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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

DENTAL PRODUCTS PANEL

of the

MEDICAL DEVICE ADVISORY COMMITTEE

OPEN SESSION

Friday, October 6, 2000

9 o'clock a.m.

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Leslie Heffez, D.M.D., M.S. Chairperson
Pamela D. Scott, Executive Secretary

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Mark R. Patters, D.D.S., Ph.D.

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INDUSTRY REPRESENTATIVE

Floyd Larson

PATIENT REPRESENTATIVE

Sue Warman

CONSULTANTS

Peter Bertrand, D.D.S.
Marcus Besser, Ph.D.
Richard Burton, D.D.S.
David Cochran, D.D.S., Ph.D.
Willie Stephens, D.D.S.

FDA

Timothy Ulatowski

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P R O C E E D I N G S

Welcome and Introductory Remarks

MS. SCOTT: Welcome to the meeting for the Dental Products Panel. To start off the meeting, I would like to introduce our panel for today.

Our chair for today's meeting is Dr. Leslie Heffez. He is Professor and Department Head of Oral and Maxillofacial Surgery with the University of Illinois at Chicago.

We also have with us today Dr. Kristi Anseth. She is Patten Associate Professor in the Department of Chemical Engineering at the University of Colorado.

We also have Dr. Edmond Hewlett. He is Associate Professor with the Division of Cariology and Restorative Dentistry with the University of California at Los Angeles, in the School of Dentistry.

We also have Dr. Janine Janosky. She is Assistant Professor with the Department of Family Medicine and Clinical Epidemiology within the School of Medicine at the University of Pittsburgh.

We have Dr. Mark Patters, who is Chair of the Department of Periodontology within the College of Dentistry at the University of Tennessee.

Our consumer representative for today is Ms. Lynn Morris. She is Deputy Director of the Board of

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Relations with the California Department of Consumer Affairs, Executive Office.

Our industry representative is Mr. Floyd Larson. He is President of PacMed International. I have to apologize for the mistake in the program; it states Pacific Materials and Interfaces.

MR. LARSON: Former name; same thing.

MS. SCOTT: Former name; same company. Our patient representative today is Ms. Sue Warman. She is a TMJ patient, with past experience as a patient. Also, in the mid-80's she was the head for a local TMJ support group for about two years.

We also have with us today Dr. Peter Bertrand. He is the Director of the Orofacial Pain Clinic and specialty adviser for oral facial pain and TMD with the National Naval Medical Center.

We also have Dr. Marcus Besser, who is Assistant Professor in the Department of Physical Therapy at Thomas Jefferson University.

Also on our panel today is Dr. Richard Burton. He is Assistant Professor of Oral and Maxillofacial Surgery with the Department of Hospital Dentistry at the University of Iowa Hospitals and Clinics.

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We also have Dr. David Cochran, who is Professor and Chair of the Department of Periodontics at the University of Texas Health Science Center at San Antonio.

Also, we have Dr. Willie Stephens. He is Associate Surgeon for the Harvard Oral and Maxillofacial Surgery Associates.

Our FDA participants for today include Mr. Tim Ulatowski, who is the Director of the Division of Dental, Infection Control and General Hospital Devices. Also, we have Dr. Susan Runner, the Branch Chief for the Dental Devices Branch; and Ms. Angela Blackwell who is a reviewer within the Dental Devices Branch.

Before we get into the meeting, I have several administrative items to take care of. The first is the reading of the conflict of interest statement for today's meeting.

The following announcement addresses conflict of interest issues associated with this meeting, and is made part of the record to preclude even the appearance of an impropriety.

The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employers' financial interest. To determine if any conflict existed, the agency reviewed the submitted agenda and all

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financial interests reported by the committee participants. The agency has determined that no conflicts exist. However, we would like to note for the record that the agency took into consideration a matter regarding Dr. Willie Stephens who reported interest but no financial involvement in firms at issue. The agency has determined that Dr. Stephens may participate fully in all deliberations.

In the event that the discussions involve any other products of firms not already on the agenda for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement and the exclusion will be noted for the record.

With respect to all other participants, we ask in the interest of fairness that all persons making statements or presentations disclose any current or previous financial involvement with any firm whose products they may wish to comment upon.

