Then we'll give  
17 our summary to the FDA, if that would be okay with Dr.  
18 Witten.

19 DR. WITTEN: Yes.

20 DR. YASZEMSKI: And Dr. Holden, can you  
21 read just the (b) part of the question, please?

22 DR. HOLDEN: Given the historical success

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1 rates for laminectomy, please discuss what impact the  
2 effectiveness results of this study have in relation  
3 to our interpretation of the risks and benefits of  
4 treatment with the X STOP device.

5 DR. YASZEMSKI: Thanks Dr. Holden. Dr.  
6 Diaz?

7 DR. DIAZ: As I had mentioned earlier, the  
8 non-homogeneity of the population makes a decision to  
9 proceed with surgery in this group of people very  
10 difficult. Many of the patients that were treated in  
11 this study with what were considered mild to moderate  
12 symptoms in my opinion had severe symptoms that were  
13 incapacitating enough for them to have failed best  
14 available medical treatment, and warranted certainly a  
15 surgical decision. The comparison made with the best  
16 medical treatment available was in my mind the  
17 evaluation of no treatment versus some form of  
18 treatment. In my mind, the comparison should have  
19 been made better, and with a good statistical ability  
20 to validate the procedure, by comparing laminectomy,  
21 which is something that is surgically invasive, can be  
22 minimally invasive as well. Many of our patients can

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1 be treated through relative small incisions, be  
2 admitted to the hospital for the exact length of time  
3 that these patients were admitted, be ambulatory the  
4 night of the surgery with a laminectomy, and in  
5 essence have a relatively blinded ability to assess  
6 these patients. In my mind, the right comparison  
7 should have been with laminectomy. My question to the  
8 sponsor is why was that not the decision made.

9 DR. YASZEMSKI: Thank you Dr. Diaz. Dr.  
10 Andersson?

11 DR. ANDERSSON: Well, we thought long and  
12 hard about this, and had a very difficult decision to  
13 make. When you're comparing a procedure which is  
14 somewhere in between to other alternatives, the choice  
15 of which alternative to use as your comparison group  
16 becomes difficult.

17 There were really three things that moved  
18 us in the direction of the non-operative treatment.  
19 One had to do with the fact that the majority of  
20 patients when they were enrolled in the study were  
21 really not ready for a laminectomy. Their symptoms  
22 were moderate, and although their qualities of life

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1 were significantly impaired in some cases, they were  
2 not looking for a major surgical procedure. And I do  
3 agree that you can do laminectomies as outpatient  
4 procedures or as same-day-home procedures, but they  
5 are still much, much bigger procedures, and you enter  
6 the spinal canal, and it does raise the opportunity of  
7 complications which are not really there when you use  
8 the X STOP device.

9 The second reason was that the salvage  
10 procedure for both non-operative treatment and the X  
11 STOP is a laminectomy. And so we felt that it was  
12 somewhat inappropriate to compare the X STOP to the  
13 salvage procedure for the X STOP.

14 And the third had to do with the risk  
15 profile, which the X STOP is much closer to that of  
16 non-operative treatment than a laminectomy. And so  
17 for those reasons we ended up choosing the non-  
18 operative treatment, went to the FDA, and as stated  
19 previously, had discussions with them about this, and  
20 eventually agreed that that would be the appropriate  
21 comparison.

22 DR. YASZEMSKI: Thank you Dr. Andersson.

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1 Dr. Rudicel, let's come around this way to you this  
2 time. Sorry for the surprise.

3 DR. RUDICEL: I would just add that I  
4 prefer the study design that they had to comparing it  
5 to laminectomies for the reasons that Dr. Andersson  
6 has stated. While it's not a perfect design, and it  
7 certainly presents problems with blinding, I think  
8 that it is a less invasive procedure. And so I  
9 thought it was, that part of it anyway was the way I  
10 would have done it too.

11 DR. YASZEMSKI: Thank you Dr. Rudicel.  
12 Dr. Finnegan?

13 DR. FINNEGAN: I agree with Dr. Diaz.

14 DR. YASZEMSKI: Thank you Dr. Finnegan.  
15 Dr. Ellenberg? It's 4(b).

16 DR. ELLENBERG: I'm sorry, my version is  
17 earlier. I just want to make sure I'm understanding.

18 DR. YASZEMSKI: Would you like a moment to  
19 think about, and I'll come back to you?

20 DR. ELLENBERG: Yes. I pass, and then  
21 come back.

22 DR. YASZEMSKI: Okay. Dr. Li?

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1 DR. LI: I agree with Dr. Diaz.

2 DR. YASZEMSKI: Thank you. Dr.  
3 Kirkpatrick?

4 DR. KIRKPATRICK: I have to be on the  
5 fence. I think a laminectomy control group would have  
6 been an excellent addition to this. I still would  
7 want to see the non-operative control. But to get to  
8 the specifics of the question, I think in perspective,  
9 compared to laminectomy, this option would be one on a  
10 scale of gradually increasing risk but gradually  
11 improving clinical results. I see this as between  
12 non-operative interventions and the success rate of a  
13 laminectomy as far as success, and I see it as between  
14 non-operative treatment and laminectomy as far as  
15 surgical risk.

16 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
17 Dr. Naidu?

18 DR. NAIDU: I have nothing more to add.

19 DR. YASZEMSKI: Thank you. Dr. Kim?

20 DR. KIM: I would concur with Dr.  
21 Kirkpatrick.

22 DR. YASZEMSKI: Thank you. Dr. Doyle?

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1 DR. DOYLE: I agree with Dr. Diaz.

2 DR. YASZEMSKI: Thank you. Ms. Maher?

3 MS. MAHER: Nothing to add.

4 DR. YASZEMSKI: Thank you. Dr. Ellenberg?

5 DR. ELLENBERG: I'm sorry, I have to  
6 apologize. I've been working from a different set of  
7 questions. My sense is that the historical success  
8 rates for the laminectomy are what they are. They are  
9 historical, they are not controlled. And throughout  
10 the readings and preparation for this meeting, I'm not  
11 sure I really ever understood and still don't  
12 understand the question this regards. So I prefer not  
13 to make any comments in regard to this question.

14 DR. YASZEMSKI: Thank you. Entirely  
15 appropriate, thank you. Other comments? Dr. Witten,  
16 Question 4 has, again, as some of the previous  
17 questions, a spectrum of responses. Dr. Diaz  
18 articulated it well when he said this population is  
19 non-homogenous. There are many different subgroups,  
20 if you will, anatomically, that result in the symptoms  
21 we see in spinal surgery patients. Dr. Finnegan,  
22 however, mentioned that she sees from the data

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1 presented some groups that would be appropriate, those  
2 who would have difficulty with general anesthesia,  
3 those who would for other comorbidity reasons be in  
4 increased surgical risk, and other discussers, for  
5 example, talked about the one versus two sides, and  
6 perhaps to stratify the patients by initial severity.

