

1 conducted an S/N curve fatigue testing with post-fatigue  
2 strength testing using this worst case scenario. In  
3 addition, static load was conducted using this  
4 configuration.

5 The actual fossa device by itself was utilized for  
6 our kinematic analysis, which is the only type of analysis  
7 we know that was conducted using a partial joint; retrieval  
8 analysis, dimethylgloxime testing, limulus testing, finite  
9 element analysis and our casting and finishing analysis.

10 So, in summary, procedure testing for the Fossa-  
11 Eminence Prosthesis, utilizing representative samples and  
12 devices, worst case combinations and the actual devices have  
13 been performed and submitted in the PMA. The justification  
14 and rationale for this testing has been explained in the PMA  
15 and has been discussed and explained to the Center. Thank  
16 you.

17 MR. COLE: Thank you, Mr. Durnell.

18 DR. HEFFEZ: This concludes the industry  
19 presentation and now we will move on to the FDA  
20 presentations. The first presenter will be Mr. Timothy  
21 Ulatowski, the Director, Division of Dental, Infection  
22 Control and General Hospital Devices.

23 MS. SCOTT: While Mr. Ulatowski is coming to the  
24 podium, I would like to confirm that the engineering data  
25 that was submitted by the company is included in the packet

1 that you received today. The additional engineering data  
2 that was submitted by the company is included in the panel  
3 packet for today.

4 **FDA Presentation**

5 MR. ULATOWSKI: We need a little time to set up  
6 here but I would like to take that moment just to thank and  
7 appreciate the attendance of the panel today to discuss this  
8 topic, and recognize all the speakers this morning in regard  
9 to their presentation. FDA considers all of the information  
10 presented, both pro and con, and the presenters this morning  
11 have been very helpful.

12 There is the potential that we will shorten the  
13 lunch period in order to proceed with discussions, or even  
14 have a working lunch. The chair will consider what he wants  
15 to do with that so that we can complete our day in a  
16 reasonable amount of time.

17 [Slide]

18 So, we are going to begin. What I want to discuss  
19 very briefly before my staff presents the FDA review, is to  
20 go over the goals for today's meeting, to discuss in a  
21 little more detail the timing and events that will occur,  
22 provide some background to our discussions this morning and  
23 for the afternoon, and then to move on to the other  
24 speakers.

25 [Slide]

1 My goal today in discussion with the panel is to  
2 respond to the panel's request to revisit the data for TMJ  
3 Implants, Inc. in regard to the fossa-eminence device. We  
4 want to obtain today the panel's vote based on the current  
5 set of data for the Fossa-Eminence Prosthesis. We want to  
6 obtain the panel's comments on labeling for the metal-on-  
7 metal total joint. So, there is a difference between our  
8 discussion today on the Fossa-Eminence Prosthesis compared  
9 to the metal-on-metal total joint. Time permitting, we will  
10 see how we proceed with the comment period on labeling this  
11 afternoon.

12 [Slide]

13 We have already had our public comment on the  
14 fossa-eminence and the industry presentation. We will have  
15 our say now before you, and then discussion and vote. In  
16 the afternoon, with the total joint, I will make some  
17 introductory statements regarding the labeling for the total  
18 joint and then we will have further discussion and comments  
19 on the labeling.

20 [Slide]

21 We are discussing today a type of device FDA  
22 called pre-1976 class III device, otherwise known as 515(b)  
23 type devices. As we all know, certain devices were on the  
24 market prior to when FDA started regulating medical devices  
25 in the premarket fashion, and we classified those devices.

1 Some devices were ultimately classified as class III, which  
2 means they require a premarket approval by the agency,  
3 submission of a premarket approval application to the  
4 agency, and this is the type of device we are discussing  
5 today.

6 Now, the timing of when FDA required premarket  
7 approval applications has played out since 1976 for various  
8 types of devices. For this particular type of device, TMJ  
9 Implants, it has been relatively recent when we asked for  
10 submission of premarket approval applications for one reason  
11 or another. FDA has its priorities; there are other issues  
12 going on. That is just the way it plays out.

13 [Slide]

14 Even though we are discussing pre-1976 devices, or  
15 devices found equivalent to those devices along the way  
16 since that time, one may ask, well, is there a different  
17 threshold for clearance of these types of devices versus new  
18 devices we might receive today. And, the answer is no.  
19 There one set of expectations, one law, one set of  
20 regulations regarding the safety and effectiveness  
21 determinations for premarket approval applications, and you  
22 have had training and discussion regarding reasonable  
23 assurance of safety and effectiveness.

24 In May or 1999 a prior panel discussed the partial  
25 implant, and from the public discussion and disclosures in

1 the press and elsewhere, it is self-evident that the outcome  
2 was that FDA did not move to approve that product after the  
3 panel discussion.

4 Let me clarify one respect, as speakers have  
5 already discussed, but let me just reemphasize that the  
6 panel around the table, here today, makes recommendations to  
7 the agency, and those are recommendations. Food and Drug  
8 Administration makes the final determination whether to  
9 approve or disapprove. We consider what you say. We  
10 consider what everyone has to say on the public record and  
11 make our decisions based upon the criteria that our Congress  
12 has outlined to us for making those decisions of reasonable  
13 assurance of safety and effectiveness.

14 At the last discussion, in May, FDA considered the  
15 discussion and the comments by the panel, and we actually  
16 took the comments to heart in regard to the type of  
17 information and data that we ought to be receiving.  
18 However, the vote did not reach the threshold that FDA  
19 considered to be appropriate for approval at that time.

20 Now, we moved on. Today is a new day. We have a  
21 new presentation of information before you, more extensive  
22 information, more extensive engineering data, more extensive  
23 clinical data. I trust that the panel will consider all the  
24 speakers today and the information provided to you today in  
25 making a recommendation to the Food and Drug Administration.

1 [Slide]

2 We are going to proceed with a discussion of the  
3 engineering review, Angela Blackwell, the chief reviewer for  
4 this application from the engineering point of view. I  
5 might add that Ms. Blackwell was superbly supported in the  
6 engineering review and analysis by our Office of Science and  
7 Technology, Dr. Gary Fishman assisting us in the evaluation  
8 and I appreciate that assistance.

9 A clinical review, Food and Drug Administration's  
10 review of the clinical data, Dr. Susan Runner. So, without  
11 further ado, Angela?

12 MS. BLACKWELL: I am Angela Blackwell, biomedical  
13 engineer in the Dental Devices Branch. I am the lead  
14 reviewer for this PMA.

15 [Slide]

16 This review focuses on data from the total joint  
17 device. The total joint device includes the fossa-eminence  
18 and the condylar prostheses.

19 As Mr. Durnell mentioned, most of the testing data  
20 was on the total, which includes the fossa but there wasn't  
21 testing on the fossa alone, therefore, evaluation must be  
22 made by extrapolating from the total joint data.

23 [Slide]

24 I am going to give you brief information about  
25 four different types of testing that were provided. Finite

1 element analysis, fatigue tests, wear tests and  
2 metallurgical analysis.

3 [Slide]

4 Finite element analysis uses computer models of  
5 the implants to compare the device's mechanical properties  
6 by loading them in the same manner.

7 Patient specific and stock total joints were  
8 compared. The models demonstrated that for mechanical  
9 testing purposes the stock device is a worse case than the  
10 patient specific.

11 [Slide]

12 Worse case means that the stock device is  
13 mechanically weaker than the patient specific device. The  
14 patient specific devices are larger than the stock devices,  
15 so this result was expected.

16 Mechanical testing of the stock device will be  
17 adequate to substitute for mechanical testing of the patient  
18 specific joint.

19 [Slide]

20 Fatigue tests -- several different tests were run  
21 with different parameters. These were all run on the total  
22 joint devices. The different fatigue tests were combined in  
23 order to get a fatigue limit. Justification for pooling the  
24 data was provided. The finite element analysis was used to  
25 justify testing only the stock devices.

1 [Slide]

2 Taken all together, the tests conclude that the  
3 fatigue limit of the device is approximately 130 lbs. If a  
4 3 times safety factor is used, the maximum load would be 43  
5 lbs. Some patients, such as unilateral patients, could have  
6 a TMJ load larger than 43 lbs.

7 [Slide]

8 Evaluation of the engineering data, in conjunction  
9 with clinical input, led to the following labeling  
10 recommendations:

11 [Slide]

12 The labeling should advise to exclude any patients  
13 who have habits which increase the load on the joint.  
14 Examples would be patients who brux or grind, and the  
15 surgeons should be warned why they are being excluded. The  
16 approvable labeling for the total joints has these  
17 restrictions.

18 [Slide]

19 Wear tests -- information on wear of the total  
20 joint was provided. FDA assessed the data, the conditions  
21 of wear, and the failure mode of the device, and determined  
22 no additional testing would be required. No preclinical  
23 information on the wear of the partial joint on the natural  
24 condyle was provided.

25 [Slide]

1 Metallurgical analysis -- analysis showed that the  
2 heat treatment used to dissolve secondary carbides does not  
3 always work. Gas porosity was shown to be on the surface of  
4 the implants. We have concerns about the effect of carbides  
5 or gas porosity in the fossa on the condyle whether it is  
6 natural or metal.

7 [Slide]

8 We have worked with the sponsor to address these  
9 concerns through changes in their quality control system.  
10 Thank you.

11 MR. ULATOWSKI: Now Dr. Susan Runner, the Branch  
12 Chief for the Dental Devices Branch.

13 DR. RUNNER: Good morning. In his introduction  
14 today, Mr. Ulatowski has outlined the background leading up  
15 to today's meeting and the goals of today's meeting.

16 [Slide]

17 FDA is requesting your recommendations this  
18 morning on the TMJ Implants, Inc. premarket approval  
19 application for two models of their Fossa-Eminence  
20 Prosthesis, the patient specific Fossa-Eminence Prosthesis  
21 and the stock prosthesis. The labeling for the total joint,  
22 consisting of the fossa and the condyle, will be separately  
23 considered this afternoon, time permitting.

24 [Slide]

25 The patient specific Fossa-Eminence Prosthesis and

1 the Stock Prosthesis are used for the partial reconstruction  
2 of the temporomandibular joint. The indications for use  
3 proposed by the applicant are for one or more of the  
4 following conditions:

5           Internal derangement, with or without meniscal  
6 perforation, not responsive to other modalities of  
7 treatment; inflammatory arthritis involving the  
8 temporomandibular joint, not responsive to other modalities  
9 of treatment; recurrent fibrosis and/or bony ankylosis, not  
10 responsive to other modalities of treatment; failed tissue  
11 graft; and failed alloplastic partial joint reconstruction.

12           [Slide]

13           The clinical review of a PMA involves a careful  
14 consideration of all the data presented by the applicant.  
15 FDA reviews all the data. FDA provides comments to the  
16 applicant during the course of the review, and FDA and the  
17 applicant present their case before the panel.

18           You recommend, based on the data presented,  
19 whether you believe the device is safe and effective for its  
20 intended use. Since there are risks with the use of any  
21 device, your recommendation must consider whether the  
22 demonstrated benefits of the device outweigh any known or  
23 possible risks.

24           Almost every term that we use here at FDA has a  
25 regulatory definition. Some are quite complicated. Quote,

1 safety and effectiveness are defined by regulation,  
2 specifically in 21 CFR, 860.7. Pam Scott will go over these  
3 later today as we get to the end of the day. But one of the  
4 points that is very important is that we must consider in  
5 our review, number one, the persons for whom the device is  
6 represented or intended; the conditions of use for the  
7 device, including conditions of use prescribed, recommended  
8 or suggested in the labeling; the probable benefit to health  
9 from the use of the device weighted against any probable  
10 injury or illness from such use; and, the reliability of the  
11 device.

12 [Slide]

13 Now, onto the specifics of the clinical data for  
14 the fossa as presented in the PMA. The applicant has  
15 presented two primary data sets, a retrospective study,  
16 known as the registry, and a prospective study that is  
17 ongoing. The sponsor has also submitted data from a  
18 clinician to document the effect of the Fossa-Eminence  
19 Prosthesis on the natural condyle.

20 [Slide]

21 TMJ Implants, Inc. developed the registry to track  
22 their implants. This is a retrospective evaluation  
23 collected from implanting surgeons. TMJ Implants, Inc.  
24 requested baseline and follow-up information from surgeons  
25 including data related to pain, diet restriction, and

1 interincisal opening limitations. Surgeons voluntarily  
2 responded to the company with monthly clinical research  
3 forms. The registry was designed to collect follow-up  
4 information beginning at six months.

5 [Slide]

6 The potential retrospective data pool consists of  
7 1358 patients receiving partial joint replacements.  
8 Emphasis, however, should be placed on the 88 patients for  
9 whom they have complete data sets through 36 months. The  
10 applicant concludes from this data that the use of the  
11 Fossa-Eminence Prosthesis results in a reduction of pain in  
12 a cohort of patients with a diagnosis of, quote, severe  
13 temporomandibular joint disorders.

14 [Slide]

15 Our statistician has reviewed the data on this  
16 patient set and a repeated measures ANOVA F-test gave a p-  
17 value of less than 0.0001. This particular retrospective  
18 study does not elaborate on the diagnostic criteria for the  
19 selection of patients in this cohort.

20 The applicant also presents data from a  
21 prospective study that is ongoing. This is a multi-center,  
22 open-label, single-arm study to evaluate the safety and  
23 effectiveness of the TMJ Fossa-Eminence Prosthesis. The  
24 primary objective of this study is to determine the  
25 reduction of pain as recorded by the patient. Secondary

1 objectives include assessment of adverse events, improvement  
2 in diet and improvement in interincisal opening.

3 [Slide]

4 The preoperative work-up includes a dentofacial  
5 exam, clinical and radiological exams, and a VAS scale.  
6 Patients are screened for the following inclusion criteria:  
7 Multiple joint operations; severe trauma to the joint;  
8 previous failed joint implant surgery; inflammatory or  
9 resorptive joint pathology; temporomandibular joint disease,  
10 defined as greater than or equal to Wilkes stage II;  
11 osteochondritis dissecans; avascular necrosis; intrinsic or  
12 neoplastic or congenital bone disease; ankylosis; internal  
13 derangement; and degenerative bone disease.

14 [Slide]

15 Additional questions on the patient screening form  
16 include, "does the patient's condition warrant partial  
17 and/or total temporomandibular joint replacement," and  
18 screening tests for other systemic diseases. The  
19 dentofacial exam includes evaluation of occlusion, range of  
20 motion, muscle palpation, notation of clicking, locking and  
21 crepitus, and evaluation of facial nerve impairment.