The second item that I need to read into the record is our appointment to temporary voting status. Pursuant to the authority granted under the Medical Devices Advisory Committee charter, dated October 22nd, 1990, as amended April 20th, 1995, I appoint the following people as voting members of the Dental Products

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Panel for this panel meeting, on October 6th, 2000, Dr. Peter Bertrand, Dr. Richard Burton, Dr. Marcus Besser and Dr. Willie Stephens. For the record, these people are special government employees and are consultants to this panel under the Medical Devices Advisory Committee. They have undergone the customary conflict of interest review. They have reviewed the material to be considered at this meeting. Signed, Dr. David Feigal, Director for the Center for Devices and Radiological Health, October 2nd, 2000.

At this time, I would like to turn the meeting over to our Chair, Dr. Leslie Heffez.

DR. HEFFEZ: I want to welcome everyone to the meeting. I would like to hold this open public hearing in an organized fashion. In order to do this, we have a number of presenters and I will ask each presenter to stick to a time limit of five minutes. If it appears that you are going to extend beyond the five minutes I will give you a little warning and interrupt your presentation. Prior to your presentation, I would like you to restate your name. I would like you to state if there is any financial interest present regarding your presentation and yourself and, in particular, if your attendance currently, today, is supported by a company or other.

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Without further ado, I would like to start the public hearing and ask Antoinette Hosford to present.

Open Public Hearing

MS. HOSFORD: My name is Antoinette Hosford. I have no financial stake in the company.

In about 1989, I began to have three to four migraines a month and my jaw would pop really loudly across the room. Then I began to have severe constant pain in my jaw all the time. Finally, after the third or fourth visit to my family doctor, telling him about the migraines and the pain, I was referred to a neurosurgeon who then referred me back to my family doctor and said I had no brain problems, who then ordered an x-ray and an MRI of my jaw and determined that I had problems with my TM joint.

I was sent to a dentist who tried several different programs to help me without doing surgery. We tried to splint. We tried medication. Eating with the splint, I had no relief in pain. It just gradually got worse and I could not eat hardly anything, except soft food and just liquid things.

We were then referred back to my oral surgeon who advised me and counseled me on having surgery with the Christensen implant. I had the surgery April 15th, 1992 and for eight and a half years have had no problem

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whatsoever with my jaw. I have the Fossa, the partial implant, and have just been really pleased with it. I have a friend who had two different surgeries. They were unsuccessful and I know that she is now trying to have the Christensen implant, and hopes that that will give her relief. Her husband had advised me not to have the surgery but we went ahead with it.

And, I am just here to let you know that I think the Christensen Fossa implant is wonderful. This is the only surgery that I have ever had. I have never had any other surgery before or after. We did try the splint and medication but they didn't seem to help at all. I couldn't open my jaw; I had migraines. Since I have had the surgery I have been really pleased with it, and I don't know where I would have been had I not had the surgery the first time. I might have had several other surgeries until coming upon the Christensen implant and I am very pleased that that was the first and only surgery that I have ever had.

DR. HEFFEZ: Thank you. Just for the record, was your attendance supported by the company?

MS. HOSFORD: No.

DR. HEFFEZ: Okay. The next speaker will be Charlene Jaspersen.

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MS. JASPERSEN: Good morning, panel. My name is Charlene Jaspersen, and I do not have any financial interest in the company.

I am here in support of the Christensen Fossa-Eminence prosthesis. My story began several years ago. I suffered with TMJ for about fifteen years. I tried all of the conservative treatments, soft food diets, pain meds, muscle relaxants, tranquilizers, splints and three arthroscopic surgeries that did not work for me. I was given a non-chew cookbook and told there is nothing else that can be done for me.

Then, I was given a "don't" list, and that consisted of: Don't chew gum. Don't eat hard or chewy foods. Don't clench down on your teeth. Don't sing or talk for any long periods of time. Do not do vigorous exercise. Don't chew on fingernails, pencils, bobby pins, and so forth." Don't yell or open mouth wide. Don't drink through a straw. Don't smoke. Don't carry heavy bags, purse and so forth.

My "do" list was: Do support your lower jaw when yawning. Do apply hot and cold compresses on the jaw. Do eat a soft diet and cut food very small. Do try to avoid stressful situations and get a good night's sleep.

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None of these procedures relieved my pain and suffering from this debilitating disease. I was even told to learn how to live with it and make the best of it. I could not eat, smile, talk, laugh or even have my teeth worked on. Kissing my husband was such an effort and caused me so much pain. I lived on a diet of baby food, soups, mashed potatoes and so forth.