7 Dr. Kirkpatrick, however, I think is in agreement  
8 with Dr. Diaz when he said that there were not a  
9 homogenous subgroup, and that he considers this  
10 somewhere in the middle. It's a little more risky  
11 than non-operative techniques, but not quite as risky  
12 as a formal decompression. However, it's looked at as  
13 another step, perhaps, in the care of these patients.

14 Have we discussed this to your  
15 satisfaction?

16 DR. WITTEN: Yes, thank you.

17 DR. YASZEMSKI: Thank you. We're going to  
18 move on to Number 5. Dr. Holden?

19 DR. HOLDEN: In this study, the protocol  
20 did not define what criteria were to be used in either  
21 group to determine when or whether patients proceeded  
22 to laminectomy. It also did not define whether to

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1 administer additional epidural injections to patients  
2 in the control group. Some patients in the  
3 investigational X STOP group received the control  
4 treatment, epidural injection for pain, rather than  
5 proceeding to laminectomy, and it is not clear whether  
6 success in those patients was due to temporary relief  
7 from the injection, or to the X STOP. Please describe  
8 the potential impact on the interpretation of the  
9 study result of these confounding factors.

10 DR. YASZEMSKI: Thanks very much. We'll  
11 start with Dr. Ellenberg this time, and we'll come  
12 around this way through Dr. Li and Dr. Kirkpatrick.

13 DR. ELLENBERG: My sense in response to  
14 this question is that the lack of a protocol for the  
15 use of either epidurals or laminectomy can be added to  
16 the potential for the informed consent being  
17 optimistic for patients going onto the X STOP  
18 procedure, can be added to the issue of the trial  
19 being unmasked for whatever reasons, and can be added  
20 to the nature of the other outcomes that are  
21 subjective, the self-scoring by patients. So my sense  
22 is that there are a whole host of things that could be

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1 influenced by investigators, could be influenced by  
2 the patients' feeling about what their expectations  
3 are for the X STOP procedure. So in my mind, all of  
4 these things, including the two that are specifically  
5 mentioned here, the use of epidurals and the reasons  
6 for going on to a laminectomy, could have an impact on  
7 the interpretation of this study. However, having  
8 said that, in my going through the data and trying to  
9 simulate what would happen, looking at a multitude of  
10 what-if scenarios, if this were in one extreme or  
11 another extreme, in the end the results appear to be  
12 impressive, and that the difference between the X STOP  
13 and the control group appeared to stay no matter what  
14 I could do with the data. But all of the data are  
15 subjective. So in my view, the interpretation that  
16 the panel considers in terms of the efficacy has to be  
17 tempered by the fact that the foundation for the study  
18 is subjective, and the use of the epidural and the  
19 laminectomy are just two more elements in that vein.

20 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.  
21 Li?

22 DR. LI: I have nothing to add.

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1 DR. YASZEMSKI: Thank you Dr. Li. Dr.  
2 Kirkpatrick?

3 DR. KIRKPATRICK: I think the key issue in  
4 this question in my mind is the fact that I would have  
5 considered an epidural after the X STOP as a failure  
6 period. So I would have taken those as being an  
7 endpoint. Because if the X STOP is doing what it's  
8 supposed to do, the epidural wouldn't ever be required  
9 unless they can demonstrate as the sponsor that they  
10 were doing an epidural block for a different level  
11 than the X STOP was intended for, which I did not see  
12 any data to show any specificity with the epidurals.  
13 I couldn't tell whether they were transforaminal at  
14 particular levels and that sort of thing. So I think  
15 that's not going to be answerable.

16 Whether that is a particular thing that's  
17 a high enough incidence to change the overall results  
18 I can't tell you, but my sense is it is not. And as  
19 far as the laminectomy failure, or the steps going to  
20 laminectomy, I think that is too general of an  
21 indication with regard to individual patients and the  
22 multiple individual surgeons that has to be reserved

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1 on a one-to-one basis. And so I don't think they  
2 could standardize when and whom would proceed to  
3 laminectomy. So I don't fault that at all as far as  
4 the study design. Thank you.

5 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
6 I'd like to give an opportunity. Would anybody from  
7 the sponsor like to address the epidurals after X  
8 STOP? If you do, please do so. If not, we'll move  
9 on. Dr. Zucherman.

10 DR. ZUCHERMAN: As Dr. Kirkpatrick said,  
11 really the timing of these things was left up to the  
12 patient-doctor relationship. There were 10 patients  
13 who had one epidural in the control group and  
14 proceeded on to laminectomy. Seven of those occurred  
15 within two months, and the other three occurred after  
16 a year. And in the rest of the control group they had  
17 varying numbers of epidurals and the length of time --  
18 this is in the group that went on to laminectomy --  
19 the length of time reflects the number of epidurals  
20 they had because they got a period of relief after  
21 them. And likewise for a decision to go on to  
22 laminectomy, if the conservative treatment was not

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1 being effective, the epidurals weren't effective, a  
2 patient could proceed to laminectomy at his  
3 discretion.

4 In the cases of the X STOP groups who  
5 received epidurals, there were eight. Six of those  
6 were failures, and the only two that weren't failures  
7 were patients who both had motor vehicle accidents,  
8 had an epidural. They were successes before the  
9 accident. After their shots, they recovered and  
10 regained success at 2-year follow-up. And if you take  
11 them out of the database, it still remains very  
12 strongly statistically significant.

13 DR. YASZEMSKI: Thanks Dr. Zucherman. Dr.  
14 Naidu?

15 DR. NAIDU: I have nothing more to add.

16 DR. YASZEMSKI: Thank you. Dr. Kim?

17 DR. KIM: I just wanted to reemphasize  
18 that I agree with Dr. Ellenberg about the subjective  
19 nature of this study. But if you look at the X STOP  
20 patients that had this, only two of them are  
21 considered in the success rate. So I agree with Dr.  
22 Kirkpatrick that it probably wouldn't have made a

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1 difference. And in the end despite this flaw, the  
2 results are probably the same, that the X STOP did  
3 provide some benefit.

4 DR. YASZEMSKI: Thanks Dr. Kim. Dr.  
5 Doyle?

6 DR. DOYLE: I have nothing to add.

7 DR. YASZEMSKI: Thank you. Ms. Maher?

8 MS. MAHER: Nothing to add.

9 DR. YASZEMSKI: Thank you. Dr. Diaz?

10 DR. DIAZ: I agree with Dr. Kirkpatrick  
11 and the issues that are being considered in this  
12 question are bothersome in the aggregate of the  
13 inconsistencies, or the several inconsistencies that  
14 exist in this study.