22 [Slide]

23 The radiological exam requires a panoramic x-ray.  
24 Optional CT scans and MRI evaluations are included.

25 [Slide]

1 Patients are also asked to rate pain on a VAS  
2 scale and rate interference with eating on a VAS scale, and  
3 rate interference caused by the TMJ disorder with life in  
4 general.

5 In their clinical report, 106 patients have been  
6 enrolled with data available from 98 patients. The  
7 applicant reports that the most frequently reported  
8 indication for partial joint replacement was 81 percent with  
9 internal derangement.

10 Adverse events reported included facial nerve and  
11 muscle weakness, paralysis, degenerative joint changes and  
12 development of adhesions, postoperative pain, swelling, and  
13 jaw muscle spasm, trauma, dislocation of the natural  
14 condyle, malocclusion, prosthesis did not fit, nausea and  
15 blurry vision.

16 The results, as you see on the screen, indicate  
17 that at 12 months 29 patients have a reduction in pain from  
18 a mean of 7.5 to a mean of 2 on the VAS scale; 15 patients  
19 out to 24 months reveal a reduction to a mean of 1.0 on the  
20 VAS scale; and 2 patients out to 36 months have a mean pain  
21 score of 0. Similar reductions were noted in the VAS score  
22 for reduction in diet restriction. Note that these are mean  
23 values and standard deviations are reported.

24 Finally, the sponsor has also provided information  
25 from a patient set that indicates that patients who receive

1 the partial joint prosthesis do not have clinical evidence  
2 of increased wear on the natural mandibular condyle, and you  
3 hear that information from Dr. Curry previously.

4 [Slide]

5 The applicant has stated, in material that has  
6 been provided to the panel, that for patients who do not  
7 respond to non-surgical therapies and when there is evidence  
8 of damage to the interarticular disk, a patient may be a  
9 candidate for a surgical approach. The applicant has also  
10 stated that early surgical intervention with the placement  
11 of the Fossa-Eminence Prosthesis is recommended for the  
12 treatment of internal derangement after failure of other  
13 treatment options. The applicant also states that this  
14 prosthesis may be indicated to, quote, protect the base of  
15 the skull and the head of the condyle from any further  
16 degeneration.

17 The preliminary data presented from the  
18 prospective study indicates that the use of the Fossa-  
19 Eminence Prosthesis may result in a decrease in pain and a  
20 reduction in dietary restrictions in certain patients. The  
21 applicant's most frequent preop diagnostic category is  
22 internal derangement. FDA has concerns about the adequacy  
23 of the characterization of this patient population. This  
24 category of patients may not be sufficiently precise to be  
25 able to identify the target population for this device.

1           As you have heard before, the standard of care and  
2 the history of TMJ disease and diagnosis suggest that  
3 surgical intervention with this patient population may be  
4 approached cautiously. The applicant's concept of early  
5 surgical intervention as an option for this patient  
6 population should be based on prospective data that compares  
7 treatment options. We are asking you, as representatives of  
8 the clinical community, to provide input in defining the  
9 target patient population, and in determining if there is  
10 adequate data to support these indications.

11           During the May, 1999 panel meeting, the panel  
12 asked questions in reference to indications for use of these  
13 implants. Specifically, they questioned characterization of  
14 the pain prior to surgery, the heterogeneous nature of the  
15 population, the nature of indications for the Fossa-Eminence  
16 Prosthesis, and the need to accurately look at the  
17 indications and diagnosis. The panel also stated that the  
18 use of these devices should no be a primary modality but  
19 used as a salvage modality.

20           As I noted at the beginning, we are seeking your  
21 input on the applicant's proposed indications for use and  
22 the data presented to support these indications, and any  
23 effect that the Fossa-Eminence Prosthesis has on the natural  
24 mandibular condyle. Thank you.

25           DR. HEFFEZ: Does the panel have any questions to

1 industry or FDA presenters? We certainly will have the  
2 opportunity after lunch, and I would like to tell you it is  
3 12:10. We were scheduled for lunch at 12:00. So, depending  
4 on the level of questions, we will see what we will do  
5 concerning coming back. So, any specific questions from the  
6 panel? Yes, Dr. Patters?

7 DR. PATTERS: Mark Patters. The individual from  
8 the company that presented the clinical data -- I am sorry,  
9 I don't recall your name, but I have a question. You stated  
10 that 93 percent of the partial prostheses were still  
11 functioning, and I wondered if the data actually said 93 of  
12 those available to follow-up were still functioning.

13 MR. ALBRECHT: The 93 percent reflects that  
14 patient population, the cohort of 88 patients. Out of that  
15 cohort of 88 patients, 93 percent of those 88 were still  
16 functioning after 3 years, as well as in the cross-section,  
17 if you look at the 1350-some odd patients that initially  
18 gave us preoperative data, out of those 1300 patients, 93  
19 percent of them still had the device functioning at 5 years.

20 DR. PATTERS: Those available to follow-up?

21 MR. ALBRECHT: Yes, sir.

22 DR. HEFFEZ: For the record, could you state your  
23 name?

24 MR. ALBRECHT: I am sorry, Doug Albrecht, TMJ  
25 Implants.

1 DR. BURTON: Mr. Albrecht, I have a question for  
2 you as well. This is Richard Burton, University of Iowa.  
3 You know, in your data set, particularly from your registry  
4 numbers, you had a pretty abysmal set of numbers by 24-36  
5 months. In most cases it was 10 or 15 percent of the  
6 enrolled patients. If you look at the N numbers, you know,  
7 that is a very, very small data set when you have numbers  
8 that were under 100 out of 1300 that were originally  
9 employed, and it is a little difficult to draw what a long-  
10 term assumption is from a number that is small. You can put  
11 the slide back up if you have it available, but at 24-36  
12 months with the registry data -- can you explain that at  
13 all?

14 DR. HEFFEZ: State your name again.

15 MR. ALBRECHT: Mr. Albrecht, TMJ Implants The  
16 registry follow-up is a voluntary method. We send out the  
17 forms to the physicians every six months after surgery to  
18 get the data. A good portion of them do return them, but if  
19 they don't return them -- it is not a clinical study; it is  
20 purely just a clinical follow-up voluntarily done by the  
21 physicians. So, if we don't get the forms back we are not  
22 going to go out and monitor because the physicians are  
23 scattered all over the country.

24 These data were presented to support the data that  
25 is being presented for the prospective clinical study, which

1 is a controlled study followed by a clinical protocol. As I  
2 indicated at the end of my presentation, no matter how you  
3 slice the pie, either from the registry or from the  
4 prospective study, we are seeing the same results out to at  
5 least three years after implant.

6 DR. BURTON: And, in your prospective study what  
7 is your N number that is at the 36-month point?

8 MR. ALBRECHT: I don't have the number at the top  
9 of my head. Can I get my notes?

10 DR. BURTON: Yes, that would be fine.

11 MR. ALBRECHT: At 36 months I have 5 patients  
12 right now in the prospective study.

13 DR. BURTON: Out of?

14 MR. ALBRECHT: Approximately 100 patients, give or  
15 take.

16 DR. BURTON: And, what was it at 24 months?

17 MR. ALBRECHT: Somewhere around 20, I believe --  
18 if I recall correctly. I want to add that the study began  
19 early in 1997 so patients are now just reaching their 3-year  
20 follow-up. So, as the study goes on, that number will  
21 increase rather quickly.

22 DR. HEFFEZ: Dr. Patters?

23 DR. PATTERS: Yes, Mr. Albrecht, one more  
24 question. In that prospective study of the 106 patients --  
25 is that right?

1 MR. ALBRECHT: Yes, 106. Right now it is 113  
2 since that was submitted to you, yes

3 DR. PATTERS: Regardless of what stage they are  
4 in, how many are still available to you for follow-up?

5 MR. ALBRECHT: We have lost approximately between  
6 10-15 percent of the patients, but I am talking about the  
7 total population, total joints and partial joints. I don't  
8 have it separated out to partial joints right now, but I  
9 would say the majority of the partial joint patients are  
10 still being followed up. We have lost a few to follow-up.  
11 A few have requested not to participate any longer, but I  
12 would say probably 90 percent of the patients with partial  
13 joints are still being followed.

14 DR. HEFFEZ: Dr. Bertrand?

15 DR. BERTRAND: Peter Bertrand. I have a question  
16 for Dr. Alexander. Sir, for the internal derangement  
17 population, you said that conservative treatment comprised a  
18 1-6 month time period in general before their pain is  
19 refractory for which a surgical intervention is necessary.  
20 What I have a difficult time understanding is the report in  
21 the literature which says patients with internal  
22 derangements, after 18 months without any treatment, 70  
23 percent of the time their symptoms will dissipate. That is  
24 not necessarily correlated to what the shape of the condyle  
25 appears as with imaging. Can you help me understand that

1 dichotomy?

2 DR. ALEXANDER: Rick Alexander. Again, I think I  
3 said that this has to be a decision that is made between the  
4 patient and the surgeon. If you have a surgeon that has a  
5 closed lock and can only open their mouth 10-15 mm, has pain  
6 -- you know, are you going to wait 18 months before you do  
7 anything? You know, I don't have too many patients that  
8 want to do that, and you start with some of the other  
9 procedures. Arthroscopy would be a start. But, you know,  
10 the goal here is to decrease pain, increase opening or do  
11 away with dysfunction and do away with noises. I mean,  
12 there are patients out there that have an internal  
13 derangement that have no pain, open to 42 or 50 mm, hyper-  
14 mobile patients, where the noise is so loud that they can't  
15 sit in a restaurant and eat. Are you going to wait around  
16 18 months? Most of these patients are just dying to have  
17 this taken care of.

18 So, you know, I think it is a decision that has to  
19 be made between the surgeon and the patient, and if a pat  
20 wants to wait 18 months, then that is a reason to wait but I  
21 think you will find that patients that have serious internal  
22 derangement problems, by the time I see them, generally  
23 speaking are looking for something to solve the problem and  
24 they have already been through probably, some of them,  
25 years. I have a patient right now who has gone through

1 three years of conservative therapy, has spent \$22,000 on  
2 conservative therapy, and has a Wilkes class V internal  
3 derangement.

4 DR. BERTRAND: So the duration of pain for the  
5 patient population that you are seeing for surgery -- they  
6 have had pain greater than 18 months almost always?

7 DR. ALEXANDER: Some of them have and some of them  
8 haven't.

9 DR. BERTRAND: Do you have any figures on that?

10 DR. ALEXANDER: No, I don't think there are -- I  
11 am not aware of any published data that will give you that  
12 figure and, again, I don't think you can treat these  
13 patients based on published data in terms of when you are  
14 going to operate on them. I think when the patient's pain,  
15 dysfunction and/or noise is sufficient to interfere with  
16 their quality of life, that is an indication for surgery,  
17 and I don't know who can make that decision other than the  
18 surgeon and the patient together.

19 In terms of the prolonged internal derangement,  
20 you know, there are some studies that show that as many as  
21 30 percent of the people walking around have asymptomatic  
22 displaced disks.

23 DR. BERTRAND: Probably greater than that.

24 DR. ALEXANDER: And that ranges to studies where  
25 they show 50 percent. Am I going to operate on those

1 patients? No. But I will tell you one thing I am going to  
2 tell those patients, that it is crystal-clear that long-term  
3 internal derangement leads to degenerative joint disease,  
4 and if they start to have pain, and they start to have  
5 noise, and they start to have dysfunction they need to be  
6 reevaluated. But I am not going to operate on asymptomatic  
7 patients.

8 DR. BERTRAND: It is crystal-clear that long-term  
9 internal derangement always leads to arthritic degeneration?

10 DR. ALEXANDER: I don't think anything is one  
11 hundred percent but I think there is sufficient evidence out  
12 there to show that the step that occurs after long-term  
13 internal derangement in many patients is degenerative joint  
14 disease. Patients don't just go from a normal functioning  
15 disk with no internal derangement to degenerative joint  
16 disease. That doesn't happen. Something goes on internally  
17 with disk problems before they get to the degenerative joint  
18 stage.

19 DR. BERTRAND: There is also, wouldn't you agree,  
20 considerable evidence that degenerative joint disease  
21 doesn't necessarily correlate with pain in a large group of  
22 patients.

23 DR. ALEXANDER: Degenerative joint disease can  
24 burn out and never require any treatment but, again, I think  
25 that is something that the patient and the surgeon have to

1 decide on an individual basis.

2 DR. BERTRAND: Thank you.

3 DR. HEFFEZ: Dr. Besser?

4 DR. BESSER: I have a couple of questions for Dr.  
5 Urbanek.

6 DR. URBANEK: Tony Urbanek, Nashville, Tennessee.

7 DR. BESSER: I wondered as to the 16 patients you  
8 stated were waiting for this prosthesis, and its  
9 unavailability. Is there a reason that they would not be  
10 candidates to be included in the prospective study that is  
11 currently going on?

12 DR. URBANEK: Yes, one big reason, the biggest  
13 reason is because there is a certain limitation. I have  
14 been allotted 35 patients in this study and have topped out  
15 at 35 patients. A secondary reason is to make any variation  
16 of that, it has to go before the hospital review board.  
17 That process was attempted once, and with every effort on  
18 the review board and all the members spending days of their  
19 personal time, it took two months to get that one patient  
20 through the review process so that it could be done.

21 DR. BESSER: Thank you. I have questions about  
22 your experience with this prosthesis. You listed 217  
23 partial joints that you had done. All of these were with  
24 the Fossa-Eminence Prosthesis?

25 DR. URBANEK: That is correct. Actually, I

1 believe it was 345 joints, 217 patients.

2 DR. BESSER: So, that is even better then. I have  
3 a question as to how many of those were sort of more recent.  
4 You said you started very slow. You did one; you waited six  
5 months; you did a second one.

6 DR. URBANEK: Right.

7 DR. BESSER: Do you have a feel for how many of  
8 those 350 joints were in the last three years, one year?

9 DR. URBANEK: Well, in the last year it has  
10 trailed off to nothing. In the past three years -- well, I  
11 can give you this statistic, approximately three operated  
12 patients per month for the past three years.

13 DR. BESSER: So, give or take 120.

14 DR. URBANEK: Yes, it is pretty well distributed  
15 from 1994 to the present time -- recent time.

16 DR. BESSER: In your experience with your  
17 patients, what adverse events have you seen in your  
18 experience?

19 DR. URBANEK: Would you like me to address  
20 surgical adverse events or postoperative effects? I can go  
21 through the whole litany; I know it well.

22 DR. BESSER: What might be considered a poor  
23 outcome, so problems during the surgery that might not be  
24 specific to the device but set those aside for a minute and  
25 look at problems probably associated with the device.