My family and friends had had enough of the pain and suffering I was going through. I was even giving up on life. I knew then it was time to find some answers to this TMJ pain that I was living with, and the doctor I was seeing at that time told me I need not come back to him anymore if I had found another procedure.

I heard of the Christensen implant from a friend of mine. I then made an appointment to meet with a doctor who specialized in TMJ treatments to see if I was a good candidate for the prosthesis. In December of 1990 I had the Christensen Fossa-Eminence prosthesis implanted bilateral in place of my disk that had badly deteriorated with the rheumatoid arthritis. I am now ten and a half years postop and doing great, with no pain in the TM area. I am eating everything I want, including steaks and hamburgers, sub sandwiches. I can even eat hard candy. I have no restrictions or limitations, and I can smile and have my teeth worked on without any problems,

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and without my jaw locking either open or closed. I am living a normal life and I sometimes forget that I ever had TMJ.

In May of 1990 I had a CT scan on my jaws. My implants, the Fossa-Eminence prosthesis, looks as good as the day they were implanted. There are no loose screws on the implants and they are still in place in the disk area. My own condyles were not replaced at the time of the Fossa-Eminence implant in December of 1990. My condyles showed a slight deterioration from the rheumatoid arthritis at the time. To this date, my own condyles still look great and, in fact, they do look better than before and do not need to be replaced. The Fossa-Eminence prosthesis has done the job and stopped the process of deterioration to my condyles.

I feel very fortunate that I have the Christensen implant as I have friends that have other types of implants, like the Vitek and Silastic and Teflon Proplast. They have caused them so much damage to their TM joint, along with pain and suffering. The Christensen implant, the Fossa-Eminence prosthesis has given me back my life. I have not had to have many multiple surgeries and I feel normal once again.

In closing, I would like to say I don't know where I would be today if it had not been for the

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Christensen Fossa-Eminence. I feel truly blessed. Thank you.

DR. HEFFEZ: Thank you. Miss Jaspersen, and for others who are going to present, there is a slight difference between someone having no financial interest and whether your attendance was supported.

MS. JASPERSEN: My attendance was not supported.

DR. HEFFEZ: Thank you. And, future presenters, please address those three issues. The next presenter is Ellen Lucus.

MS. LUCUS: My name is Ellen Lucus, and I have no financial or involvement with any other joint. You are looking at a three-time failure. Three failed total jaw joints. I know this meeting is about the all-metal Christensen joint but I would like you to humor me as I discuss all three of my failed joints.

First, there was the Vitek VKII, and I feel the need to express to you my extreme disappointment in the way you, the FDA, has handled this failure. You allowed these joints on the market without strict safety guidelines. Then, when you discovered the horrible problems with Vitek you covered your butts by "grandfathering" in the rest of the joints instead of thoroughly checking the safety of these joints. If you had checked out these joints back in '91 and '92, we

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wouldn't be here right now discussing the all-metal joint problems.

Also, there are many people still out there that don't know that the joints in their heads have been recalled, and I know this for a fact because I have had to tell six people their joints were recalled over eight years ago, instead of the doctor telling them, and that is not fair to them or me. All you required of Amos is that they inform their patients and you haven't enforced that.

Now I would like to address the acrylic head Christensen. Whatever happened to this joint? It mysteriously went off the market. From what I can gather, around '93, '94, Dr. Christensen no longer provided these joints to doctors. Should I assume that he recognizes the problems with this joint? First he says there haven't been wear problems with the condylar heads, but during the May 11th panel sessions he admits that they wear down, but this somehow makes them better. I would like to know what is the FDA's position on this joint, and if they are considered to be bad is there anything official from FDA stating this and if there isn't, why isn't there?

Now I would like to discuss the all-metal Christensen joints. I want to know why this joint was

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even allowed on the market to begin with. Around '93 or '94, Dr. Christensen started replacing the acrylic head joints with the all-metal. He told the FDA they have been on the market for, I think, around thirty years. Where is the data to prove this? And, if there is any proof, then they were introduced after you grandfathered the existing joints in. I want to know what type of testing you have done to justify that this is a safe joint.

My metal Christensen caused immediate pain and swelling. This pain and swelling got so bad that the joints had to be removed last July. My op reports, which I mailed to you with my Medwatch form, says that these joints caused metalosis. If you did a thorough job of testing these joints, why was I never asked to submit my joints to you for testing?