15 DR. YASZEMSKI: Thank you Dr. Diaz. Dr.  
16 Rudicel?

17 DR. RUDICEL: I agree with Dr.  
18 Kirkpatrick.

19 DR. YASZEMSKI: Thank you. Dr. Finnegan?

20 DR. FINNEGAN: The only thing I would add  
21 is that this is perhaps one area where doing a further  
22 follow-up from the two years may give more information

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1 and be more of a help.

2 DR. YASZEMSKI: Thanks Dr. Finnegan.

3 Other comments?

4 DR. ELLENBERG: Yes, I'm sorry.

5 DR. YASZEMSKI: Dr. Ellenberg?

6 DR. ELLENBERG: It seems to me that it's  
7 potentially possible, and I can't be secure in this,  
8 that if you looked at the patients that went on to  
9 laminectomy in both the control group and the X STOP  
10 group sequentially over time, and you looked at the  
11 measurements for the three components of the ZCQ  
12 score, it may be informative to the FDA post panel  
13 deliberations to see whether or not there's any nature  
14 that we can glean from the succession of scores of  
15 both the physical and severity and the satisfaction  
16 levels over time that would distinguish between the  
17 control group and the X STOP group in terms of what  
18 actually happened in this trial with regard to who is  
19 chosen to have the laminectomy. But obviously we  
20 don't have that here.

21 DR. YASZEMSKI: Thanks Dr. Ellenberg.

22 Further comments? Dr. Witten, with respect to

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1 Question Number 5, Dr. Ellenberg's summary, which I  
2 think was confirmed by the other comments, was that  
3 there are a host of confounding factors. The two that  
4 are listed here are just two additional ones to add to  
5 the list. He indicated, though, that after looking at  
6 many what-if situations, the results were still the  
7 same. Dr. Kirkpatrick commented that the epidural  
8 after X STOP should be a failure, and we had a  
9 description and a discussion of that by the sponsor.  
10 And Dr. Finnegan added that perhaps this is one  
11 question which further follow-up past two years might  
12 yield results. However, the overall conjecture is  
13 that this is a subjective endpoint, and there are many  
14 confounding factors.

15 Have we discussed this adequately from  
16 your perspective at FDA?

17 DR. WITTEN: Yes, thanks.

18 DR. YASZEMSKI: Thank you. We're going to  
19 move on to Number 6. Dr. Holden?

20 DR. HOLDEN: Under CFR 860.7(d)(1), safety  
21 is defined as "reasonable assurance based on valid  
22 scientific evidence that the probable benefits to

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1 health under conditions of the intended use when  
2 accompanied by adequate directions for use and  
3 warnings against unsafe use outweigh any probable  
4 risks." Do the clinical data in the PMA provide  
5 reasonable assurance that the device is safe?

6 DR. YASZEMSKI: Thanks Dr. Holden. We're  
7 going to start with Dr. Naidu and come around this way  
8 through Dr. Kirkpatrick. Dr. Naidu?

9 DR. NAIDU: Based on the valid scientific  
10 evidence, in this study it's quite obvious that it's  
11 based on subjective evidence, which is mainly the ZCQ  
12 scores. Based on this, my thoughts are that the  
13 events related to device or implantation were few or  
14 relatively minor. And I think that it could be  
15 considered reasonable for such a procedure as Dr.  
16 Kirkpatrick presented in his presentation. And life-  
17 threatening complications appeared to be more related  
18 to patient population than intervention. So based on  
19 the subjective scientific evidence, I think it's  
20 reasonably safe.

21 DR. YASZEMSKI: Thank you Dr. Naidu. Dr.  
22 Kirkpatrick?

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1 DR. KIRKPATRICK: I think that the answer  
2 to the question 'is it safe' the answer is yes. But I  
3 do have to put an asterisk by that, and modify the  
4 definition of "intended use" to "appropriate use."

5 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
6 Dr. Li?

7 DR. LI: I'm going to agree with that.

8 DR. YASZEMSKI: Thank you Dr. Li. Dr.  
9 Ellenberg?

10 DR. ELLENBERG: My sense is that this  
11 device is safe. But the regulations ask us to weigh  
12 the safety against the efficacy in this particular  
13 question. So I'm not sure until we answer Question 7  
14 that we can definitively respond to Question 6.

15 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.  
16 Finnegan?

17 DR. FINNEGAN: I have to ask him, did you  
18 go to law school? That was a great answer.

19 (Laughter)

20 DR. FINNEGAN: I agree with Dr. Naidu.

21 DR. YASZEMSKI: Thank you. Dr. Rudicel?

22 DR. RUDICEL: I think the device is safe.

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1 DR. YASZEMSKI: Thank you. Dr. Diaz?

2 DR. DIAZ: I agree with Dr. Kirkpatrick.

3 DR. YASZEMSKI: Thank you. Ms. Maher?

4 MS. MAHER: I think the device is safe.

5 DR. YASZEMSKI: Thank you. Dr. Doyle?

6 DR. DOYLE: I agree, simply because it  
7 hasn't been proven unsafe.

8 DR. YASZEMSKI: Thank you Dr. Doyle. Dr.  
9 Kim?

10 DR. KIM: I would agree with Dr.  
11 Kirkpatrick.

12 DR. YASZEMSKI: Thanks very much. Other  
13 comments? Dr. Witten?

14 DR. WITTEN: Thank you.

15 DR. YASZEMSKI: Thank you. Number 7.

16 DR. HOLDEN: Under CFR 860.7(e)(1),  
17 effectiveness is defined as "reasonable assurance that  
18 in a significant portion of the population, the use of  
19 the device for its intended uses and conditions of use  
20 when accompanied by adequate directions for use and  
21 warnings against unsafe use will provide clinically  
22 significant results. Do the clinical data in the PMA

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1 provide reasonable assurance that the device is  
2 effective?

3 DR. YASZEMSKI: Thanks Dr. Holden. Dr.  
4 Li, and we're going to go around through Dr.  
5 Ellenberg.

6 DR. LI: There's enough ambiguous words in  
7 here to make any lawyer happy. I guess the issues  
8 here are the judgment calls, right? They're asking  
9 for a reasonable assurance, significant portions of  
10 the population, adequate directions, and clinically  
11 significant results, none of which have hard  
12 definitions. So that being said, as far as the device  
13 goes, I think the success rate is very low. Even  
14 including the St. Mary's population, the success rate  
15 is 45 percent, less than 50 percent. If you take the  
16 St. Mary's group out because it's so much higher than  
17 all the rest, the success rate is down to one-third.  
18 And you superimpose upon that we're not exactly sure  
19 what the best patient population is that benefits from  
20 this particular result. So it seems like at best you  
21 have kind of one chance in three of having improved  
22 yourself. Now, I think it's safe because it doesn't

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1 seem to cause the patient any harm if it doesn't work.