1 DR. URBANEK: I have seen no problems associated  
2 directly with the device. I have seen no device fractures.  
3 After opening, as I said, four or five joints for traumatic  
4 reasons, I have seen no giant cell formation, degenerative  
5 change of the tissue surrounding the implant in the glenoid  
6 fossa or degenerative change of the condyle itself by  
7 visualization. I follow the patients along with Panorex on  
8 a yearly basis for several years after surgery. I have seen  
9 no gross degenerative change of the condyle on Panorex, on  
10 x-ray examination.

11 There are a few immediate postoperative  
12 considerations that have to be taken into consideration of  
13 doing the surgery correctly. If it is done correctly  
14 patients do extremely well immediately after surgery and  
15 thereafter. I can address that at great length and lecture  
16 on that, for that matter. In the long-term, I have seen no  
17 adverse events related to the prosthesis itself.

18 Out of that number of patients that I did, to my  
19 knowledge, there is one patient -- one patient -- who had  
20 had the prosthesis in place -- this particular patient was  
21 injured at work, was a workman's compensation patient. The  
22 prosthesis went in and, no matter what I did for the  
23 patient, I couldn't make the patient better. The prosthesis  
24 came out. I still couldn't make the patient any better, and  
25 I will let the panel draw its own conclusions.

1 I won't say that 100 percent of my patients are  
2 doing perfectly, but I can say with certainty that 95-plus  
3 percent of my patients, and I do follow them for years after  
4 surgery and I don't charge them to come back; I encourage  
5 them -- most patients in Tennessee, once they reach a  
6 certain level, they won't come back and I invite them. When  
7 I finish and discharge a patient I say, if there is any  
8 problem at all, under any circumstances at any time, I want  
9 you to come back to see me. That is one way I know that  
10 they are not having problems. Of the patients I have done  
11 in this series, 95 percent report to me that they are happy,  
12 doing well; their life has changed; they are comfortable.  
13 You know, my job is to get them out of pain. That is really  
14 what they want and that is what they report to me -- they  
15 are out of pain and their life has changed.

16 DR. BESSER: Thank you.

17 DR. URBANEK: Certainly.

18 DR. HEFFEZ: Go ahead.

19 DR. COCHRAN: David Cochran. I was wondering, you  
20 have done 345 joints in 200-and some patients. Have you  
21 considered doing a retrospective analysis of that and look  
22 to see what your percentage of dropout was, and actually get  
23 numbers on that?

24 DR. URBANEK: Yes, I have given it lots of  
25 consideration, especially recently once I became, let me

1 say, embroiled in these discussions. In fact, I will do  
2 that.

3 DR. BURTON: Dr. Urbanek, you mentioned the fact  
4 that between 1983 and 1987 that you placed 80 Proplast  
5 implants and I believe you have removed 78 of them at this  
6 point of time. How long after 1987 did you start to see  
7 problems in your patient population personally that then led  
8 to your adoption of the fossa implant in 1991 or started to  
9 look at that as a treatment modality?

10 DR. URBANEK: I believe I understand your  
11 question, just let me repeat it to be certain. In 1987 I  
12 became aware of the problem with Proplast, and at that point  
13 in time I no longer used Proplast. It was between 1987 and  
14 1991, late in 1991 that I used no alloplastic prosthetic  
15 devices at all.

16 DR. BURTON: But just looking at the time frame  
17 and the length of time that these have been more widely  
18 used, and the same thing with the Vitek, you know, you had a  
19 four-year period where they were being implanted and then  
20 how long after the information became available --  
21 obviously, along with everyone else, you stopped utilizing  
22 those -- that you started to see problems in your own  
23 patient pool?

24 DR. URBANEK: In my own patient pool?

25 DR. BURTON: Yes, sir.

1 DR. URBANEK: Well, let's define problems. With  
2 the Vitek, there were many, many, many patients out there  
3 who did not have any pain even to the point where I took the  
4 prosthesis out but we immediately began to see and review  
5 and find many radiographic evidence of degenerative change  
6 of the condyle and the surrounding glenoid fossa and other  
7 tissues. So, the answer to your question is immediately.

8 DR. STEPHENS: Dr. Urbanek, I am Willie Stephens.  
9 After opening some of these joints that you treated, what is  
10 your sense as to why this procedure works, and what is the  
11 difference between this procedure and a meniscectomy alone?

12 DR. URBANEK: Let me answer the second question  
13 first. A meniscectomy I have lots of experience with.  
14 Between 1981 and 1993 or 1994 I did lots of meniscectomies.  
15 Meniscectomy trailed off between 1991 and 1994 when I found  
16 that meniscectomy was consistently not working; patients  
17 were returning. Meniscectomy alone does not work because,  
18 whether it encourages fibrosis, it allows fibrosis to occur  
19 within the joint space, and when you reoperate a patient  
20 that has had only meniscectomy, that is what you will find  
21 visually, fibrosis scarring within the joint space. On the  
22 other hand, with the Christensen prosthesis, on opening  
23 several of these cases, I see no fibrosis at all. None.

24 DR. STEPHENS: Have you been able to note if there  
25 is any synovial fluid in these joints?

1 DR. URBANEK: In the operated joint?

2 DR. STEPHENS: When you have reopened the joints  
3 with the prostheses.

4 DR. URBANEK: Let's just say that the cartilage  
5 covering of the condyle is intact. Not to avoid your  
6 question, I don't note any obvious synovial fluid, although  
7 the joint space is moist. In fact, joint fluid within an  
8 operated joint, when you open the joint and the fluid pops  
9 out at you is a bad indicator of inflammatory joint disease.  
10 So, what I see when I reoperated, in the few cases I have  
11 gone into joints with the prosthesis in place, is a smooth  
12 joint, a nice condylar surface on the condyle itself, and an  
13 appropriate amount of synovial moisture or fluid.

14 DR. HEFFEZ: Dr. Janosky?

15 DR. URBANEK: Excuse me, could I just add to  
16 answer the question specifically, the reason I think that  
17 the prosthesis works, in my opinion, is that it is extremely  
18 inert. I see no reaction of soft tissue, hard tissue. I do  
19 not see any bone resorption whatsoever clinically, visually  
20 or radiographically.

21 DR. JANOSKY: I have some questions for Mr.  
22 Albrecht. It might be helpful for me if the slides though,  
23 so give them a chance to get those up and take another  
24 question in the interim.

25 DR. HEFFEZ: In the interim, is there another

1 question? Yes, Dr. Besser?

2 DR. BESSER: Dr. Besser. I have a question for  
3 Dr. Curry.

4 DR. CURRY: Jim Curry, from Colorado.

5 DR. BESSER: Dr. Curry, you made a statement in  
6 the volume of data that we got that there was evidence that  
7 the Fossa-Eminence Prosthesis has actually protected the  
8 bone from further deterioration, and you mentioned it again  
9 during your presentation today. Other than the one set of  
10 radiographs you showed us where a patient who was not  
11 operated experienced joint degeneration, is there other  
12 evidence that leads you to this conclusion? Can you share  
13 it?

14 DR. CURRY: Well, I am not sure I ever made the  
15 statement that it absolutely prevents --

16 DR. BESSER: No, the statement was there is  
17 evidence that the Fossa-Eminence Prosthesis has actually  
18 protected the bone from further deterioration.

19 DR. CURRY: What I am referring to there is I have  
20 had one occasion to reoperate a joint that had a total joint  
21 prosthesis in place where actually the phalange of the  
22 condylar element fractured after about eleven years. So,  
23 when I went in to replace the prosthesis, and when I took  
24 the glenoid fossa prosthesis out to replace it, I took some  
25 photographs of the base of the skull and it was my clinical

1 observation at that point in time that if I had brought a  
2 person into the operating room to look at the glenoid fossa  
3 of this patient, and they didn't have any clinical history  
4 or anything of what was going on there, they would not be  
5 able to distinguish that fossa from one that had never been  
6 operated before.

7           The observation that I have is very similar to Dr.  
8 Urbanek's. In the very few number of cases that I have had  
9 the occasion to reoperate, either from trauma or whatever, I  
10 have not seen a single case of severe condylar degeneration.  
11 I just haven't seen that happen and we have, of course, seen  
12 that with other cases. I have seen it with people who have  
13 had surgery that had never had anything but just a standard  
14 placcation, for example, or something of that nature, and I  
15 just haven't been able to see that in any of the several  
16 hundred patients that I have dealt with personally, and it  
17 leads me to -- I mean, God gave me a mind and I have just  
18 common sense and I make a statement like that just based on  
19 pure clinical observation.

20           DR. BESSER: Thank you very much.

21           DR. CURRY: Yes, sir.

22           DR. HEFFEZ: We will go back to the question by  
23 Dr. Janosky.

24           [Slide]

25           DR. JANOSKY: I want to just spend some time

1 looking at your prospective study and your registry data.  
2 You presented two graphs, one from each of those. They are  
3 very similar. One was the pain score. This is a follow-up  
4 on some other questions that were asked and then sort of  
5 looking at it a different way.

6 Let me understand this, this is from your  
7 prospective study. So, that was an N of how many starting,  
8 again?

9 MR. ALBRECHT: Right now we have 113 partial  
10 joints implanted.

11 DR. JANOSKY: Okay, 113, and if we just use the  
12 estimate, let's say, of 70 percent rate of return, what time  
13 point would that classify as? If we just say 70 percent of  
14 the patients, where do we have the point at which we have 70  
15 percent of the data still available? What is the time point  
16 that that would classify? Would that be three months worth  
17 of data?

18 Let me ask the question a little differently. If  
19 I look at your 36 months, you have 2 patients, data  
20 available on 2 patients within that first group. Is that  
21 correct within that first group?

22 MR. ALBRECHT: Okay, 2 patients with perf, 3  
23 patients without perf.

24 DR. JANOSKY: Right. So, you have 2 within the  
25 first group out of a start of 25. So, you have

1 approximately 10 percent of your patients remaining at 36  
2 months within that first group.

3 MR. ALBRECHT: Right.

4 DR. JANOSKY: So, what if I use the rule of thumb  
5 and I want to find where you have data on at least 70  
6 percent of the patients, at what point would that be? Is  
7 that 3 months worth of data? Is it 6 months worth of data?

8 MR. ALBRECHT: If you do the math, at 12 months I  
9 have half the patients, I have 50 percent of the patients.

10 DR. JANOSKY: I am looking for approximately 70  
11 percent.

12 MR. ALBRECHT: Okay, 70 percent, probably between  
13 3 and 6 months.

14 DR. JANOSKY: Between 3 and 6 months. So, this is  
15 for pain reduction within the prospective study. Could you  
16 do the same exercise with the other study and for the other  
17 outcome for me, please?

18 MR. ALBRECHT: For the registry?

19 DR. JANOSKY: Yes. You have pain reduction and  
20 you also have opening. Correct?

21 MR. ALBRECHT: I do.

22 DR. JANOSKY: And is the data the same for opening  
23 as it is for pain reduction in terms of the sample size?

24 MR. ALBRECHT: Yes. Please put up the cohort for  
25 the registry, the 88 patients.

1 [Slide]

2 DR. JANOSKY: So, we can conclude from the  
3 prospective study you have 70 percent of the patient data  
4 available with 3-6 months follow-up, and that was a total N  
5 of 113.

6 MR. ALBRECHT: Out of that 113, 78 percent had the  
7 definition of internal derangement. So, we are not looking  
8 at a total of 113 patients. So, we are talking somewhere  
9 around 80 patients with internal derangement, and at about  
10 3-6 months I have about 70 percent of the data.

11 DR. JANOSKY: So, if we use 70 percent as our cut-  
12 off point you have 3-6 months worth of data in terms of that  
13 study. Within your registry again, I want to use the same  
14 yardstick. At what point do you have 70 percent of your  
15 data?

16 MS. ALBRECHT: This is the cohort of 88 complete  
17 patients, of which we have class III, IV and V in the Wilkes  
18 classification here.

19 DR. JANOSKY: Did you not have a table with the  
20 patient numbers?

21 MR. ALBRECHT: This is 46 out of the 88 patients.  
22 I have a complete set of 20 patients with class V, 18 with  
23 class IV and 8 with class III from beginning to end.

24 [Slide]

25 In the registry cross-section, with internal

1 derangement anywhere between class V and class III we have  
2 over 800 patients to begin with.

3 DR. JANOSKY: And were using 70 percent again?

4 MR. ALBRECHT: Seventy percent, so you are talking  
5 about maybe 300 patients, so probably around 6-12 months  
6 would be 70 percent.

7 DR. JANOSKY: No, that is 30 percent.

8 MR. ALBRECHT: I am sorry.

9 DR. JANOSKY: So, is it 6 months? It looks like  
10 less than 6 months. Let me just conclude what I think we  
11 have just walked through, just to make sure it is clear in  
12 my mind. You have two studies, one is a prospective study  
13 and one is a registry study. Within the prospective study  
14 you have 70 percent completers up to 3-6 months for  
15 approximately 50 patients at that 3-6 months mark.

16 MR. ALBRECHT: Right.

17 DR. JANOSKY: And with the registry you have  
18 approximately 300 and, again, the completers of 70 percent  
19 is about 6 months or less.

20 MR. ALBRECHT: Yes.

21 DR. JANOSKY: So, in terms of long-term data,  
22 there is very little in either one of the studies past  
23 essentially 6 months.

24 MR. ALBRECHT: If you look at the math, yes.

25 DR. JANOSKY: Thank you. I have some more

1 questions later but I think I will stop for now.

2 DR. HEFFEZ: I just have one follow-up question.  
3 Are you only considering the class III and above, because  
4 you have down there listed class I and II --

5 MR. ALBRECHT: I just put that in there for  
6 observation.

7 DR. HEFFEZ: I want to finish the question.  
8 Because class I and II, according to your criteria, you have  
9 been speaking mostly about class III and above and, yet, the  
10 criteria for the protocol indicates class II and above and,  
11 yet, I see class I and II. So, is the data that you have  
12 just reported, is that including class I and II, or just  
13 class III and above?

14 MR. ALBRECHT: The data in the prospective  
15 clinical trial?

16 DR. HEFFEZ: Answer for both.

17 MR. ALBRECHT: In the prospective clinical trial  
18 the inclusion criteria call for Wilkes II and above. But if  
19 you look at the diagnosis of internal derangement and how  
20 the physicians have provided that to us, they all fall into  
21 the categories of III and above.

22 In the registry, if we go back and look at what  
23 the physicians have provided us, the overwhelming majority  
24 provided class III, IV and V. Only 21 out of the 800-some  
25 odd returns gave us a class I and II. I think, to answer

1 the question, we are looking for an indication of Wilkes  
2 class III, IV and V.