I would like to know more about the green material that has been oozing out of some of thee joints. Has it ever been identified and, if so, what is it? And what kind of damage to my body should I expect from this?

We, the public, can't afford to have another medical catastrophe caused by a bad jaw joint, especially since we see how poorly you have helped us after Proplast. If my husband performed his job as well as some of you have performed yours he probably would have

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been fired by now, and you guys probably make a lot more than he does.

I am asking you to do your job based on thorough research, not pressure from big business. If these joints are allowed back on the market without proof to me that they are safe, I will be forced to put my op pathology and a copy of my Medwatch out there on the web for anyone who would like to see it.

Dr. Christensen and you, the FDA, were aware of the problems with metalosis and this joint, just from what I have submitted to you. And, I would like to make one last comment. Every once in a while I get really hard on myself for foolishly allowing three bad joints to be put in me, and it dawned on me that I keep giving you, the FDA, the benefit of the doubt that you are looking out for me but you keep letting me down, and all I am asking is that you don't let me down again. Thank you very much.

DR. HEFFEZ: Ms. Lucus, I will invite you to come back again. You are listed twice, for Sue Schweikert.

MS. LUCUS: I will just say it right now, Sue is a friend of mine and she can't be here right now because she is in real bad condition right now. Her teeth are crumbling. She has had the all-metal. Like I said, she

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is in such a bad position that she can't attend right now. Thank you.

DR. HEFFEZ: Thank you. Our next speaker will be Terrie Cowley.

MS. COWLEY: Good morning. In 1992 I made my first visit to Congressman Ted Weiss's office --

DR. HEFFEZ: Excuse me, just restate your name for the record.

MS. COWLEY: Terrie Cowley, and I have no financial interests in any company. In 1992 I made my first visit to Congressman Ted Weiss's office to describe to his legislative staffer what I knew about the Vitek and Silastic implants. She asked me what I knew about other devices on the market and when I said, "not much," she admonished me by saying, "if you are going to be a patient advocate, you darn well better know everything about every device out there." That meeting led to the congressional hearings called, "Are the FDA and NIH Ignoring the Dangers of TMJ Implants?" and the subsequent initiation of the classification process of these devices.

In the eight years since that congressional visit, I have made it my business to learn as much as I can about all TMJ devices. This has been facilitated because the TMJ Association has become the 911 for most

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patients. From the May, 1999 Dental Products Panel meeting I learned the following about the Christensen models: First, the testing data on all Christensen devices were woefully inadequate. The May, 1990 panel went on to say that evaluation of TMJ Implants clinical data was impossible as all Christensen products were blended into one reservoir of anecdotal, case study, and retrospective data, a body of haphazardly collected information without the benefit of a clinical trial protocol. Over 80 percent of the patients were lost to follow-up.

Regarding the devices under discussion today, the TMJ Association has heard the following problems from patients: When the Fossa-Eminence prosthesis is used, the patient suffers what surgeons refer to as condyle "shredding" or degeneration, as well as Fossa-Eminence prosthesis fracture. Of the all-metal total joint, the primary complaints we hear are metalosis, allergic reactions to the materials, and shattering of the fossa piece. Screw loosening is a complaint common to all of these devices.

Conspicuous by its absence at this meeting is discussion of the polymethylmethacrylate condylar head device, on the market since 1961 and, following the recall of the Vitek devices in 1990, aggressively

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marketed. Compelling evidence of the safety and efficacy of this device was not presented at the May, 1999 meeting. The PMMA shreds, leaving a nail-like projection to abrade against the metal fossa, which can then shatter. It is apparent that a PMA for this device has not been submitted by the manufacturer and it is no longer being marketed. Where does this leave the patients who have been implanted with this device? If it is found to be unsafe, shouldn't the FDA initiate appropriate action, such as a recall, alert or warning?

The most troubling information revealed at the 1999 panel meeting was that the manufacturer received 361 MDR reports and determined that only 4 were device related and reportable to the FDA. He blamed the remaining reports on the patients and the surgeons. This is a chilling reminder to us of Dr. Charles Homsey's defense of the Vitek devices -- he blamed the patients and the surgeons for the failures.