2 So it's safe in that regard. And maybe it's a good  
3 adequate mid-step like Dr. Kirkpatrick said. But it  
4 seems to me, from the data in and of itself, based on  
5 the success rates, that I don't believe this device is  
6 particularly effective.

7 DR. YASZEMSKI: Thanks Dr. Li. Dr.  
8 Ellenberg?

9 DR. ELLENBERG: I will concur with Dr. Li.

10 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.  
11 Finnegan?

12 DR. FINNEGAN: I don't know if it's  
13 effective or not because I don't think the clinical  
14 data in this PMA gives us that information.

15 DR. YASZEMSKI: Thanks Dr. Finnegan. Dr.  
16 Rudicel?

17 DR. RUDICEL: I think we're dealing with a  
18 problem that has a low success rate with other, with  
19 laminectomies or other ways of treating it. So while  
20 the success rates are low, I think we're dealing with  
21 a problem that doesn't have the normal types of  
22 success rates that we like to see, certainly in

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1 orthopedics. But I would say with that caveat that I  
2 think the device is effective.

3 DR. YASZEMSKI: Thank you Dr. Rudicel.  
4 Dr. Diaz?

5 DR. DIAZ: I concur with Dr. Li. I don't  
6 believe that the sponsors have presented to my  
7 satisfaction the fact that there is a significant  
8 proportion of the population that is benefited by this  
9 device. The population, as we heard earlier by the  
10 sponsors themselves, constitutes approximately an  
11 annual incidence of 700,000 patients. The non-  
12 homogeneity of the population as such, that a group of  
13 200 patients that they started with and came down to  
14 170. If we put into it all the varieties of possible  
15 etiological reasons, we cannot have a statistically  
16 meaningful analysis for any of them. So in my mind,  
17 the significant component of the definition is not  
18 met.

19 Furthermore, I cannot think of a patient  
20 who is more grateful than a patient with spinal  
21 stenosis who has had a laminectomy. People who have  
22 spinal stenosis literally spring out of bed and kiss

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1 you they feel so much better after an operation. And  
2 I can't imagine that based on what I have seen as Dr.  
3 Li indicated that a third of these patients get  
4 better, that this is really achieving the efficacy  
5 that we are asked to opine on. In my assessment, the  
6 efficacy assessment has not been met.

7 DR. YASZEMSKI: Thank you Dr. Diaz. Ms.  
8 Maher?

9 MS. MAHER: Well, I'd like to start by  
10 reminding everybody that we're actually going to  
11 alternately be talking about a risk versus benefit,  
12 and that's why -- and it has to be safe and effective.

13 But it is a risk-benefit analysis that we're looking  
14 at. This also gets to the question that I asked  
15 earlier of what does a 0.5 change really mean, even if  
16 it is in only 33 percent of the population. And if as  
17 Dr. Kirkpatrick said this is a good potential mid-step  
18 in between conservative care and laminectomy, is it  
19 the right way to consider going? And if the sponsor  
20 has any more information that they want to provide us  
21 on what the 0.5 meant. And I understand it has to be  
22 subjective, and it's not a hard number or a hard

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1 thing, but for a patient who's had a laminectomy, it  
2 is a very risky procedure, a relatively risky  
3 procedure, a bigger procedure than this one. So is  
4 this a good mid-step? And I think at least for the 33  
5 percent of the population that were successes, this  
6 was effective.

7 DR. YASZEMSKI: Thanks Ms. Maher. Dr.  
8 Andersson?

9 DR. ANDERSSON: I would be happy to  
10 address that more fully. I think what hurts treatment  
11 studies in spinal stenosis generally is that the  
12 results are generally so poor, almost no matter what  
13 treatment you apply as we showed in some of our slides  
14 earlier. What also hurts us is the aggregate score,  
15 because if you look at the results on the pain side  
16 it's almost 70 percent, and if you look at them on the  
17 function side it's almost 70 percent. It's a little  
18 over 70 percent.

19 Thinking about a grateful patient, you  
20 remember Ms. Miller, our first patient this morning.  
21 Her improvement was 0.8. The average for our patients  
22 was 0.99. Certainly she is an example of a very

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1 grateful patient. 0.5 applies to all questions in  
2 each domain. And typically the patients don't change  
3 by 0.5 for every question. More often there is a  
4 change, for example, in pain from severe to mild. But  
5 these patients may still have mild pain every day,  
6 which is another question. In the physical function  
7 domain, a patient may move from walking 50 feet to  
8 more than two miles, or from shopping always in pain  
9 to occasionally in pain. And these are typical  
10 examples of the results with this device.

11 DR. YASZEMSKI: Thanks Dr. Andersson. Dr.  
12 Doyle?

13 DR. DOYLE: I don't have anything to add.

14 DR. YASZEMSKI: Thank you. Dr. Kim?

15 DR. KIM: This PMA is unfortunately  
16 burdened with a lot of problems, particularly with  
17 bias during the randomization and things that we have  
18 discussed. But I think that the success criteria, my  
19 sense is that it's very stringent. In fact, too  
20 stringent. So I'm not too worried about the success  
21 rate being one-third or 0.5 because that number can be  
22 varied depending on how strict you want to be with the

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1 definition of success.

2 To get at this question is this treatment  
3 effective, I think a number of different, if I heard  
4 correctly, a number of different statistical tests  
5 were done for worst case scenarios. And in the end,  
6 the X STOP device still wins out. So I don't know how  
7 much better patients are going to be, but it looks  
8 like they're going to be better. And then I combine  
9 that with its safety profile, which I think is very  
10 safe. So it's a close call, but I feel that it is  
11 effective, since the benefits outweigh the potential  
12 risks.

13 DR. YASZEMSKI: Thanks Dr. Kim. Dr.  
14 Naidu?

15 DR. NAIDU: Based on the ZCQ scores, the  
16 sponsors have shown definitively that the device is  
17 effective based on the subjective criteria. Again,  
18 Dr. Ellenberg clarified this for us. 0.5 improvement,  
19 albeit minimum, is actually one standard deviation  
20 improvement. And he has shown you distribution  
21 curves, and he has even gone up to a stricter criteria  
22 of improvement by one point, and it still didn't make

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1 a difference. And it showed definitively that the X  
2 STOP was superior based on the ZCQ criteria.  
3 Unfortunately, we don't have any objective criteria.  
4 But based on the clinical definition of this study,  
5 based on the clinical criteria, I'd have to conclude,  
6 even though the success rates are low, I would have to  
7 conclude that it is effective.