3 DR. HEFFEZ: Thank you. Any other questions from  
4 the panel?

5 DR. BURTON: Yes, for Dr. Curry.

6 DR. CURRY: Jim Curry, from Denver.

7 DR. BURTON: Yes, Dr. Richard Burton, University  
8 of Iowa. Dr. Curry, you provided to us a review in August  
9 of '99, looking at 17 patients that were reviewed for the  
10 stability of the condyle versus the Fossa-Eminence  
11 Prosthesis. What percentage of your patients, or the  
12 patients who had had the eminence prosthesis during that  
13 period does this 17 represent?

14 DR. CURRY: I don't know. The inclusion criteria  
15 for this study was a minimum of three years that I was able  
16 to look at patients that had data that I could look at that  
17 were at least three years old. So, I don't know what  
18 percentage of patients that would be. My original group of  
19 patients included about 64, of which probably 85 percent  
20 were partial joints. So, if we stood here and did the math  
21 a little bit we might be able to figure that out but I  
22 didn't look at that.

23 DR. BURTON: I guess what I am getting at is what  
24 were your selection criteria? To me at least, it wasn't  
25 completely clear. Was it strictly the fact that you had

1 three-year follow-up records on this particular group of  
2 patients?

3 DR. CURRY: That is correct, and that they were  
4 partial joints.

5 DR. BURTON: And, from 1992 on, you do not have  
6 any patients that are more current -- let's say who were  
7 done in 1994 and three years would have been 1997, that  
8 would have met that criteria? I guess I am curious why the  
9 last patient falls in the '92 time frame.

10 DR. CURRY: Well, I don't know that I even thought  
11 about that. I just went through my patient records. I had  
12 my staff do that, and picked the patients that I had  
13 available records for and x-rays for and that I could  
14 actually contact and get back into the office. So, that was  
15 the reason for that.

16 DR. HEFFEZ: Do you have a follow-up question, Dr.  
17 Burton?

18 DR. BURTON: No, not at this time.

19 DR. HEFFEZ: I would like to have some indication  
20 of any further questions from the panel. Dr. Anseth?

21 DR. ANSETH: Kristi Anseth, from the University of  
22 Colorado. I have a question for Dr. Durnell regarding some  
23 of the dynamic material testing data that you have. Is  
24 there any information available on how the fossa-eminence  
25 interacts with a material other than just the cobalt chrome

1 head or the polymethylmethacrylate head?

2 MR. DURNELL: John Durnell. To bench test an  
3 alloplast against bone doesn't really make sense. We chose  
4 the articulation of the metal-on-metal as the worst case  
5 because it was single point contact and it was hard  
6 alloplast on hard alloplast. It is difficult to reproduce  
7 either cadaver bone or anything with kind of a cartilage  
8 covering to articulate that and get any kind of meaningful  
9 test results.

10 DR. ANSETH: And, when you say worst case, you  
11 mean looking at a worst-case scenario with respect to the  
12 fossa-eminence?

13 MR. DURNELL: Correct. In a partial joint  
14 situation, the natural condyle distributes the forces and is  
15 a softer material than the metal. So, in our test  
16 preparation we chose the total joint situation as worst  
17 case.

18 DR. ANSETH: Thank you.

19 DR. HEFFEZ: You will have an opportunity -- is  
20 this to answer --

21 MR. ALBRECHT: Just to response to Dr. Janosky's  
22 question. Is that possible?

23 DR. HEFFEZ: Okay, but be brief. State your name.

24 MR. ALBRECHT: Doug Albrecht, TMJ Implants. The  
25 data we were talking about, Dr. Janosky, was to response to

1 Dr. Runner's comments regarding what type of internal  
2 derangements do we want to indicate this for, and I agree  
3 with you, the numbers are small. But if you look at the  
4 clinical report that I believe the panel was given prior to  
5 this meeting, on page 6 of that clinical report the numbers  
6 are much larger. Again, we have a cohort of 88 patients  
7 that are followed from preop all the way out to 3 years,  
8 the same group of patients, which is very revealing as far  
9 as pain reduction.

10 As far as the cross-section, the numbers, again,  
11 of all patients that we have data on, at 12 months we have  
12 just under 50 percent; at 24 months we have approximately 25  
13 percent of the patients reporting. Again, this is a  
14 voluntary system. But even though it is only 25 percent,  
15 the numbers are still substantial. We are talking about  
16 close to 300 patients reporting a pain level at 24 months of  
17 2.1 on a scale of 10.

18 So, again, the cross-section sort of gives you an  
19 idea of what is going on with the patients, and you look at  
20 the cohort of the same group of patients followed all the  
21 way through and you are getting the exact same results. It  
22 sort of confirms what we see in the cross-section but the  
23 numbers are higher when you look at the entire population.  
24 We were able to break it down by classification just to sort  
25 of give an idea of what type of classifications are being

1 operated on and to propose our indications with.

2 DR. HEFFEZ: At this time, I would like to break  
3 for lunch. The lunch will only be 20 minutes, giving new  
4 meaning to the word indigestion. At 2:10 we will reconvene.

5 [Whereupon, at 1:50 p.m., the proceedings were  
6 recessed for lunch, to reconvene at 2:20 p.m.]

## AFTERNOON PROCEEDINGS

[2:30 p.m.]

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DR. HEFFEZ: Let's get started. While we wait for others to join us, I will ask Dr. Besser to present. I am going to ask the panel if they have any questions from the FDA presentations that they wish to ask.

DR. BURTON: Yes, for Miss Blackwell.

DR. HEFFEZ: Miss Blackwell, could you answer a question?

DR. BURTON: Richard Burton, University of Iowa. Miss Blackwell, what wasn't clear -- I was on the May, '99 panel so some of this relates back to my review of what we have in this package versus before. There were certain questions regarding carbide issues and you made a comment about some of these being resolved through quality control. Could you explain that a little bit more fully, what you meant by that?

MS. BLACKWELL: Well, some of that information I wasn't able to put on a slide because it is proprietary. So, that is why it came across like that.

DR. BURTON: That is fine. Do you feel, from an engineering standpoint, that those concerns that were presented at that previous panel -- that the metallurgical issues that were raised at that point have been adequately resolved?

1 MS. BLACKWELL: I think the company has found a  
2 way to resolve them. They aren't resolved at this point,  
3 but the company is not under production right now in a  
4 significant number so resolving them is a bit of a problem  
5 with no production going on.

6 DR. BURTON: But they have things in place that  
7 should resolve those issues?

8 MS. BLACKWELL: Yes.

9 DR. BURTON: Thank you.

10 MS. SCOTT: I will mention that if the panel has  
11 questions regarding confidential data and they feel as  
12 though that information needs to be discussed, we can ask  
13 the sponsor whether or not they would like to close a  
14 portion of the meeting to discuss that confidential  
15 information, if the panel really feels strongly that a  
16 portion of that data needs to be discussed or a question  
17 needs to be answered regarding that.

18 DR. HEFFEZ: Miss Blackwell, in your presentation  
19 you said you had concerns about the effects of carbides or  
20 gas porosity in the fossa and the condyle whether it was  
21 natural or metal. What were those concerns? Could you  
22 iterate them?

23 MS. BLACKWELL: Well, both the carbides and the  
24 porosity can cause a location in the device where you would  
25 get a stress concentrator. For instance, in the fossa if

1 you had a place of porosity or a carbide, that could be the  
2 place where the fossa might crack. The fossa is very thin.  
3 So, the carbide issue and the gas porosity issue is much  
4 more of a concern in the fossa because it is so thin. It is  
5 possible you could have a carbide or a gas porosity for  
6 almost the entire thickness of the fossa.

7 DR. HEFFEZ: Thank you. Yes?

8 DR. BERTRAND: Peter Bertrand. If there is a  
9 potential for a crack, there has to be some wear preceding  
10 that crack, and is the particulate matter of that wear  
11 absorbable into the system systemically?

12 MS. BLACKWELL: The particulate matter? You mean  
13 pieces of the fossa?

14 DR. BERTRAND: Before a crack, would there be some  
15 particulate wear?

16 MS. BLACKWELL: Not necessarily, particularly if  
17 it was a carbide or gas porosity it might not generate much  
18 in the way of wear. I mean, you could get particulate  
19 matter once it was cracked and if it remained in place and  
20 then, you know, the condyle wore on the crack. Then you  
21 would be more likely to get particulates.

22 DR. HEFFEZ: Any other questions from the panel  
23 for FDA?

24 [No response]

25 Thank you, Miss Blackwell. I would like to

1 proceed with Dr. Besser's presentation.

2 **Presentation by Panel Members**

3 DR. BESSER: Mark Besser. I am going to try not  
4 to repeat too many of the things that Miss Blackwell talked  
5 about. If I agree with her, I will just say that I did.

6 I did want to bring up a few of my concerns  
7 concerning the preclinical testing that was done on this  
8 prosthesis. I agree with Miss Blackwell's analysis of the  
9 finite element analysis and the use of the stock prosthesis  
10 as the worst-case prosthesis.

11 The fatigue tests that were presented in the data,  
12 both from the original PMA and the information presented for  
13 this meeting -- I have a great amount of problems with the  
14 load that was used. The test load that was used at which  
15 the test specimens failed, and then was lowered to find sort  
16 of fatigue limits at 130 lbs -- I believe that using any  
17 kind of a safety factor, the loads associated with chewing  
18 or with clenching would far exceed the loads that were used  
19 in this testing. And, one of the things I would like to see  
20 is either justification for why such a low loading was  
21 chosen and/or retesting at a higher load.

22 Also, in one of the presentations they presented  
23 data from, I guess, 6/10 prostheses that have been tested  
24 and concluded that only 2 of these 10 had failed. They  
25 excluded 4 from the regression analysis that failed at very

1 low numbers of cycles. I would like to hear some more from  
2 the company as far as why those 4 were excluded, leaving  
3 only the 2 that scored the best. In the material presented  
4 it was difficult to determine exactly what the criteria were  
5 for excluding those failed specimens from their regression  
6 analysis.

7 I also have concerns as to the wear testing. All  
8 the wear testing was done for the total joint prosthesis,  
9 nothing for the partial. I am not sure I have a solution to  
10 how best to look at wear on the intact condyle, which is  
11 what I would expect to show the wear as opposed to the metal  
12 prosthesis, but possibly some long-term postmarket  
13 surveillance, where an active effort was made to retrieve  
14 these prostheses further down the road to see whether, in  
15 fact, some of the things that have been presented by a  
16 couple of the doctors who spoke -- their suspicions that  
17 this protects the mandibular condyle and it actually is  
18 better than not replacing the joint are, in fact true, or  
19 whether there is wear of the bone at the condyles that we  
20 are not seeing either because the data that you presented is  
21 too new or because it can't be seen on radiographs when you  
22 have the prosthesis in place.

23 I did have a question about the carbides.  
24 However, I will defer to Miss Blackwell if that has been  
25 handled as far as the manufacturing process is proprietary,

1 and possibly someone from the company can talk to me in one  
2 of the breaks. Is that allowed?

3 DR. HEFFEZ: Well, everything should be in this  
4 forum so everyone can hear it.

5 DR. BESSER: All right, then without violating the  
6 proprietary nature of the information, I guess I will have  
7 to trust the judgment of those at FDA.

8 DR. HEFFEZ: Well, it may not be proprietary  
9 information that you are seeking.

10 DR. BESSER: Well, if there is anything you can  
11 tell me about the process used to eliminate carbides or to  
12 control for them, I would like to hear it. Those were the  
13 main questions or criticisms that I came up with in the  
14 preclinical analysis and the preclinical data.

15 DR. HEFFEZ: Mr. Ulatowski?

16 MR. ULATOWSKI: I suppose it is at the discretion  
17 of the manufacturer who may want to discuss somewhat the  
18 quality control procedure, if they so choose, or to open up  
19 a closed meeting, or we can just proceed as you recommended

20 DR. HEFFEZ: I think the best way to proceed is to  
21 just let me summarize your comments. You are looking for  
22 some justification for the low loading. Do you have a  
23 suggestion as to what loads you would like to see?

24 DR. BESSER: Somewhere between 250-500 lbs.

25 DR. HEFFEZ: You raised the question of criteria

1 for excluding certain failed specimens from the regression  
2 analysis.

3 DR. BESSER: Yes, I would like justification for  
4 that.

5 DR. HEFFEZ: And, handling of the carbides.

6 DR. BESSER: Carbide products. That is right.

7 DR. HEFFEZ: I think those are the major points.  
8 Is that correct?

9 DR. BESSER: The major points, plus also possibly  
10 later in this meeting concern about postmarket surveillance  
11 and retrieval of these prostheses further down the road in  
12 the interest of looking at wear and wear debris, and  
13 degeneration of the condyle.

14 DR. HEFFEZ: Okay. Now, what I would like to do  
15 is proceed to the next presentation by a panel member. That  
16 would be Dr. Anseth.

17 DR. ANSETH: I am Kristi Anseth, and I sort of  
18 have dual affiliations. I am at the University of Colorado  
19 at Boulder, at the Chemical Engineering Department, and I am  
20 also associated with Howard Hughes Medical Institute.

21 [Slide]

22 Again, without being too redundant about some of  
23 the issues that have already been raised, I wanted to focus  
24 mainly on two main points, the first being whether the data  
25 that is presented is relevant to both the total versus

1 partial joint prostheses, and then special issues associated  
2 with specifically the partial joint prosthesis, and then  
3 some of the information that is difficult to get from the  
4 engineering data and can we draw any inferences from the  
5 clinical data set.

6 [Slide]

7 So, first with the engineering data, a lot of data  
8 was presented on the metal-on-metal and metal-on-  
9 polymethylmethacrylate implants. So, the metal-on-metal  
10 devices were the same cobalt chrome materials that we were  
11 hearing about for the fossa-eminence. So, many of the  
12 things associated with biocompatibility and overall  
13 mechanical properties will be very similar and relevant.

14 The tests that have some unique aspects are  
15 related to those that are the dynamic testing, and you are  
16 looking at motion and movement of the fossa elements against  
17 another material. As has already been iterated this  
18 morning, the worst-case scenario was selected as the highly  
19 polished head where you can get a single point contact on  
20 the fossa-eminence, the idea being that you will get the  
21 highest load at this point, the highest wear at this point.  
22 I think that is relevant for many cases, but I think there  
23 are also some issues that I would like to bring up.

24 There was a lot of finite element analysis done to  
25 address and get at loads and stresses that the implant would

1 experience and, again, I think this is reasonable for  
2 looking at general material properties. Some of the issues  
3 come in when you are trying to look at the bone-on-metal  
4 type of interactions because finite element analysis, or at  
5 least what was presented, doesn't take into account any of  
6 the interactions at the interface or compliance of the bone,  
7 and what-not. But I do think it is relevant in terms of the  
8 bulk properties of the implant.