Upon hearing about the number of failures, we have to ask who has the responsibility for determining the cause of failures of TMJ Implants, Inc. devices? Is it the manufacturer, someone within the company? Is it an independent monitor? Does the FDA agree with the company's definition of device failure? When the FDA learned that there had been 361 failures, did the agency

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investigate the reports? If they found the company responsible for the majority of failures, at what number does the FDA take action: If the device failures were due to surgeon errors, shouldn't the company be responsible for better surgeon training? If the failures are the patient's fault, are the patient selection criteria wrong? Was the diagnosis questionable? Was the use of the device for the patient's TMJ problem wrong? Or, is the problem that there are no uniform guidelines for aftercare for implant patients in the oral surgery and device community? Instead, there are different directions given to patients by different doctors.

We know that many surgeons never file MDR or Medwatch reports. They either don't know they should or they fail to comply, or their only criterion for failure is if the device breaks. One can only wonder how many more device failures exist that have never been reported Patients hesitate to complain about their device problems to their surgeons for fear of antagonizing them. If they call the manufacturer, they are told to speak to their surgeon. If they call the FDA, the agency is limited in what they can say and patients consider it an exercise in futility.

DR. HEFFEZ: Ms. Cowley, you have thirty seconds.

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MS. COWLEY: In their frustration, patients who experience local and systemic problems related to their TMJ air these problems online with each other and with us. It will be interesting to learn how many TMJ implant-related devices have failed since the 1999 meeting. We have heard from 34 patients with device failure.

This panel has weighty matters to deliberate. Your charge is to decide whether the manufacturer has met the scientific standards of safety and efficacy demanded of jaw devices. Thank you.

DR. HEFFEZ: For the record, could you please state if your attendance is supported by an association or company.

MS. COWLEY: TMJ Associates --

DR. HEFFEZ: Could you speak up?

MS. COWLEY: I am the president of TMJ Association and we will pay for my fee.

DR. HEFFEZ: Thank you. Ms. Cowley, I can invite you back to the podium to speak on behalf of Beverly Miller.

MS. COWLEY: Ms. Wilentz will.

MS. WILENTZ: My name is Joan Wilentz. I am a volunteer with the TMJ Association. I am on the Board of

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Directors. My expenses were not paid; I am local, and I have no financial interest.

DR. HEFFEZ: May I ask you just to speak more directly into the microphone? Thank you.

MS. WILENTZ: This is a letter from a TMJ implant patient in Memphis, Tennessee, Beverly Miller. Dear Panel, everyone I know with a Christensen device has had either the head crack, the device break, screws come out. They have no end of surgeries, pain, suicidal thoughts and attempts, bankruptcy, family breakups, doctors no longer wanting to see the patients. They find disability very hard to come by and there have been no recalls. Ford and Firestone have worldwide recalls on the tires that have caused about 60 deaths. When are you going to have recalls on the TMJ implants that have caused hundreds of deaths and disabilities?

Beverly sent a photo that she would like the panel to look at. I will pass it around. This is the head of a TMJ implant where the screws came out; the shaft broke; the acrylic head broke through the patient's cheek. She developed two staphylococcal infections in her head, had to travel to another state to have surgery to have the implants removed. Her doctor refused to do further surgery to replace the implants after the staphylococcal infections had cleared up because she is

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now disabled and Medicare will not pay sufficient funds. She does not have the $10,000 cash to pay up front. Today she has no joints.

Please have all TMJ implants go through the strictest of testing and do not put others in this situation. One day it may be someone you love. Thank you, Beverly Miller.

This is the picture of the patient with the protrusion of the joint implant through the skin. I will pass it around.

DR. HEFFEZ: Just for the record, you are here representing --

MS. WILENTZ: TMJ Association.

DR. HEFFEZ: The Association or Beverly Miller?

MS. WILENTZ: Well, I was asked by the Association to read the letter that came to the panel from Beverly.

MR. ULATOWSKI: Mr. Chair, I want to make it clear that each entity has one opportunity to speak, and the understanding that you spoke for the patient and not again for the Association, that is permitted but each entity has one shot.

DR. HEFFEZ: Thank you. I will invite Dr. Doran Ryan.

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DR. RYAN: Good morning. I am Dr. Doran Ryan. I am not representing anyone but myself. My trip was paid for by myself, except I had breakfast paid for by TMJ Concepts. I had breakfast with them this morning.