8 DR. YASZEMSKI: Thank you Dr. Naidu. Dr.  
9 Kirkpatrick?

10 DR. KIRKPATRICK: Well, being from Alabama  
11 I have to put this in perspective of what my patients  
12 experience. It sounds to me like what this device  
13 might enable some of my patients to do is instead of  
14 getting their stenosis symptoms at the end of their  
15 shopping at the supermarket, they would get it at the  
16 end of their shopping at Wal-Mart. Or perhaps, if  
17 they're getting their pain at the end of shopping at  
18 Wal-Mart, they can now go to the mall. For a large  
19 number of my patients that's a significant  
20 improvement. However, I can tell you that most of  
21 them would feel it probably wouldn't be worth a  
22 surgical procedure to get that.

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1           The second thing about my patients is they  
2 understand a couple of things about percentage  
3 chances. They understand 50/50 because they toss a  
4 coin. They understand about the top 15 percent,  
5 because NASCAR interviews at the end of the races  
6 involve the top five drivers, and that's about the top  
7 15 percent in the race. So when I give them an odd of  
8 being in the top five suggestive of, as I mentioned  
9 earlier, a joint replacement where they've got a 90  
10 percent change of significant improvement over a long  
11 period of time, they're willing to put up with  
12 surgical risk. When I talk to them about a 50/50  
13 shot, they're not so excited. Basically, from what  
14 I'm hearing the sponsors tell us is that 45 to 50  
15 percent of the patient population as defined, which is  
16 all elements of lumbar stenosis, may see a 25 percent  
17 improvement in their function and their symptom  
18 severity scores according to the recomputation of our  
19 Table Number 35. So I appreciate your help on making  
20 sure that's correct.

21           So if we look at that spectrum, I don't  
22 see from a patient standpoint that we have enough

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1 effectiveness to demonstrate the balance against the  
2 safety. In addition, the stratification of the  
3 results, I think, in different areas of lumbar spinal  
4 stenosis leads great promise, and I would very much  
5 like to hear if we can define a specific area of  
6 lumbar stenosis that does benefit better than a  
7 general category of lumbar stenosis. In other words,  
8 specific indication of a regional anatomic deficit  
9 that we can improve with this device. Because I  
10 believe it's an innovative device and has great  
11 promise.

12 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
13 Other comments? Dr. Witten, have we discussed this to  
14 the FDA's satisfaction?

15 DR. WITTEN: Yes, thank you.

16 DR. YASZEMSKI: Thanks so much, Dr.  
17 Witten. We're going to proceed now to the second open  
18 public hearing, now that we've discussed the FDA  
19 questions. Is there anyone else in the room who  
20 wishes to address the panel at this time? If so,  
21 please come forward to the podium. Seeing none, we're  
22 going to proceed to the FDA and sponsor summations.

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1 I'll ask the sponsors -- the sponsors have indicated  
2 to me that they have an answer to Dr. Kirkpatrick's  
3 earlier question regarding the table, and please  
4 include that in your summation when you come up, if  
5 you would please. FDA?

6 DR. WITTEN: Perhaps can we have a 10-  
7 minute break before the summation?

8 DR. YASZEMSKI: Yes, ma'am. We'll have a  
9 10-minute break. It's now 2:25. We'll pick up again  
10 at 2:35. Thanks.

11 (Whereupon, the foregoing matter went off  
12 the record at 2:26 p.m. and went back on the record at  
13 2:38 p.m.)

14 DR. YASZEMSKI: Alright folks. If I could  
15 ask everybody to wander to your seats, we'll go ahead  
16 and get started. As I said, we were going to start  
17 with presentations by both, but the FDA will not give  
18 a summation. We're going to proceed right to the  
19 sponsor summation. If the sponsors are ready, please  
20 do come forward and give your summary. Dr. Andersson?

21 DR. ANDERSSON: Thank you very much, Mr.  
22 Chairman and members of the panel. Outcomes of

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1 clinical studies depends on your measurement tool. As  
2 I showed in my presentation, result of non-operative  
3 treatment in our study was similar to that reported in  
4 the literature, and yet we had only a four percent  
5 success rate by our criteria. Similarly, the X STOP  
6 results are similar to those of laminectomy reported  
7 in the literature, and yet the aggregate was only  
8 about 40 percent. Despite the high requirements, we  
9 met our primary endpoint as we had agreed upon with  
10 the FDA. We anticipated a difference of 22.5 percent  
11 between the groups, and ended up with a 40 percent  
12 difference. The patient satisfaction was 70 percent,  
13 symptom severity improved by 58.3 percent.

14 We did choose non-operative treatment as  
15 control, and I would choose non-operative treatment as  
16 my control if I were to redo this study, for the  
17 reasons that I mentioned before. The patient  
18 population, while not homogenous, really can't be  
19 homogenous because spinal stenosis is, as we've heard  
20 from panel members, such a varying disease entity,  
21 with all sorts of presentations clinically, and with  
22 all sorts of dimensions on the spinal canal

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1 addressable by different types of procedures.

2           The X STOP is a very innovative device.  
3 It is unusual in the sense that it addresses a problem  
4 within the spinal canal without entering the spinal  
5 canal. It's also unusual in the sense that it leaves  
6 the door open for additional procedures should they be  
7 necessary. And so we're not closing the door as with  
8 the laminectomy, where we really have no return. To  
9 provide patients the opportunity given the low risk in  
10 my opinion would be a major step in the right  
11 direction. Thank you for the opportunity.

12           DR. YASZEMSKI: Thanks very much Dr.  
13 Andersson. I'd also like to ask, Dr. Yerby did you  
14 discuss with Dr. Kirkpatrick the numbers. And if you  
15 haven't and would like to do so, now is -- just a  
16 closing answer to a prior question.

17           DR. YERBY: Sure. Based on your question  
18 earlier, I recalculated everything that we discussed  
19 and I agree with what you said earlier.

20           DR. YASZEMSKI: Okay, thanks Dr. Yerby.  
21 Ms. Scudiero will now read the three possible panel  
22 recommendations options for pre-market approval

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1 applications. Ms. Scudiero?

2 MS. SCUDIERO: The Medical Device  
3 Amendments to the Federal Food, Drug and Cosmetic Act,  
4 as amended by the Safe Medical Devices Act of 1990,  
5 allows the Food and Drug Administration to obtain a  
6 recommendation from an expert advisory panel on  
7 designated medical device pre-market approval  
8 applications, PMAs, that are filed with the agency.  
9 The PMA must stand on its own merits, and your  
10 recommendation must be supported by the safety and  
11 effectiveness data in the application, or by  
12 applicable publicly available information. Safety is  
13 defined in the act as the reasonable assurance based  
14 on valid scientific evidence that the probable  
15 benefits to health under the conditions of intended  
16 use outweigh any probable risks. Effectiveness is  
17 defined as reasonable assurance that in a significant  
18 portion of the population, the use of the device for  
19 its intended uses and conditions of use when labeled  
20 will provide clinically significant results.