9           The fatigue testing -- I think I have similar  
10 issues that were already raised in terms of the fatigue  
11 limit being 130 lbs. and, depending upon the safety factor,  
12 whether that is within reason. Static load testing I  
13 thought was fine in terms of the studies that were performed  
14 and the outcomes measured.

15           One of the issues I had was with the wear testing,  
16 and I just threw up this example from the data set which  
17 showed wear of the metal-on-metal versus the metal-on-  
18 polymethylmethacrylate head, and just to bring out the point  
19 that when you have two dissimilar materials you are going to  
20 get very different wear rates, which makes it more  
21 complicated when you want to look at the fossa-eminence on  
22 the bone. I would agree that the fossa-eminence worst wear  
23 rate is probably predicted by the studies that were done for  
24 the metal-on-metal. But when you look at the perspective of  
25 the bone or the native tissue, that may be where the concern

1 lies, and that is not the case.

2 [Slide]

3 So, from the partial joint prosthesis, from the  
4 data that I just discussed briefly, when I say no additional  
5 tests I mean no additional tests that were just specific to  
6 the partial joint in terms of that dynamic environment. In  
7 particular, I was curious and would like to hear more about  
8 what the company thinks in terms of any potential issues or  
9 new issues that might result when you only have the fossa-  
10 eminence in place. And, I alluded to the perspective that  
11 you are looking at. Are you looking at the mechanical  
12 performance of the fossa-eminence? Are you looking at the  
13 wear of the fossa-eminence? Are you looking at what is  
14 happening to the condyle or if the disk is in place? And,  
15 wear is a very complicated process that is influenced by  
16 your number of contact points, the roughness, whether there  
17 is a third body present from wear debris and what-not. So,  
18 I think for the worst-case situation you need to be careful  
19 in terms of what perspective you are looking at.

20 So, because the company iterates that it is  
21 difficult to do this in vitro experiment with living bone  
22 against their fossa-eminence, there wasn't any data to try  
23 to extrapolate or compare to other systems, I looked a  
24 little bit at the clinical data to see if we could find if  
25 there was evidence for this occurring or should it be an

1 issue. I think we heard about the clinical data already  
2 today and I just wrote down some of the basic numbers.

3 I think one of the concerns again is the very low  
4 N at the three-year period. So, if we are looking for an  
5 adverse effect that would be caused by wear on either the  
6 condyle or the meniscus or whatever that might be, it is  
7 difficult to assess what is causing any adverse effect. We  
8 have heard a lot that it is not related to the implant  
9 itself but more related to the procedure or the patient, and  
10 that was a little difficult to quantify and I would like to  
11 hear more about that.

12 [Slide]

13 So, in terms of degeneration of the condyle, what  
14 I was able to find -- mainly I took out excerpts from  
15 different reports from collaborators. What you see is  
16 something that is not necessarily so easy to quantify, and I  
17 think it is difficult to quantify but Dr. Levine and Abbey,  
18 in their letters, say that there is minimal condylar  
19 remodeling secondary to the prosthesis, and in the small  
20 population where it has been noted it cannot be related to  
21 the prosthesis but correlates to the natural course of the  
22 pathology itself. I think it is really difficult to assess  
23 whether it is from the prosthesis or whether it is from  
24 disease progression, and I would like to hear a little bit  
25 more about that as well.

1           Again, these are just excerpts and I don't feel  
2 the need to read them all, but I think there is also a point  
3 of view, in the last quote, where Dr. Garrett says that in  
4 cases where you do see resorption of the condyle, he points  
5 out that it is not the fault of the prosthesis as surgeons  
6 may think who are not clinically experienced. Other  
7 surgeons may call this a failure of the Fossa-Eminence  
8 Prosthesis even though there is absolutely no evidence of  
9 reaction to the prosthesis. I think to some extent we have  
10 to also assess where the burden lies. Is it up to us to  
11 find whether the implant is causing negative impact or  
12 resorption of the condyle, or does the company need to  
13 provide more quantitative data on that?

14           [Slide]

15           Again, these are just sample quotes again. In  
16 general, I think that we have heard from many of the  
17 patients as well that certainly people have benefited from  
18 this, and I think we have heard the negative on this as  
19 well, and it is very difficult to quantify this issue and  
20 that is one thing I would also like to hear more discussion  
21 about.

22           [Slide]

23           Again related to this issue, it wasn't clear to me  
24 either whether the disk should be removed or left in place,  
25 and whether this mattered at all with the Fossa-Eminence

1 Prosthesis. There was one study of 17 patients and 10 of  
2 the patients did not have the disk removed when they were  
3 implanted, but subsequently 4 of these had to have their  
4 disk removed to treat their symptoms. I think it at least  
5 brings up a question. If there is wear of the fossa-  
6 eminence, what happens to the debris? Does the debris get  
7 into the disk or not? I mean, that is one common thing in  
8 terns of polishing things or looking at different kinds of  
9 grinding wheels, you put particles in a soft adhesive and  
10 you use that as a means to polish something. So, I think  
11 this might be one issue I would like to hear more about.

12           So, it is difficult to get to the information that  
13 you would like but are there ways to quantify the  
14 interaction of the implants with the natural condyle and  
15 tissues, and can we look at things like a control where  
16 there is no implant put in place -- the disk is removed and  
17 no implant, and what are the relatively measures compared to  
18 those with implant?

19           [Slide]

20           I guess the last is that clearly one of the  
21 benefits of this device, as stated, is to salvage the  
22 natural condyle, and are there benefits associated with that  
23 early surgical intervention, and the clinical study that is  
24 ongoing to evaluate primarily the pain and to assess  
25 different safety issues and opening issues, but are there

1 things associated with the study where we can better  
2 quantify these effects on the natural tissues? Thank you.

3 DR. HEFFEZ: Thank you very much. Dr. Burton, I  
4 will ask for your presentation.

5 DR. BURTON: Thank you. Dr. Richard Burton,  
6 University of Iowa. My review personally led more to some  
7 of the clinical issues, and I will try to be brief in  
8 covering those as I think we need to carefully assess them  
9 as we move through the deliberation process.

10 We had Dr. Curry's paper that was presented to us.  
11 I have concerns, as I mentioned earlier, regarding the N for  
12 that being 17 out of what I feel was more than likely a  
13 larger number, and the criteria for inclusion for those 17  
14 with the conclusion that there were no condylar changes.  
15 Some of the other papers presented, they talked about a  
16 reoperation rate of 10-15 percent. That particular group  
17 had a reoperation percentage in the low 20 percentile range.

18 Again, a number of the papers and presentations --  
19 there is never a clear delineation of how you determine  
20 adaptive bone changes in the condyle versus degenerative  
21 bone changes. In all the cases, they keep going back to the  
22 fact that none of these seemed to be implant related. I  
23 guess it is very unclear to me how that is being determined.  
24 There may be some changes and I think that may eve be  
25 acceptable. The question is, can they be implant related or

1 are they normal adaptive changes, and I don't feel that that  
2 has been addressed, candidly, on any level.

3 We have large numbers of letters of support that  
4 were part of our packages. In reading through those,  
5 unfortunately, most of those didn't provide any good, hard  
6 data that was, again, normally just related to clinical  
7 observation, both pro and con.

8 We had some earlier discussions regarding the  
9 registry data numbers and the cohort data numbers, and the  
10 fact that they are very similar, however, as you get out to  
11 the 24 or 36 month period the cohort numbers in essence  
12 really become the registry because that is all that is left  
13 of the registry that is still being reported. So the  
14 similarities are from the fact that we are really probably  
15 talking about the same group and, again, we are dealing with  
16 a data set that by the point in time where many other  
17 studies and other procedures and other situations show  
18 patients returning with problems at the 18 to the 24 to the  
19 36 month point -- our data set has become extremely small,  
20 to the point that we may not be seeing those patients.  
21 Certainly, in the reports we have we don't have that but,  
22 again, that small data set may not adequately reflect what  
23 the overall condition of those patients at that point of  
24 time is.

25 Another issue that runs through all this is the

1 question of internal derangement and whether the fossa  
2 implant should be a primary treatment for that. It seems to  
3 me that as a means of preventing further treatment -- we did  
4 have the letter from Dr. Keller which the company presented  
5 as support, with some other questions from Dr. Curry. In  
6 Dr. Keller's letter, he asks us to consider the fact that  
7 that particular case was more of a salvage procedure versus  
8 a treatment, and he actually said not for internal  
9 derangement.

10 I think one of the concerns that I had looking  
11 through the various data sets is, again, that there don't  
12 appear to be any real controls to that. We don't have a  
13 comparison group other than those that have received this  
14 procedure and these particular implants. Either a control  
15 group without treatment, and I don't think it even has to be  
16 run by the company per se but I think there are other  
17 studies out there that show the changes both in pain, range  
18 of motion, and groups that have other treatments or no  
19 treatment at all out to a reasonable length of time to act a  
20 as a control, and there is no comparison to that type of  
21 group.

22 In looking at some of the materials that were  
23 presented to us, I have some concerns regarding the informed  
24 consent process and I think that Dr. Anseth provided a  
25 quotation from Dr. Garry about the failure of the implant

1 versus a progression of disease, and I have concerns that in  
2 each of the things that were presented to us, every time  
3 there seemed to be anything that was either adverse or could  
4 be interpreted as adverse, it always seems to be either  
5 operator or patient dependent and at no time shows any  
6 correlation with the implant itself and I think, you know,  
7 that after all a bad result with proper consultation,  
8 informed consent is not a surgical failure or failure of the  
9 prosthesis, it becomes an indication for the next procedure  
10 which has already been discussed as a possibility with the  
11 patient.

12 I am happy to hear from Miss Blackwell that the  
13 metallurgy issues have been resolved. I certainly had  
14 concerns about that from the prior panel meeting, and it  
15 appears that those issues have been dealt with. In the  
16 materials that we have here that was not clear.

17 But in my particular view what this boils down to  
18 is whether or not, particularly the fossa implant, is,  
19 first, safe as an implant and, secondly, what those  
20 indications are. Whether the indications are for that  
21 subset or that grouping which includes things such as  
22 ankylosis or infection or tumor or internal derangement. I  
23 think probably with the latter indications most of us feel  
24 much more comfortable with those as a potential implant  
25 situation.

1           Unfortunately, it appears from what I can see in  
2 the data that the majority of the patients who are receiving  
3 these are receiving these for internal derangement -- the  
4 great majority for that, and that seems to be the primary  
5 indication for its utilization. Certainly the other ones  
6 fall into that but the majority of the patients being  
7 selected for this particular implant are due to internal  
8 derangement. So, we have a question of safety, and it  
9 appears, at least from the metallurgical standpoint and  
10 possibly from some of the engineering standpoints that that  
11 may be resolved. The question then secondarily is, is it an  
12 efficacious treatment for internal derangement?

13           A number of the letters refer back to the fact  
14 that it seems to be somewhat operator dependent, and one  
15 thing which is certainly not clear is if you look at the  
16 number of these particular implants that have been used, how  
17 many surgeons are placing the majority of these versus a  
18 widespread utilization within the oral surgery community.  
19 And, are those failures that are out there not being tracked  
20 back and could they be, in fact, again, not prosthesis  
21 related but perhaps a training issue or a labeling issue  
22 which needs to be addressed as well so that we may have what  
23 is a safe implant or prosthesis but requires additional  
24 efforts by the company to provide adequate training and  
25 oversight of the selection and placement of these implants.

1           So, like I said, I think we need to look at the  
2 safety and the efficacy and, most importantly, what are the  
3 clinical indications for the utilization of the implant.

4           DR. HEFFEZ: Thank you very much.

5                           **Open Committee Discussion**

6           At this time, I would like to proceed to open  
7 committee discussion regarding the issues. The best way  
8 that I believe we could approach this efficiently is to look  
9 at the questions that have been asked for us to answer as a  
10 panel. They are available on the power-point presentation  
11 and format so that everybody will be familiar with them.

12                           Question one is the following: Given the  
13 justification and the data presented in the current PMA, is  
14 there valid scientific evidence to support effective use of  
15 the Fossa-Eminence Prosthesis for the indication of internal  
16 derangement?

17                           So I would like the discussion just to exclusively  
18 deal with this problem, and not to deal with the second  
19 question, which is other disease entities. I know after  
20 that heavy lunch, delicious lunch it will be hard to evoke  
21 good questions or discussion.

22                           DR. BERTRAND: I have a comment. Given the small  
23 N number of 24 and 36 months, it is hard for me to feel  
24 convinced that entering a virgin joint and placing a  
25 metallic implant is always indicated when, at that same time

1 period, a large percentage of symptomatic patients with  
2 internal derangement become asymptomatic. When 75 percent,  
3 70 percent of those patients at 18 months, in a controlled  
4 comparison, are getting better we don't have that same kind  
5 of data with the eminence device to say we are going to  
6 achieve, for the whole group of patients being operated,  
7 that same success. Does anybody have any comments on that?

8 DR. BURTON: Richard Burton. Dr. Bertrand, I have  
9 the same questions as well, and the fact that it is  
10 difficult to see what certainly is an evasive procedure  
11 being the first stop in the treatment for these patients.  
12 If it could be shown conclusively enough that there was a  
13 prevention of further surgery or that this would arrest that  
14 safely long-term, that might be true but I am not convinced  
15 that the data that we currently have really indicates that.

16 DR. HEFFEZ: I believe to avoid some difficulty in  
17 interpreting this question, I think we should clarify  
18 internal derangement because people have been using the  
19 Wilkes classification -- there are several classifications  
20 available, but if we go through the Wilkes classification  
21 since its name has been evoked here several times, it has  
22 grade I through V. So, one could easily say grade V  
23 internal derangement, but I don't want to preempt it. But  
24 the second question is going to refer to degenerative  
25 processes. So, I believe that if we, as a committee, look

1 at this question indicating earlier internal derangement  
2 problems rather than the later one, which are usually in  
3 relationship to a degenerative process, we may be able to  
4 answer this question easier. So, I would like to hear from  
5 the committee how they feel about that -- the term internal  
6 derangement not referring to the degenerative process and,  
7 therefore, it would be earlier stages of internal  
8 derangement. How does this committee feel about that?

9 DR. BESSER: Mark Besser. I will ask you for  
10 clarification. Wilkes class I?

11 DR. HEFFEZ: I and II are earlier classifications  
12 -- are earlier in the disease process.

13 DR. BESSER: Would a class I be an internal  
14 derangement?

15 DR. HEFFEZ: Yes, those could be internal  
16 derangements. Class II could be internal derangements.  
17 Class III could -- it is all just increasingly severe. It  
18 is on a grade of severity.

19 DR. BESSER: Could someone for us review exactly  
20 the Wilkes classification so that whole panel is aware of  
21 it?

22 DR. HEFFEZ: To make it easier, I think that  
23 industry, I believe, had one slide with the Wilkes  
24 classification. We could put it up there and I think  
25 everybody will understand.