I want to thank you for the opportunity to address this panel regarding the all-metal total joint prosthesis of TMJ Implants, Inc. I am an oral and maxillofacial surgeon in private practice, in Oshkosh, Wisconsin. I am also president of the American Society of Temporomandibular Joint Surgeons. I have published numerous articles regarding the use and disuse of alloplastic implants in the temporomandibular joint. I have had the opportunity to do research on implants in animals both to find the results and the uses of these implants.

I really represent the oral maxillofacial surgeons who practiced during the Proplast Teflon era and has witnessed the pain and suffering of over 10,000 patients who had FDA approved Proplast Teflon placed in their temporomandibular joints. Many of those patients continued to suffer even after removal of those implants. In the early 1980s the FDA approved the Proplast Teflon as safe and effective for the use in the temporomandibular joint even though no independent testing of the product, nor any controlled clinical

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trials were established. The FDA relied on undocumented information from the company, that being Vitek.

In 1986, six years after the Proplast Teflon started to be used, I wrote a letter to Dr. Singleton of the FDA and to the editor of the Journal of the Oral Maxillofacial Surgery. I recommended the product not be used; all the patients be recalled and evaluated for removal of the implant. I had animal research to back up these recommendations. At least ten doctors wrote rebuttals to Dr. Singleton and to the Journal. The implants were working for them and I was wrong. They claimed the problem was the technique and not the product.

Unfortunately, it was more than six years before the FDA acted on the recommendations, with the debate finally ending in 1992. The law suits continue today against the doctors. Patients continue to suffer, and the FDA did say they were sorry.

How quickly we forget. Now, in the year 2000 we are faced again with a novel approach to the reconstruction of the temporomandibular joint, that is the all-metal total joint. Is this product safe and effective? And, will it pass the test of time? I don't know that answer, but I don't think the FDA does either.

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Here are the reasons why I question the approval of this product: There is no history of metal-to-metal temporomandibular joints. This is truly a new idea. Two articles were published, one in 1997 and the other in 1998, in a non-refereed book with the manufacturer as one of the co-authors. The mean follow-up time was 7.5 months and 26 months. Keep in mind, we didn't acknowledge Proplast Teflon failures for 8 years. That means we almost have 5 years of debt on this product. I have not seen any published controlled clinical studies with this product.

The only other joint in the body using metal-to-metal total joints is the hip. It is a constrained joint, unlike the temporomandibular joint. The knee is closer in function and metal total joints are not used in the knee. The metal-to-metal hip joint failed in the '60s and '70s. Failure was attributed to poor control of sphericity, inadequate radial clearance via matched head and cup pairs, and unpredictable cobalt chrome molybdium microstructure secondary casting of the metal. This led to two and three-body wear. Excessive wear, metal fatigue and corrosion led to ultimate failure.

New guidelines, published by the American Society of Testing and Materials, include the following: The fossa and condyle need to be well matched and

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spherically controlled. As the difference in the radius increases, point contact occurs and a new product can lead to excessive wear. Cobalt chrome molybdium is more homogeneous and stronger than cast metals, which is the way this product is made. The fossa used in the system is cast metal, which is very thin, and combined with the point contact with the system has been shown to fracture.

The question of independent evaluation of this product must be answered. Who is independent, and does the testing follow the standards? I remember vividly being told by the manufacturer that acrylic on the condyle of the previous total joint of TMJ Incorporation didn't wear -- no wear. We all know that that is not true. I was shown independent studies that demonstrated this fact. Yet, we know that the acrylic condyle did, and still does, wear.

Now the same company is offering up a new all-metal-to-metal total joint with, the best I can tell, five years of uncontrolled data. Have they followed the published guidelines of testing this material, and who is doing the testing?

DR. HEFFEZ: Dr. Ryan, you have thirty seconds.

DR. RYAN: I do not know those answers, but I know that you need to look very closely at that data. In conclusion, I hope I am wrong about this product and I

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hope that it does not fail but, please, don't give us another Proplast Teflon clone. Most importantly, please do not sentence more patients to a life of severe chronic pain and suffering because power and money is placed in front of science and research. I hope that this time if the product fails the FDA will take responsibility for their action and not just say, "I'm sorry," and leave the results of failure for others to manage. Thank you for your time and attention.

DR. HEFFEZ: Thank you. The next presenter invited to come to the podium is Michael Billingsley.

DR. BILLINGSLEY: Good morning, ladies and gentlemen. I am Dr. Mike Billingsley. I am a private practice oral and maxillofacial surgeon from Colorado Springs, Colorado.