21 Your recommendation options for the PMA  
22 vote are as follows. Approval, if there are no

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1 conditions attached. Approvable with conditions: the  
2 panel may recommend that the PMA be found approvable  
3 subject to specific condition, such as patient or  
4 physician or patient education, labeling changes, or a  
5 further analysis of existing data. Prior to voting,  
6 all the conditions should be discussed by the panel.  
7 Not approvable: the panel may recommend that the PMA  
8 is not approvable if the data do not provide a  
9 reasonable assurance that the device is safe, or if a  
10 reasonable assurance has not been given that the  
11 device is effective under the conditions of use  
12 prescribed, recommended, or suggested in the proposed  
13 labeling. Following the voting, the chair will ask  
14 each panel member to present a brief statement  
15 outlining the reasons for his or her vote.

16 DR. YASZEMSKI: Thanks Ms. Scudiero. Are  
17 there any questions from the panel members about these  
18 voting options before I ask for a main motion on the  
19 approvability of this PMA? Seeing none, I'm going to  
20 ask for a motion. I'm going to ask our lead clinical  
21 reviewer, Dr. Kirkpatrick, if he has a motion. Dr.  
22 Kirkpatrick?

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1 DR. KIRKPATRICK: I can put forth the  
2 motion, sir.

3 DR. YASZEMSKI: Please do.

4 DR. KIRKPATRICK: And if I may, I will  
5 give my reasons and then my motion so that my vote  
6 would be clear in my motion. While verified in the  
7 cadaver model, the concept of preventing the narrowing  
8 of the canal, lateral recess, and foramen was not  
9 verified in the clinical study. And while the  
10 specific population in my mind has not been adequately  
11 defined as far as who will benefit from this device,  
12 and the improvement in the device seemed reasonably  
13 small, although definitely measurable, I would move  
14 not approvable, with all due respect to my colleagues  
15 and friends in the sponsor's area, and my  
16 encouragement to them to define those areas so that we  
17 can have this device available for the appropriate  
18 patients.

19 DR. YASZEMSKI: Okay, we have a motion for  
20 not approvable. And what we'll need to do is ask if  
21 there is a second for that motion.

22 DR. DIAZ: Second.

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1 DR. YASZEMSKI: We have a second so we'll  
2 no vote on that motion. I'll go around the room and  
3 ask everybody to vote. If you vote for the motion,  
4 you are voting to not approve this device. If this  
5 motion passes, then this panel's work is done. If  
6 not, I'll then ask Dr. Kirkpatrick for an alternate  
7 motion. We have a motion for not approvable. Dr.  
8 Kirkpatrick, you made it, and I'm going to just ask  
9 you formally to state your vote.

10 DR. KIRKPATRICK: My vote would be for the  
11 motion, and the reasons are in the motion.

12 DR. YASZEMSKI: And we're going to go  
13 around the room. I'm going to go around the room  
14 counter-clockwise and go to Dr. Naidu. Dr. Naidu?

15 DR. NAIDU: I will -- I'm not with the  
16 motion.

17 DR. YASZEMSKI: You're voting against the  
18 motion?

19 DR. NAIDU: I'm voting against the motion.

20 DR. YASZEMSKI: Dr. Naidu votes no,  
21 against the motion. Dr. Kim?

22 DR. KIM: Even though I agree with so many

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1 things that Dr. Kirkpatrick states, and the fact that  
2 he's so thorough and thoughtful, unfortunately I will  
3 have to disagree with this motion.

4 DR. YASZEMSKI: Dr. Kim votes against the  
5 motion. Dr. Diaz?

6 DR. DIAZ: For the motion.

7 DR. YASZEMSKI: Dr. Diaz votes for the  
8 motion. Dr. Rudicel?

9 DR. RUDICEL: I vote against the motion.

10 DR. YASZEMSKI: Dr. Rudicel votes against  
11 the motion. Dr. Finnegan?

12 DR. FINNEGAN: I vote for the motion.

13 DR. YASZEMSKI: Dr. Finnegan votes for the  
14 motion. Dr. Ellenberg?

15 DR. ELLENBERG: I vote for the motion.

16 DR. YASZEMSKI: Dr. Ellenberg votes for  
17 the motion. Dr. Li?

18 DR. LI: For the motion.

19 DR. YASZEMSKI: Dr. Li votes for the  
20 motion. The votes is 5 for the motion, and 3 against  
21 the motion. The motion for non-approvability passes.

22 I'd like to go around the room now and ask

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1 everybody to comment on their reasons. Dr.  
2 Kirkpatrick, you've already given a description of  
3 your reasons. If you'd like to add to that, please do  
4 so.

5 DR. KIRKPATRICK: I don't really have an  
6 addition to my reasons, just a further encouragement  
7 to precisely define which of my patients will benefit  
8 from this device.

9 DR. YASZEMSKI: Thank you. Dr. Naidu, you  
10 voted against the motion. Your comments?

11 DR. NAIDU: Yes, I have several. I think  
12 it is a less invasive procedure, it's a middle of the  
13 road approach. I'm not a spine surgeon, but it makes  
14 sense that this a safe device. I mean, the biggest  
15 concern here is dislodgement of the device  
16 posteriorly. And provided the sponsor was going to  
17 set up a training camp to do this, I think that this  
18 is a good middle of the road approach because the  
19 sponsor met the primary endpoints, three out of four  
20 primary endpoints. They met the physical function  
21 measurements by the ZCQ at 24 months. Symptom  
22 severity was also significantly improved at 24 months.

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1 Patient satisfaction was also improved. And the only  
2 thing that really they did not demonstrate is  
3 radiographic efficacy. And so I thought it was  
4 approvable, based on the data presented.

5 DR. YASZEMSKI: Thanks Dr. Naidu. Dr.  
6 Naidu brought up an important point that I'd like to  
7 ask the remaining panel members to address when it  
8 becomes their turn. And that is since the panel voted  
9 for not approvable, please make a comment to the FDA  
10 and to the sponsor as to what the sponsor needs to do  
11 to move the application from non-approvable to  
12 approvable. Dr. Naidu has indicated that he thinks  
13 radiographic confirmation would be necessary. And  
14 when we come back around, since I didn't specifically  
15 ask Dr. Kirkpatrick and Dr. Naidu, I'll ask them again  
16 if they have additional comments. Dr. Naidu, is that  
17 the only thing you feel the sponsor needs to do to  
18 make this approvable, get radiographic confirmation?

19 DR. NAIDU: I'm not even so sure that  
20 should be a strict criteria. All I'm saying is it's  
21 approvable mainly because the primary efficacy  
22 endpoints were met.

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1 DR. YASZEMSKI: Okay. Thank you. Dr.  
2 Kim?