1 In the interim, while they are kind enough to set  
2 up their presentation and show that slide, are there other  
3 questions regarding this issue? Dr. Patters?

4 DR. PATTERS: Mark Patters from Tennessee. A  
5 question that I would pose to the panel, if I am quoting Mr.  
6 Albrecht correctly, he said the registry was not a study. I  
7 would have to agree that the registry is not a valid  
8 scientific study because the rates of lost-to-follow-up are  
9 so high. In order for it to be valid, one would have to be  
10 able to make the assumption that those lost-to-follow-up had  
11 the same success rate as those not lost-to-follow-up.

12 I don't think that is an assumption that can be  
13 made at this point. So the valid study, the scientifically  
14 valid study, is, no doubt, the prospective study but,  
15 unfortunately, it appears to be premature to evaluate the  
16 data since most of the patients have not reached the long-  
17 term stage in the study.

18 So I am at a loss, then, to find the valid  
19 scientific data to even answer this question since I don't  
20 believe the registry study is a true clinical study and the  
21 prospective study is not complete at this time.

22 DR. HEFFEZ: Mr. Ulatowski?

23 MR. ULATOWSKI: The panel is considering valid  
24 scientific evidence which is a range of possibilities, not  
25 necessarily consisting of a prospective study. So you need

1 to assess and find the merits of the elements of the data  
2 presented and whether it is supportive or not supportive.  
3 Registries are, I won't say often used, but for 515(b)  
4 devices, these pre-'76 devices, that sort of information is  
5 more common in regard to supportive data, data over the  
6 years, where you necessarily have to go back and look back  
7 at what has been going on rather than what we traditionally  
8 do now with the newer devices.

9           So I wouldn't necessarily discard it, but it has  
10 to be factored in.

11           MR. ALBRECHT: Doug Albrecht, TMJ-Implants.

12           [Slide.]

13           This is the slide with basically the symptoms that  
14 a patient would experience with Wilkes clarification.  
15 Radiologically, for class I, you may see a slight forward  
16 displacement with good anatomic contour of the disc. For  
17 class II, you will see, again, a slight forward  
18 displacement, some deformity of the disc that is beginning  
19 and some thickening of the posterior edge of the disc.

20           Class III is where you will see an anterior disc  
21 displacement with significant deformity, prolapse of the  
22 disc and increased thickening, again, of the posterior edge.  
23 Stage IV, you will see an increase in severity of the  
24 symptoms over class III with positive tomograms showing  
25 early to moderate degenerative changes, flattening of the

1 eminence and deformed condylar head sclerosis.

2 Last stage IV, you will see a disc or attachment  
3 perforation, filling defects, gross anatomic deformity of  
4 the disc and hard tissues, positive tomograms with  
5 essentially degenerative arthritic changes.

6 DR. HEFFEZ: Thank you. So, essentially, we are  
7 looking at the internal derangement process, if you want, I  
8 through III not showing radiographic evidence and IV and V  
9 showing radiographic evidence consistent with the  
10 degenerative process.

11 So one could consider that the degenerative  
12 process be included in the second question to come and  
13 consider internal derangement as the early process.

14 Does the committee feel that there is scientific  
15 evidence to warrant the use of the Fossa-Eminence Prothesis  
16 in that situation? Let me stimulate some discussion, then.  
17 Dr. Besser, do you have something to say?

18 DR. BESSER: Dr. Besser. I don't think the  
19 questioning can be answered the way it has been asked so  
20 far, and I think that is a lot of the reason, at least, I am  
21 sitting here unable to think of a way to respond to it.

22 It is presented as a yes/no question and the  
23 answer is not yes or no. I think I have seen evidence  
24 presented today that, for patients in category IV where  
25 there is significant joint degeneration going on, and these

1 are obviously candidates for both surgery and for an  
2 implant, in these cases, I think, you can see some  
3 indication for the Fossa-Eminence Prosthesis.

4           Likely, I would also state that patients in  
5 category I, unless there is some other reason, and I don't  
6 want to take that decision, the making of that decision,  
7 away from the surgeon or the physician or dentist who is  
8 seeing that patient, but I don't think you can routinely say  
9 that yes, everybody who starts to have a clicking jaw should  
10 have one of these Fossa-Eminence Prostheses put in. I don't  
11 think that is the manufacturer's contention either.

12           Somewhere in the middle, we may cross that line.  
13 So possibly, if we can look at--unless there is a need to  
14 only use the two words "internal derangement--to look at  
15 indications or subheadings of internal derangement that  
16 might be easier to say yes or no to when asked the question.

17           DR. HEFFEZ: Certainly, we are permissible to  
18 qualify the question saying the early process in which there  
19 is no evidence of any degeneration in the condyle is the  
20 evidence, scientific or supportive evidence, for use of the  
21 Fossa-Eminence Prosthesis.

22           You raised one point regarding loading. You felt  
23 that loading wasn't satisfactory. One could raise the  
24 question whether, in the early problem when there is mild  
25 clicking, for example, that the loads across that joint

1 might be greater than later on in the cycle of the disease  
2 and that might help you in your thinking process.

3 Dr. Bertrand, I think you had something you wanted  
4 to say?

5 DR. BERTRAND: In looking at these indications,  
6 the degree of internal derangement, with new evidence these  
7 types of patient present as, out of the University of  
8 Michigan, more than 70 percent of these patients with  
9 perceived facial pain have pain in other parts of the body  
10 concurrently.

11 Published in the Annals of Internal Medicine in  
12 January, 2000, less than--about 15 percent of patients with  
13 continuous pain, crepitus, painful function, 83 percent of  
14 them have a comorbidity of many other factors. My concern  
15 about doing something surgically to this group of patients,  
16 how well have those comorbid factors been included in the  
17 documentation and treated right from the onset.

18 If, indeed, those comorbid factors, like headache,  
19 irritable bowel syndrome, many other factors, fibromyalgia,  
20 have been ruled out and, perhaps, there is an indication.  
21 When we look at the failure of conservative therapy, what is  
22 the expertise of that conservative therapy and how are all  
23 the risk factors identified from the onset.

24 With the emerging evidence that, perhaps, bruxism  
25 is a serotoninerically effect, has that been addressed?

1 What are the medications that might be contributing to the  
2 factors that are producing this type of presentation to  
3 start?

4 I don't think hardly any of those questions have  
5 been addressed. To do something where a large majority of  
6 patients followed for thirty years in Holland do resolve  
7 rather well, regardless of the image conformity of the  
8 joints, seems a little bit premature with the amount of data  
9 that is available right now.

10 DR. HEFFEZ: Thank you.

11 Dr. Burton?

12 DR. BURTON: In response to Dr. Besser's comment  
13 over there, I would agree. I think that the problem is  
14 that, and in reviewing what was presented to us, we all know  
15 that internal derangement is a broad diagnosis with a lot of  
16 different facets and levels to that.

17 My concern is the fact that, in the materials that  
18 have been presented to us from the company, it just says,  
19 internal derangement. It does not either quantify or  
20 identify that. In their selection and inclusion criteria,  
21 internal derangement alone fits the inclusion criteria for  
22 that. It is not quantified and there are patients that are  
23 in the ones that they presented that were Wilkes I and II.

24 So I guess I have concerns about utilizing the  
25 indication of internal derangement as an indication for the

1 fossa prosthesis. We can discuss whether or not we should  
2 try to quantify it and that, obviously, will become much  
3 more difficult.

4 But our first question is, does the effective use  
5 of the Fossa-Eminence Prosthesis for the indication of  
6 internal derangement as a non-quantified statement and, on a  
7 non-quantified basis, I would say that it doesn't.

8 DR. HEFFEZ: So, the inclusion criteria, actually,  
9 that industry presented in their proposal is greater than or  
10 equal to class II of Wilkes, but their data did have  
11 combined I and II on their slide. The majority were, though,  
12 in III, IV and V.

13 We are permitted to look at this question in more  
14 detail and think of the process, whether internal  
15 derangement, as a primary diagnosis or when the internal  
16 derangement is more severe, whether, when there is presence  
17 of degeneration in the joint, whether we want to consider  
18 that as an alternative pathological problem.

19 I think we should not use specifically a  
20 classification, for example the Wilkes classification. We  
21 would be talking in generic terms, whether the early process  
22 or the last process, and maybe discount the late internal  
23 derangement and consider that indicative of degeneration.

24 Dr. Stephens, did you have a comment?

25 DR. STEPHENS: I think that makes sense because,

1 even though internal derangement is a broad term, I think  
2 that when you open this up and start to define what areas of  
3 internal derangement that we are going to use, it starts to  
4 move toward clinical decision making. These patients, I  
5 don't there is any way to take a lot of the decision making  
6 out of the surgeon's hand at the time that he is evaluating  
7 the patients because they really do present very  
8 differently.

9           It is very possible to have patients with very  
10 severe radiographic changes who are essentially  
11 asymptomatic. On the other hand, many patients with severe  
12 pain really show very little change on their MRI. So I  
13 think we have to be careful if we start to break it down. I  
14 think that it has to remain somewhat generic.

15           DR. HEWLETT: Ed Hewlett. While certainly the  
16 question of the disposition of the internal-derangement  
17 indication and how that should actually be more specific is  
18 important. I just want to, again, draw attention to another  
19 aspect of this question in so far as, for the purposes of  
20 answering the question, it may render the internal-  
21 derangement aspect moot, and that is, again, getting back to  
22 the amount of data in terms of the sample size and in terms  
23 of the length of time that has occurred allowing observation  
24 and collection of that data.

25           I am talking about what we might call the

1 scientifically valid data from the prospective clinical  
2 trial. I think that the very small amount of data and the  
3 length of time that we have a substantial number of subjects  
4 from whom data have been collected is a significant issue  
5 here and it makes it difficult for me to be able to answer  
6 this question in the affirmative.

7 DR. HEFFEZ: I think we have had enough discussion  
8 regarding this point. I would like to go on to the next  
9 question. That question; the sponsor is also requesting  
10 approval for other indications besides the internal  
11 derangement. They are listed as four. One is inflammatory  
12 arthritis involving the temporomandibular joint not  
13 responsive to other modalities of treatment. Two, recurrent  
14 fibrosis and/or bony ankylosis not responsive to other  
15 modalities. Three, failed tissue graft. Four, failed  
16 alloplastic partial joint reconstruction.

17 I think to help stimulate discussion on this  
18 question, we should be looking at each of those  
19 individually. I will ask industry to just clarify their  
20 definition of inflammatory arthritis.

21 DR. CHRISTENSEN: That can be in the early  
22 inflammatory situation involving the innermost part of that  
23 joint, from synovitis to capsulitis to any other thing that  
24 happens in that area. So that is how we have talked about  
25 it.

1 DR. HEFFEZ: How do you differentiate that from an  
2 internal-derangement process?

3 DR. CHRISTENSEN: You may not. This may be an  
4 internal internal-derangement process. The only way you are  
5 going to know on that is a biopsy of that tissue. The  
6 symptoms may be exactly the same or they could be slightly  
7 different.

8 DR. HEFFEZ: Thank you.

9 DR. BURTON: would you expect, with inflammatory  
10 arthritis, to see any radiographic, in terms of bony changes  
11 associated with the device, just an internal derangement?

12 DR. CHRISTENSEN: Not if it is early; no--if it is  
13 an early situation. If it goes on for a period of weeks or  
14 months; yes, I would expect to see something happen  
15 bonewise.

16 DR. HEFFEZ: Dr. Hewlett?

17 DR. HEWLETT: Edmond Hewlett. Even though Mr.  
18 Chair asked us to consider these individually, I would just  
19 like to point out, from a collective standpoint, that,  
20 according to the information that has been supplied to us,  
21 the number of subjects in the prospective trial that  
22 collectively fall into these categories comprises 19 percent  
23 of the subjects in the study.

24 Clearly, in what has already been characterized as  
25 a subject pool at a very preliminary stage of data

1 collection, I would submit that we really don't have a  
2 strong enough sample size of these various conditions to  
3 really answer question No. 2.

4 DR. HEFFEZ: One of the problems is when you have  
5 an all-encompassing definition of inflammatory arthritis  
6 where it encompasses basically the issue of question 1 is  
7 that it sort of makes it even more difficult because the  
8 numbers are smaller.

9 I don't remember exactly but it is certainly on  
10 the order of maybe about 10 percent, I believe, for the  
11 remaining conditions if you eliminate the first condition,  
12 inflammatory arthritis.

13 DR. BURTON: Richard Burton. My question, sort of  
14 back to an issue, then, that we have within approximately  
15 80 percent of the indications in the prospective trial are  
16 internal derangements and then what, approximately then  
17 another 10 percent are involved with some grouping of  
18 inflammatory arthritis and 10 percent in the other three  
19 indications.

20 But, again, I guess I am not clear where that line  
21 falls between internal derangement and inflammatory  
22 arthritis given at least what I have heard as the  
23 indications for that. So I guess it seems that we have got  
24 two questions, but it seems as if the inflammatory arthritis  
25 almost falls more in with the--given the fact that there may

1 or may not be radiographic findings with it, falls in with  
2 the internal-derangement grouping.

3 So we have got almost 90 percent of the group  
4 within those two, internal derangement and inflammatory  
5 arthritis, and a relatively--very, very small grouping in  
6 the other three indications.

7 DR. HEFFEZ: One of the things that might have  
8 been difficult to collect data is in the clinical-study  
9 protocol, TMJ 96-001, the way it is indicated as far as the  
10 history. There are a lot of overlapping entities,  
11 inflammatory resorptive joint pathology, temporomandibular  
12 joint disease defined as greater than or equal to Wilkes II,  
13 stage II. Internal derangement is another, and degenerative  
14 joint disease. So there is a lot of overlapping.

15 DR. BURTON: I guess that sort of goes along with-  
16 -maybe it is my lack of understanding but we had internal  
17 derangement as a separate indication from temporomandibular  
18 joint disease, Wilkes stage II or above. Which one is it?

19 DR. HEFFEZ: One entity I think that we should  
20 bring out for discussion is bony ankylosis. I think this is  
21 a problem in the sense that many clinicians grasp for--in  
22 the treatment of this problem, try to create a  
23 pseudoarthrosis and, in creating the pseudoarthrosis, they  
24 have, in the past, put alloplastic material, autografts, and  
25 nothing.

1 I believe, in certain situations, alloplasts--and  
2 I can be corrected, but I believe that silastic, for  
3 example, even though it has been pulled from the market, can  
4 be used as a interpositional graft.

5 DR. BURTON: Temporary interpositional graft.

6 DR. HEFFEZ: Temporary--for this condition. So  
7 this is a condition that stands a little bit outside of the  
8 other criteria that are placed, and I would like to hear,  
9 maybe, some discussion about ankylosis.

10 Dr. Stephens, could I maybe ask you to tell me  
11 your experience?

12 DR. STEPHENS: Are you speaking about ankylosis  
13 with respect to this specific device or--

14 DR. HEFFEZ: Yes; the use of this device. Do you  
15 think it would be indicated in treatment of bony ankylosis?

16 DR. STEPHENS: I think that, for bony ankylosis,  
17 the major problem, the major failures, in treating bony  
18 ankylosis is reankylosis around whatever device is used. It  
19 seems that this device, alone, in cases of major ankylosis,  
20 may not be thick enough, may not create enough of an  
21 interarticular gap in most cases, in my opinion.

22 DR. HEFFEZ: Any other discussion regarding these  
23 points? Dr. Burton?

24 DR. BURTON: Richard Burton. I guess I would also  
25 like, from industry, a little clarification on what the last

1 one is. It says, "failed alloplastic partial joint  
2 reconstruction." Was that one of these particular ones that  
3 needed to be replaced? Is this an indication for its  
4 replacement or--I guess I am not currently aware that there  
5 is or has been another alloplastic partial joint system on  
6 the market.

7 MR. ALBRECHT: That would have been the teflon  
8 Proplast and silastic. I presume that is what you are  
9 talking about.

10 DR. HEFFEZ: Could you please come to the  
11 microphone and identify yourself, and then make the  
12 statement.

13 DR. CHRISTENSEN: Dr. Bob Christensen. Yes; the  
14 failed Vitek interpositional implant could be one of them.  
15 You were mentioning a minute ago silastic, which has been  
16 used in there as a poor substitute for an ankylosis case.  
17 It could be one of our implants, for some reason, in which  
18 bone has grown up around us. We have seen that happen and  
19 gone in and put in either a patient-specific implant or put  
20 in a larger size implant. So that is what would fit in  
21 there.

22 We have used the Fossa-Eminence Prosthesis on a  
23 number of occasions for just bony ankylosis. I wrote papers  
24 on that back in the '60's. So if you want to look it up,  
25 it's there.

1 DR. HEFFEZ: Thank you. Does the committee feel  
2 that there are any other questions to be raised from FDA or  
3 from industry that would help them ultimately to make a  
4 decision regarding this device for these indications?

5 DR. COCHRAN: This is David Cochran. I guess it  
6 would be helpful if somehow the panel could be clarified,  
7 for instance, for failed tissue graft, what the numbers are  
8 for the data, what data exist for failed tissue graft, for  
9 instance, if we are going to break it out into these  
10 different components.

11 It would be nice to see data that related to that  
12 specific category.

13 DR. HEFFEZ: So, in order to assist us, we will  
14 ask industry to put up on the screen the distribution of the  
15 cases according to these criteria that were selected. While  
16 they are doing that, I will ask industry--when Dr. Janosky  
17 was asking you regarding the distribution of cases and how  
18 long they were studied for, were you considering all the  
19 cases or did you have a breakdown according to these  
20 different problems, these different indications?

21 MR. ALBRECHT: Doug Albrecht, TMJ Implants.

22 [Slide.]

23 On the screen now is the breakdown of the  
24 different indications that we did present data on, as I  
25 said. Nearly 90 percent include internal derangement,

1 either with perforation or without perforation or associated  
2 with arthritis. In the prospective study, itself, 3 percent  
3 of the patients had a previously failed tissue graft or  
4 alloplast before receiving our device again.

5 DR. HEFFEZ: Do you have an idea of how long they  
6 were followed for, the last two, ankylosis, fibrosis and  
7 failed tissue graft?

8 [Slide.]

9 The fibrosis and ankylosis patients, I start out  
10 with about eight patients and, at twelve months, I have  
11 three patients still reporting. At 24 months, one patient  
12 has made it that far.

13 DR. COCHRAN: If you had 3 percent of the failed  
14 alloplast, where you are talking about four or five  
15 patients, but that data is not up here as well?

16 MR. ALBRECHT: No. The N was so small, it wasn't  
17 representative of any significant results.

18 DR. HEFFEZ: I would like to move on to question  
19 No. 2--well, question No. 3, really. I will read question  
20 No. 2; has the sponsor provided valid scientific data to  
21 support effective use of the Fossa-Eminence Prosthesis for  
22 those indications that we had listed before. We will be  
23 having to look at; if not, which indications are appropriate  
24 for use of the partial joint prosthesis and what additional  
25 data, if any, are required to support the particular

1 indication?

2 Now we will move to question 3; if, after  
3 consideration of questions 1 and 2, the panel believes that  
4 there is valid scientific evidence to support these  
5 indications, what contraindications, precautions and  
6 warnings should be applied for the Fossa-Eminence Prosthesis  
7 when used as a partial joint replacement?

8 Some of you may have already developed in your  
9 mind whether you felt there are indications or  
10 contraindications to this. I have one question to industry.  
11 You considered loosening of screws as a surgical problem  
12 rather than a device problem.

13 What led you to place screw-loosening only in the  
14 surgical-related section rather than considering it in  
15 device-related? Could somebody from industry answer that?  
16 Please identify yourself.

17 DR. CHRISTENSEN: Bob Christensen. A screw, in a  
18 bone plate or an implant, can certainly loosen. It depends  
19 on the type of bone you have got there and the problems  
20 there. If you have a problem with the screw, you are going  
21 to see evidence of a pattern of loosening of screws in the  
22 ramose area or in the base of the skull.

23 Screw loosening is really extremely small  
24 considering the great number, or the fair number, of these  
25 that we have out there. We pulled up some information on

1 that. I don't think it necessarily shows all of them. So,  
2 when we see it, it is either--we consider it a surgical  
3 entity because of the bone of that patient, or it can be the  
4 way the doctor puts it in.

5 If you drill a hole through the large port, or you  
6 put it in at an odd angle, it is more likely to come out.  
7 You put one in there and strip it. But if you do it  
8 properly, and use the proper drill for it, that just  
9 generally does not happen.

10 DR. HEFFEZ: The specific question would be, then,  
11 do you feel that any screw loosening that occurred was all  
12 due to clinical application of it or was it from the device?

13 DR. CHRISTENSEN: I would say it is almost  
14 entirely clinical, either patient, or the person drilling  
15 that hole and putting it in.

16 DR. HEFFEZ: Were there any cases that you felt it  
17 was from the device, that the screw loosened due to the  
18 device?

19 DR. CHRISTENSEN: That is a hard one to totally  
20 answer. I don't have an exact answer for that.

21 DR. HEFFEZ: Thank you.

22 Any questions from panel? I had an additional  
23 question for--I would like to ask Dr. Urbanek if he could  
24 tell us what he felt the learning curve for the application  
25 of this device would be.

1 DR. URBANEK: That is a very good question. I  
2 will be happy to answer it. It is not a simple answer. I  
3 am not going to ask you to define what you think is a  
4 learning curve, but there is a learning curve. First, I say  
5 there is a learning curve to put these in correctly.

6 Certain clinical things can happen that Dr.  
7 Christensen alluded to. If the hole is drilled incorrectly,  
8 if the wrong size screw is put in, if it isn't put in the  
9 correct density of bone, the chances are pretty good that  
10 screw is going to back out at some point in time.

11 But, with the amount of bone in the glenoid-fossa  
12 area, any reasonable surgeon would be able to do that with  
13 adequate experience and care. I just hesitate--it is a very  
14 good question. I prefer to think about that a little bit.  
15 Let me put it in real terms. I will relate it to my own  
16 experience.

17 After, certainly, a dozen cases, I felt very  
18 certain that I could efficiently, correctly, insert the  
19 implant and expect a good result. Actually, that is pretty-  
20 -that is a small learning curve in comparison to some of the  
21 things that I do and have been trained to do. It is not  
22 extensive, but it isn't minimal, either.

23 Another way to describe that would be that I think  
24 that someone who does this work, inserts this prosthesis,  
25 needs to have experience gained from others, whether it be

1 in a training program or whether it be mentoring or whether  
2 it be in a clinical program where he is exposed to others  
3 who have more experience putting this in.

4 I think that is a very reasonable expectation, to  
5 put this in. Now, in the real world, it does not work that  
6 way all the time and it just doesn't apply to oral or  
7 maxillofacial surgery. I can quote chapter verse of many  
8 surgeons who don't see one do one, they just read it in a  
9 book and do one. That doesn't apply to any kind of surgery,  
10 actually, but, in the real world, that happens.

11 I would hope that, in surgeons who apply this  
12 technology to the temporomandibular joint, that they don't  
13 do that. How much mentoring they would need? On a relative  
14 scale, not that much. If I was starting off from scratch, I  
15 would feel very comfortable watching and participating in  
16 three, four, five of these before I felt comfortable enough  
17 where I would do it, myself, considering I had the broad,  
18 general surgical experience and the specific surgical  
19 experience of other types of maxillofacial reconstruction.

20 DR. HEFFEZ: Were you mentored?

21 DR. URBANEK: Yes and no. Was I mentored on the  
22 glenoid-fossa implant? No. Was I mentored by trial by  
23 fire? Yes. I was so familiar with the temporomandibular  
24 joint by the time I got to putting in the glenoid-fossa  
25 implant that, yes; I was mentored very well.

1 DR. HEFFEZ: I am just trying to get--it is very  
2 difficult, you are right, to answer the question, but I am  
3 just trying to get some idea. In your experience with  
4 temporomandibular joint, prior to placing any prosthesis,  
5 you felt that twelve cases--you felt comfortable after that.

6 DR. URBANEK: I felt very comfortable.

7 DR. HEFFEZ: Okay. Thank you very much.

8 DR. URBANEK: You are very welcome.

9 DR. STEPHENS: Just one follow-up question. I am  
10 Willie Stephens. Do you know if there have been any  
11 differences in screw loosening between the stock prosthesis  
12 and the patient-specific patient because I am wondering if  
13 the screw problems may not be the screw as much as it is the  
14 fit of the prosthesis.

15 DR. URBANEK: I can answer that question with  
16 great experience. It is not quite what you would expect,  
17 though. I do not believe that there is a difference in the  
18 screw loosening between stock and specific tailor-made  
19 prosthesis. It is my experience, as has been alluded to,  
20 that the screws loosen directly in relationship to the  
21 experience of the surgeon and the quality of the bone that  
22 is going in.

23 It happens in both the tailor-made and the stock  
24 prosthesis at about the same rate.

25 DR. HEFFEZ: Thank you very much.

1 DR. URBANEK: Thank you.

2 DR. BERTRAND: Peter Bertrand. I have a question  
3 for Dr. Urbanek. Sir, you were only able to supply thirty-  
4 five of your patients for the prospective study; is that  
5 correct?

6 DR. URBANEK: That is correct.

7 DR. BERTRAND: But you have 228 patients, as I  
8 recall.

9 DR. URBANEK: That's correct.

10 DR. BERTRAND: As for the more severe joint  
11 problems, of severe fibrous ankylosis, bony ankylosis, or  
12 failed other implants, can you give us some numbers on your  
13 experience with that group of patients?

14 DR. URBANEK: Certainly. My experience with those  
15 228 patients and 350-some odd implants pretty much coincides  
16 with the percentages that have been described to you today  
17 from industry in that, in my experience and my diagnosis,  
18 place on these patients, that the vast majority of the  
19 patients that I operate on have actually a true diagnosis of  
20 internal derangement/degenerative joint disease.

21 What I heard being argued and discussed before by  
22 you is, like, where is that line? Where do we draw that  
23 line as to--where do you say, this is indicated and that  
24 isn't.

25 I have heard from TMJ Implant, Inc. and they

1 submitted to you that their proposal is to draw that line at  
2 internal derangements at Wilkes classification III, IV and V  
3 to be indicated and degenerative joint disease and fibrosis.  
4 I would agree with that, by my experience. My diagnosis of  
5 internal derangement--when I say I diagnose 75, or 80,  
6 percent of my patients that I operate by internal  
7 derangement, those are Wilkes classification III, IV and V,  
8 not I and II.

9 Patients I and II get evaluated, get a pat on the  
10 head and I say, "Come back and see me when you have a  
11 problem. This is what you do; diet, antiinflammatories."  
12 But when they come to you with an internal derangement, by  
13 definition, as you saw up there, by Wilkes, and I would  
14 present to you that it is not a wrong tack to actually--it  
15 is a very commonly accepted--in our profession, it is  
16 totally accepted, Wilkes classification is the  
17 classification how you classify internal derangements of the  
18 temporomandibular joint.

19 It is very appropriate to use that classification  
20 in describing the label or any other aspect of this implant.  
21 So, in those patients, in those 350-some patients that I  
22 have done, the vast majority of them are internal  
23 derangements. But they are Wilkes classification III, IV  
24 and V. Fibrosis and degenerative joint disease spills in,  
25 too. You can have a three with fibrosis, internal

1 derangement, a IV with fibrosis and degenerative joint  
2 disease, and a V with fibrosis and degenerative joint  
3 disease.

4           There is no cut-and-dried answer. It is a very  
5 gray area. You didn't ask the question, but I have the  
6 opportunity to answer it. The relationship that you see  
7 between your patient, what they present with and their  
8 degree of pain, and the objective findings you see on  
9 physical examination, on the MRI, is what makes you  
10 determine that this patient is going to need surgery and  
11 this patient is not.

12           I don't like to be god, frankly. I don't enjoy  
13 it. But that is what it boils down to, is you are in the  
14 room with the patient. You have to make that determination,  
15 how can I best help this patient. Is surgery the best  
16 thing? Is it not? Can I do one surgery and prevent them  
17 having multiple surgeries to follow?

18           I did not prevent that comment or my opinion, but  
19 it has been my experience that now, with the properly placed  
20 glenoid-fossa prosthesis, Christensen glenoid-fossa  
21 prosthesis, that the patients don't come back for operation  
22 2, 3 and 4. In fact, the vast, vast, vast majority--I can  
23 find out for you if you want to know, but I would certainly  
24 say 90-plus percent of the patients of my experience, they--  
25 almost all of the patients do not require any kind of

1 operation again.

2 DR. HEFFEZ: Thank you very much.

3 DR. BURTON: Can I follow up? I would certainly  
4 agree with Dr. Urbanek that I think he is a very experienced  
5 surgeon--Richard Burton--that my questions is either for him  
6 or for Dr. Christensen. That is excellent, but when this  
7 product is approved and put out on the market, I hate to put  
8 it this way, it also has to go to the least common  
9 denominator.