3 DR. KIM: There are a number of issues  
4 related to this PMA, the most significant of which is  
5 the potential bias that we've discussed on numerous  
6 occasions that could come from both the physician and  
7 the patient. However, from what I can tell there  
8 appears to be a reasonable level of certainty that  
9 this device does provide some improvement in symptoms.  
10 And we saw this in various different statistical  
11 analyses. Furthermore, the device makes intuitive  
12 sense in the mechanism of action. It's simple, and it  
13 addresses something that we see clinically in that  
14 patients do better when they're bent forward. It's  
15 also minimally invasive, and compared to traditional  
16 open laminectomy it is far safer. I think we can all  
17 agree on that.

18 I care for many patients that are  
19 symptomatic enough that it affects their quality of  
20 life. I live in California, and I think people may  
21 want to be a lot more active than people from other  
22 parts of the country. That may or may not be true,

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1 but I do care for a lot of patients that for one  
2 reason or another do not want to undergo laminectomy,  
3 but at the same time epidural steroid injections are  
4 not enough to improve their quality of life. I think  
5 this device offers an important option in the  
6 treatment of that patient with spinal stenosis that  
7 wishes to avoid the general anesthesia and potential  
8 risks of laminectomy. For that reason, I voted  
9 against the non-approvable motion.

10 And thinking about what would make this  
11 more approvable, from the standpoint of the panel as a  
12 whole. Obtaining 3-year data to rule out concerning  
13 issue of the loss of benefit would be one. But  
14 probably the most important thing is to further  
15 analyze the data to address the potential biases that  
16 are raised. Maybe there's something within the  
17 analysis that wasn't looked at that can convince the  
18 panel that the biases that we looked at and the  
19 subjectivity is not as concerning.

20 DR. YASZEMSKI: Thanks Dr. Kim. I'm going  
21 to go around to the voting panel members first, then I  
22 want to end up with our industry and consumer

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1 representatives. I'm going to go to Dr. Diaz.

2 DR. DIAZ: From my perspective I believe  
3 that the device is an ingenious tool that will have  
4 future applications. My concern was that the study  
5 had too many inconsistencies. Far too many questions  
6 were not answered to my satisfaction. The evaluation  
7 procedures were limited to subjective criteria.  
8 Unfortunately within those evaluations, many of these  
9 patients either during or through the course of the  
10 evaluation became not mentally capable of answering  
11 those questions themselves, so that further undermined  
12 my ability to say that the subjective criteria that  
13 were already a concern in my mind were of any value at  
14 the end of the procedure. There was no assessment of  
15 objective radiographic criteria that could answer to  
16 my complete satisfaction that the process that you  
17 were trying to prove existed really happened. There  
18 were no MRIs, no CT scans that showed me that the  
19 foramina or the canal became larger with your tool,  
20 other than the seven fixed specimens you had. So in  
21 the future I do believe that there is an application  
22 for this tool. I do believe that there will be a

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1 limited number of people that will benefit from it. I  
2 think you need to parse out the population in sections  
3 of components so that you can really figure out for  
4 whom this device will be useful.

5           The disparity between the leading center  
6 and the other centers in my mind creates a huge  
7 question. There shouldn't be that huge difference  
8 between the designers and developers, and the rest of  
9 the people. It has to be a pretty homogenous  
10 population, or a pretty homogenous result for me to  
11 believe that the answer is there. So further  
12 definition of the population, further assessment with  
13 objective criteria, greater precision in the  
14 application of what it is you're trying to do, and a  
15 comparison with a surgical procedure. Laminectomy  
16 does not have to be a mutilating procedure.  
17 Laminectomies can be done with micro techniques. They  
18 can be done through limited access. And you can have  
19 exactly the same results with laminectomies as you do  
20 with a minimally invasive procedure otherwise.  
21 Laminectomies can be done other spinal anesthesia.  
22 They don't need to be done under general. So many of

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1 these things, I think, can be addressed in a different  
2 manner. I do believe you have a useful tool, you just  
3 need to refine its application.

4 DR. YASZEMSKI: Thank you Dr. Diaz. Dr.  
5 Rudicel?

6 DR. RUDICEL: I don't have a lot to add,  
7 except that I still like the comparison of a non-  
8 operative to this technique because I think it is the  
9 middle of the road, and it is good that it's much less  
10 invasive. I think we know a lot about laminectomies,  
11 and so I think your study design is a good one.  
12 Albeit as I mentioned there are known problems with  
13 that kind of a study, but I think you tried to  
14 surmount them in the best way that you could.

15 Probably the best area where you could  
16 improve something is to try to stratify those patients  
17 who did well to figure out who those patients were. I  
18 also think using subjective criteria is an excellent  
19 way, if you have the right tool, and I don't know  
20 enough about the tool that you used, but it seems that  
21 is what's used in spinal stenosis studies, and has  
22 been used. So I would just be sure that your tool is

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1 the most appropriate one, and certainly the SF-36 has  
2 been used in lots of orthopedic studies now. And I  
3 think the subjective approach is very good because we  
4 all know that we don't treat x-rays, although  
5 radiographic data to substantiate what you've done  
6 would be helpful. So other than that I don't have.

7 DR. YASZEMSKI: Okay, thank you Dr.  
8 Rudicel. Dr. Finnegan?

9 DR. FINNEGAN: First of all I want to  
10 reiterate that this is incredibly innovative and  
11 creative, and you need to be encouraged to continue to  
12 work on this. I do think there is going to be a  
13 patient population that this turns out to be useful  
14 for, but I don't think you've outlined that. I think  
15 you tried to take too big a patient population on.

16 I also think that not to beat a dead  
17 horse, but the biomechanics or the biological response  
18 to altered biomechanics are going to be important for  
19 two reasons. One, it'll help with your patient  
20 population definition, but it may also be that if you  
21 alter the material properties of your implant, that  
22 you may have different patient populations that you

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1 can work with. So I will beat that dead horse and  
2 tell you I really think you need to look at it.

3 I actually wonder if including a group  
4 with laminectomies so that you can demonstrate the  
5 difference between the conservative, your implant, and  
6 the laminectomies might not improve things. And I  
7 also agree you need some radiological backup.

8 DR. YASZEMSKI: Thanks Dr. Finnegan. Dr.  
9 Ellenberg?

10 DR. ELLENBERG: I believe all of my  
11 concerns and suggestions for improvements with one  
12 exception have been covered by those voting in favor  
13 and those voting against the motion. The only point I  
14 would raise which I didn't raise during my  
15 presentation or discussion before has to do with the  
16 validation of the Zurich scale. My understanding in  
17 reading the original paper was that was validated at  
18 six months, and the current study is using this  
19 measure as a primary endpoint at two years. And I  
20 don't know if that has been validated, and I'm not  
21 just aware of it two months out.