10 So the question is, and I am not saying that that  
11 is the company's fault, what I am saying is what is--at  
12 least one of the letters went on about a lot of different  
13 things, talked about a training program and I am unaware of  
14 that involved with the company. But what oversight or how  
15 do you support the fact that this may be--someone looks at  
16 these indications, depending on their experience level, both  
17 in terms of diagnostically and surgically, makes the  
18 determination from what is given out that this is the  
19 treatment of choice.

20 But he or she may or may not be capable of doing  
21 that safely and competently. In a couple of the letters  
22 that came in to you sort of said, well, you know, the  
23 stupidity--I believe one of them stated that--of the  
24 practitioner. But the thing is that when we put this  
25 product out there, I guess I still feel we have to look at

1 what the least common denominator that is going to be  
2 utilizing it is because that is where the danger may lie.

3 I think in your hands, very candidly, it probably  
4 does do very, very well. What I do see here is a small  
5 group of very competent, highly trained practitioners who  
6 have gotten good results. The problem is that there is also  
7 a peripheral number of people with low experience and, I  
8 hate to say, lower clinical skills, who may not easily get  
9 your level of results.

10 Unfortunately, the patient doesn't know that.

11 DR. URBANEK: That is correct.

12 DR. HEFFEZ: Before we go on, only the person at  
13 the podium should be standing. Everybody else can please  
14 sit down. If industry wishes to answer this question via  
15 another individual besides Dr. Urbanek, they he can yield  
16 the podium and let that other representative come.

17 DR. BURTON: That would be fine. Whoever you  
18 would feel would be most comfortable answering it.

19 DR. URBANEK: I would be happy to yield the podium  
20 to Dr. Christensen.

21 DR. CHRISTENSEN: The question is a very good  
22 question. It is one that we were faced with twelve years  
23 ago as this thing went on the market in a full-time way.  
24 Over the years, I had trained a number of surgeons in this  
25 device in residency programs and so forth, and I recognize

1 that some are better than others.

2 But when it came to putting this out where a  
3 larger number of people could be helped, I was concerned  
4 about that also. Fairly early, we started a teaching  
5 course, and we put on maybe three or four or five or six,  
6 sometimes, per year. We did that up until a year and a half  
7 ago when this was taken off the market, which has been a  
8 shame because there is a core of people out there that need  
9 to be taught and can be taught, and we had the opportunity  
10 to be able to teach them.

11 There are not many procedures where you can go  
12 back to the person and develop the technique to begin with  
13 and still talk to him, and so forth. But the thing that  
14 really got me, we have had over 600 or 700 surgeons who are  
15 using this device, and the amazing thing to me is the our  
16 results go from 8.5 down to 2.

17 We can't hardly beat that when I put that in one  
18 person's hands, in a very competent surgeon, and we don't  
19 look like we are doing that much better. So I am amazed how  
20 well we have done that very job. I don't know if that  
21 answers it for you but that is the answer that kind of came  
22 to me.

23 DR. BURTON: Richard Burton. Dr. Christensen,  
24 what type of training was involved for the surgeons in this  
25 course that you ran?

1 DR. CHRISTENSEN: We put on anywhere from one day  
2 or half-day courses to four-day courses. We brought in  
3 surgeons from all over, like Dr. Urbanek and Curry. These  
4 men have taught--we tried to get the best we could find  
5 around the nation.

6 So we would put it on with, sometimes, live  
7 surgeries but always with a multidisciplinary approach to  
8 the thing, not just this technique but what else might help  
9 that patient. So we try to cover quite a few things.

10 DR. HEFFEZ: Thank you.

11 I would like to go back, just for a moment, to  
12 question 2 on the powerpoint slide. I want to make sure  
13 that we addressed that if we didn't feel that there was  
14 scientific data to support effective use of the Fossa-  
15 Eminence Prosthesis for the indications listed above, those  
16 indications, which indications do you think this prosthesis  
17 would be indicated for, which could be listed.

18 If they are not listed already, are there some  
19 that could be listed? Can I stimulate any discussion? I  
20 will be happy to entertain the second part of the question  
21 at the same time which is, what additional data is needed to  
22 support any of the indications that are listed.

23 Dr. Janosky, you indicated before the time frame  
24 three to six months. What time frame would you prefer to  
25 see?

1 DR. JANOSKY: Since we are dealing with both  
2 safety and effectiveness, it seems reasonable to look at the  
3 time period when most of the failure are occurring and make  
4 sure that the follow up is at least as long as that  
5 particular period of time.

6 I don't see the data to tell me how long that is.  
7 So, to give a hard and fast answer, I can't. But that would  
8 be the way we would go about looking at what the time period  
9 should be.

10 DR. HEFFEZ: So you would like to know the  
11 distribution per time of the failures.

12 DR. JANOSKY: Right; exactly. And then have the  
13 follow-up period clearly longer than that failure  
14 distribution.

15 DR. HEFFEZ: Dr. Stephens, we talked about the  
16 ankylosis issue and the possibility of reankylosis around  
17 any prosthesis that is used. Do you think any specific data  
18 would be required, further data, to support the use of this  
19 prosthesis under those situations--ankylosis? I will give  
20 you time to think about it. I know I am putting you on the-  
21 -Dr. Burton?

22 DR. BURTON: Dr. Burton. This would probably best  
23 addressed to industry and, perhaps, Dr. Christensen. But  
24 when we looked previously at the total joint, there were a  
25 number of questions raised about heterotopic bone formation

1 around that. What have been your observations in terms of  
2 the difference in this formation or--and I know that, in  
3 some of the readings that we had this time, it talked about  
4 going back and either changing the implant or removing bone  
5 around it and sometimes I believe putting some fat, various  
6 things like that, around it.

7           What has been your experience with this as just  
8 the partial joint prosthesis and those occurrences versus  
9 the total joint formation, which I know that was an issue  
10 that was discussed at quite a bit of length, heterotopic  
11 bone formation. Could you answer that please?

12           DR. CHRISTENSEN: I would like to take a little  
13 different route to get there, if I may. In the earlier  
14 years of this test, we had twelve years of this, we were  
15 seeing too many of the post-Vitek type of patient. These  
16 patients has been injured by multiple surgeries and they had  
17 become ones much more likely to develop heterotopic bone.

18           Contrary to so many people's thought, perhaps  
19 right in this body right here and I know, certainly, in the  
20 FDA, they have the feeling that you have got to wait and let  
21 this thing be the very last thing we ever do. So you want  
22 to go in and do this surgery and that surgery and whatever.

23           That is not the experience that I have had for  
24 fifty years of operating on that joint. When you know that  
25 the disease process is involved and the degenerative process

1 of that joint and there would be severe enough internal  
2 derangement or you get some bony changes in there, your best  
3 operation is that first operation for carrying that out.

4 Your least likely chance of heterotopic bone  
5 formation is in that very surgery. The more you do that,  
6 the more likely you are to develop heterotopic bone. Dr.  
7 Curry, Dr. Urbanek and others have pulled that together with  
8 information on putting fat graft in there, by doing  
9 radiation therapy on some of these patients who have  
10 multiple procedures.

11 But the thing we don't want to do is keep our  
12 patients out there--I am going to say to Dr. Bertrand that I  
13 don't want to see a patient of mine waiting for eighteen  
14 months because they are in severe pain. I have had to take  
15 some patients that were in absolute severe pain that had a  
16 perforation of that disc, and I didn't do any alternative  
17 therapy.

18 But that patient, thirty-five years later, I have  
19 got the CT scan over here, a model, showing that implant on  
20 one side of her jaw. She never had to have another surgery.  
21 So it is so easy to get caught up in the thing that you do  
22 fourteen arthroscopies and two more something else and, by  
23 the time you get done, you have got a problem.

24 We can help that by moving that back a bit. I am  
25 not saying do it injudiciously. Hear me on that. But do it

1 correctly and I think we can stop that.

2 DR. HEFFEZ: Dr. Christensen, could you stay at  
3 the podium? Could I ask you what additional data you think  
4 you could provide which would lend further support to the  
5 use of your device on these indications?

6 DR. CHRISTENSEN: I think a play out of the  
7 information we have is probably going to be about as useful  
8 as anything we have got. I don't discount the registry as,  
9 perhaps, some of you do. I have seen these patients and I  
10 have seen the issues there. I think if we stay on course  
11 and we don't back up and we do continue to collect material-  
12 -we are trying to do the very best we can and help the  
13 surgeon do the very best he can.

14 DR. HEFFEZ: What specific data would you be  
15 looking at that would help in supporting further this?

16 DR. CHRISTENSEN: Restate the whole question,  
17 because I am missing some part of--

18 DR. HEFFEZ: I would like to know what specific  
19 data do you think you could provide, in addition to what you  
20 have, or do you feel that there are certain weaknesses in  
21 some of the data that you have been provided that you would  
22 like to provide, if you had the opportunity, more data in  
23 that area that would support the use of the device.

24 DR. CHRISTENSEN: I think we have given you about  
25 all the data we have. It is amazing how many ways we have

1 looked at this thing. In the area of the internal  
2 derangement, in the upper ends of that, III, IV and V, I  
3 think that there is more than enough indication there for  
4 it. Ankylosis is a smaller group so it takes you longer to  
5 get a long group of people in that area. But the results  
6 are very good.

7 DR. HEFFEZ: But we heard from Dr. Janosky who  
8 felt that distribution to determine the time frame for  
9 safety and effectiveness, we really need to know the  
10 distribution of the failures per time. That is a piece of  
11 data, for example, that is additional.

12 DR. CHRISTENSEN: I see.

13 DR. HEFFEZ: Do you have other ideas of other data  
14 that you think you could provide that would assist?

15 DR. CHRISTENSEN: I think that the idea of when  
16 these do tend to fail, or when the problem comes, as we  
17 heard last year at the May 10 and May 11 hearing, most of  
18 the things occur in the first few months to first year.  
19 Once you get there, things kind of level off.

20 So when you see this thing level off at a year,  
21 they pretty well stay there. So I think your first few  
22 months, and that first month or two after surgery, is when I  
23 would say you are going to see the biggest problem, 28 days  
24 later, 30 days later, two weeks later.

25 If that is the case, then we have gone out. Even

1 if it is, as a statistician, your type of look at this, we  
2 have gone out, probably, far enough to get a pretty good  
3 look at it. But we have looked at a lot of them a lot  
4 longer.

5 I don't know. Do we have anything that tells us  
6 how quickly something would happen? I am not sure.

7 MR. ALBRECHT: As far as when something may happen  
8 to the patient? Doug Albrecht, TMJ Implants. Within the  
9 prospective study, we are collecting peripheral information  
10 to help confirm our primary outcome. We are looking at  
11 occlusion. We are looking at lateral movement. We are  
12 looking at muscle tenderness. We are looking at joint  
13 noises postoperatively.

14 I can say for the vast--I don't have the data with  
15 me today but for the vast majority, just eyeballing it as  
16 the study goes on, we are not seeing anything occurring with  
17 these patients with regard to a change in occlusion which  
18 would indicate, perhaps, a change in the condylar  
19 performance.

20 We are not seeing any changes as far as noise in  
21 the joint. Muscle tenderness decreases tremendously as the  
22 patient goes out. So all this will be included when the  
23 study is completed and the final report is issued but just  
24 eyeballing the data right now, the patients are doing  
25 terrific postoperatively.

1 DR. HEFFEZ: Do you feel there would be any  
2 benefit in looking at a population, for example, a subset of  
3 population who had a discectomy or meniscectomy without any  
4 alloplastic material versus use of this alloplastic device?  
5 Do you think a controlled study in that manner would assist,  
6 Dr. Christensen? If he wants to yield the floor to you, he  
7 will.

8 DR. CHRISTENSEN: I think maybe I should answer  
9 that because of the time I have had with that. In the years  
10 past, when they did discectomies or meniscectomies and I did  
11 put something in, I found that the bulk of them became not  
12 only arthritic but they became fused, either osseous or  
13 fiber-osseous fusion.

14 So I would be hesitant to suggest to patients that  
15 you go through a meniscectomy and do nothing in there. We  
16 have had such remarkable luck with--I shouldn't say luck;  
17 that is not the word--success with this fossa on putting in  
18 there, on joints that had fibrous fusion and so forth--they  
19 have done extremely well and I don't know that I--I wouldn't  
20 want to put my wife or sister or me through a discectomy and  
21 not put a good device in there when we have got so much  
22 evidence that shows it going out forty years.

23 MR. ALBRECHT: Doug Albrecht, TMJ Implants. I  
24 think this question was also posed to Dr. Urbanek who very  
25 clearly stated that he initially did meniscectomies and he

1 found that he had to go back in and do surgeries again and  
2 then put the alloplast in.

3 To answer your first question, do I think there is  
4 any benefit to it, I think, from a scientific perspective,  
5 it is probably interesting. But, considering the data that  
6 we have and the success that we have seen from this type of  
7 device, I don't think it would change the results at all.

8 DR. BURTON: Richard Burton. Mr. Albrecht, there  
9 is interest enough, though. If you look at the literature,  
10 there are a number of long-term published studies up to  
11 30 years that have shown, both radiographically and  
12 clinically, symptomatically, large groups of patients who  
13 have had meniscectomies with no interpositional, either soft  
14 tissue, either allograft or autograft, that have done quite  
15 well.

16 So again it is sort of--I would agree. I think  
17 that your success has been very good. Conversely, there  
18 also have been other groups who have not utilized that in  
19 their hands that have had very good success with the other  
20 treatment.

21 It is sort of apples and oranges, perhaps, but,  
22 unfortunately, like I said, there are other equivalent  
23 treatments that have seen what are equivalent results.

24 MR. ALBRECHT: I would like to yield to Dr. Curry  
25 but I would like to say that we are not saying that this is

1 not the only treatment available. We are saying it is a  
2 treatment that does work very well.

3 DR. HEFFEZ: Dr. Curry?

4 DR. CURRY: Jim Curry from Denver. I would like  
5 to respond to the gentleman's comments about the literature.  
6 I reviewed five different papers on meniscectomy without  
7 interpositional materials at all. Indeed, there are two out  
8 of those five articles that showed very good, long-term,  
9 postoperative pain and opening results, horrible, horrible  
10 results, though, from radiographic looking at those  
11 patients.

12 The other three of the five articles that I  
13 reviewed, they stopped doing meniscectomy without  
14 interpositional materials because of the high incidence of  
15 postoperative ankylosis and pain. So, from my review of the  
16 literature, I determined early on that discectomy without  
17 some interpositional material was not something that I would  
18 subject my patients to.

19 DR. HEFFEZ: Panel, I would like to ask you if you  
20 feel there is any other data that you think would be helpful  
21 to support the indications that are listed.

22 DR. BERTRAND: Peter Bertrand. I do think, when  
23 we are talking about invasive procedures, we need to keep in  
24 mind the thirty-year Dutch literature that has looked at  
25 many patients, long-term, supportive therapy, we are looking