22 DR. YASZEMSKI: Thanks Dr. Ellenberg. Dr.

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1 Li?

2 DR. LI: I take no pleasure in voting  
3 against this device, because I think it's very clever  
4 in its design. I like the fact that it's non-  
5 invasive. And best of all, I kind of like that it's  
6 got a very clear potential mechanism for benefit, that  
7 is, reducing the amount of flexion-extension. That  
8 being said, I'm very frustrated that there's no  
9 clinical data that actually addresses that particular  
10 mechanism, so we don't really know if that's what's  
11 going on or not. Superimposed upon that are the very  
12 high variations, the overall success rate. And my  
13 only comment on things like they did better in  
14 severity, and did better in these other individual  
15 scores is like the coach that says, well, we out-  
16 gained them and we had more running yards but we still  
17 lost the game. So I think at the end of the day, I  
18 think you've got to -- I'm really just kind of  
19 reiterating what others have said in a different way,  
20 is that you've got an elegantly simple device that has  
21 the high potential of providing good patient benefit,  
22 but essentially the homework and the documentation to

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1 demonstrate that your hypothesis for action and what  
2 you actually got are in fact related. And things like  
3 the issues with two levels being better than one,  
4 patient age. You've identified a whole host of  
5 potential variables I think that could narrow down to  
6 a very specific patient population that you could give  
7 great comfort and care to. But I think in the absence  
8 of that, and you take on all comers, you know, you  
9 have one chance in three or four that that particular  
10 patient is going to come out ahead.

11 DR. YASZEMSKI: Thanks Dr. Li. Dr. Doyle?

12 DR. DOYLE: I think I probably would have  
13 voted no. And I feel split in this, as partially it's  
14 coming from a research background but also looking at  
15 it as a consumer, and as someone who has been an  
16 orthopedic user, I suppose I should say, in full  
17 disclosure, knowing how different it is to be pain-  
18 free. And the thing that bothered me, I think, with  
19 the study overall was that there were so many little  
20 things that I'd like to have seen a more clearly  
21 defined protocol where we didn't have epidurals in the  
22 X STOP group, and some clear, defined objectives for

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1 defining when laminectomy was done. It concerns me  
2 that at two years the data was less good than it  
3 seemed to be at one year. The fact that it truly  
4 wasn't a blinded group, and that we don't know what  
5 the manipulation, just in and of itself was doing when  
6 you did that, inserted the X STOP in the spine. I'd  
7 like clearer objective criteria for the outcome. I'd  
8 have liked a third group, too, with the laminectomies.

9 And having said all of that, as a patient,  
10 I regret that this is not going to be an option for me  
11 to have, because I don't think there's anything to  
12 indicate that all of these things prove that there was  
13 anything dangerous. I think they did prove efficacy,  
14 and they didn't prove that it was not safe, so I would  
15 have voted no.

16 DR. YASZEMSKI: Thank you Dr. Doyle. Ms.  
17 Maher?

18 MS. MAHER: Well, I'd like to comment a  
19 little bit on some of the comments I've heard thus  
20 far. First of all, I'd like to take a little bit of  
21 exception to the way Dr. Kim mentioned that the study  
22 had bias. I think when you do a random size of two, a

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1 block of two, you might give the appearance for bias  
2 but I don't think there was any evidence that there  
3 was any bias in this study. So I'd like that to be  
4 clearly on the record.

5 Second, I'd like everybody to remember  
6 that our goal is to be looking at products as a  
7 reasonableness, and we're supposed to be balancing  
8 risk versus benefit. And I heard everybody earlier  
9 say that they thought that this product was safe as it  
10 was designed. And the only thing I heard Dr.  
11 Kirkpatrick say was that it wasn't effective in  
12 radiographs because we didn't have radiographs to show  
13 it. But that in the patients that actually had done  
14 better through the subjective methods, it had been  
15 effective, at least in that 33 percent. So I guess my  
16 feeling is a little bit of similar to what Dr. Rudicel  
17 said. So you have a bad x-ray or a good x-ray. That  
18 doesn't stop you from having the pain. And this did  
19 help the pain in that 33 percent of the patients. It  
20 would have been and would be a good middle step. And  
21 I think it's something that as a panel everybody needs  
22 to continue to look at and think about is reasonable

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1        assurances of safety and effectiveness, and least  
2        burdensome to get where we're going. We have now told  
3        this company that they have to go back -- or told the  
4        FDA, recommended, that it's not approvable with the  
5        data that they have here, even for a more limited  
6        population. Whereas, is it possible we could have  
7        come up with some conditions for them to go and slice  
8        and dice the data to get where we needed to go as  
9        well. So I'm a little disappointed.

10                    DR. YASZEMSKI: Thank you Ms. Maher. Dr.  
11        Kirkpatrick, would you like to close up?

12                    DR. KIRKPATRICK: Well, you asked after  
13        the motion what specifics would I suggest for the  
14        proposer or the sponsor to address for resubmission,  
15        and I fully hope that we'll see one soon. I'm not  
16        fully aware of what regulations you'd have to go  
17        through to get to the panel again, but from my  
18        standpoint if you validate clinically what you showed  
19        in the lab with a reasonable radiographic study post-  
20        op with the X STOP, that would satisfy one of the  
21        three problems I had with the whole thing. And that's  
22        a key issue, because you based your philosophy on

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1 preventing the foramen from narrowing, or preventing  
2 the canal from narrowing on extension, and yet in your  
3 clinical study you showed no evidence that that was  
4 stopped.

5 I think the other issues are related to  
6 the specifics of the indications which patients will  
7 benefit. I firmly believe that if you do study the  
8 anatomic types, you will get good information there  
9 which indicates which patients do better and which  
10 patients don't do better, as well as I have a  
11 hypothesis that two-leg symptoms versus one-leg  
12 symptom may also give you a little bit of a  
13 difference, if not a larger difference. I think those  
14 things are potentially available to you. But when we  
15 asked during the presentations, nobody could provide  
16 that information. So those three things would be what  
17 I would suggest to be able to come back to panel.

18 DR. YASZEMSKI: Thanks Dr. Kirkpatrick.  
19 Dr. Witten, have you any comments?

20 DR. WITTEN: No. I'd like to thank the  
21 panel for their work today.

22 DR. YASZEMSKI: Thank you Dr. Witten. I

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1 also would like to take care of one final thing. We  
2 thank the panel for their work. I specifically thank  
3 three members of the panel for whom this is the last  
4 meeting, Dr. Li, Dr. Finnegan, and Ms. Maher. I thank  
5 you all three for your service to this panel. I thank  
6 the sponsors for a thorough presentation. And we're  
7 adjourned.

8 (Whereupon, the foregoing matter went off  
9 the record at 3:25 p.m.)

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