I am here to support the application --

DR. HEFFEZ: Could you please state your financial interest.

DR. BILLINGSLEY: Oh, yes. I am here to support the application for FDA approval for the Christensen Fossa-Eminence prosthesis manufactured by TMJ Implants, Incubation. My travel expenses were reimbursed by the company but I am not a stockholder and have no other financial interest in the company.

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I represent a group of eight private practice oral and maxillofacial surgeons based in Colorado Springs, with satellite offices in Pueblo, Trinidad, Canyon City and Castle Rock. Our service area includes a population of nearly 750,000 in southern Colorado and northeastern Mexico. Our TMJ referrals come from a large base of dental practices and a number of physicians involved in chronic pain management.

Most patients referred to our group have an extensive history of non-surgical care by the time we see them, including medications, bite splints, physical therapy and psychological management. Some are under the care of orthodontic and prosthodontic specialists. In an average year, about 75 patients receive surgical evaluation in our practice for their TMJ and dysfunction complaints. A thorough diagnostic protocol is observed, including extensive history and physical, response to prior treatment and x-rays and MRI evaluation.

Of this group, approximately 15-20 patients are identified each year as surgical candidates. Most are offered arthrocentesis if surgery is indicated, which has been a useful diagnostic and therapeutic aid for many patients. This is followed by at least 3-4 more months of non-surgical care with splints and physical therapy.

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Out of this group, usually 8-10 in a year will still be found to have painful dysfunction and are offered a surgical arthrotomy. Now, the decision to operate requires the patient have continued painful dysfunction in spite of non-surgical or arthrocentesis care, with clinical and MRI evidence of internal disk arrangement and Wilkes categories III or higher.

There are patients who have failed non-surgical and arthrocentesis therapies in most cases, but the final determination for diskectomy and placement of a Fossa-Eminence prosthesis is reserved for the time of surgery, when the disk and associated tissues can be directly observed. If the disk is found to be anteriorly and medially displaced, perforated or tightly bound down with fibrous adhesions, and on repositioning of the disk is found to be contracted with inadequate space between the anterior and posterior bands of the disk, this, to us, is a clear indication for disk removal and placement of a Fossa-Eminence prosthesis.

Using the stock templates, our doctors have always been able to achieve a good Fossa-Eminence fit, except in rare cases of severe bone destruction which requires a custom fossa prosthesis designed on the cadcam model. After selection of the proper size implant, the final Fossa-Eminence prosthesis is inserted. The dental

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occlusion and joint function are carefully checked, and the device is secured at the lateral aspect of the zygomatic base in the eminence with chrome cobalt screws. Following surgery, the patient is immediately placed on physical therapy to prevent early development of joint adhesions, and splint management is continued and the patient is carefully followed.

Our experience since 1991 with these devices includes over 80 Fossa-Eminence Prosthesis placements in 50 patients, and in this group 5 cases include total joint reconstruction with the condylar prosthesis, including 1 cadcam-base custom prosthesis. The total joint cases were in trauma, tumor and rheumatic arthritic situations. To date, no Fossa-Eminence Prosthesis only cases have required subsequent placement of the condylar prosthesis. Our success rate is over 90 percent based on our criteria of 35 mm of pain reduction from the usual level of 8 or higher on the VAS scale down to less than 2.

No major complications have been observed due to the device itself. In two cases, patients had implants removed by other surgeons but we were not provided with either the reason for explantation or any evidence of pathology related to the Fossa-Eminence Prosthesis.

DR. HEFFEZ: You have thirty seconds.

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DR. BILLINGSLEY: One of the patients eventually proved to be emotionally unstable and has continued to seek multiple surgeries. Two patients, in the initial placements early on, required replacement with larger prostheses due to range of motion limitations, and have subsequently done well. One loose screw was removed under local anesthesia with no further problems. We have observed condylar surface remodeling in some cases on follow-up x-ray but no condylar resorption has been seen.

In conclusion, our experience with the Fossa-Eminence Prosthesis has been very rewarding. This device is extremely valuable in the surgical management of articular disk disorders and early degenerative disease.

DR. HEFFEZ: Your time is up.

DR. BILLINGSLEY: Thank you.

DR. HEFFEZ: I will invite the next speaker, Dr. Joseph Niamtu.

DR. NIAMTU: Good morning. My name is Dr. Joe Niamtu. I am a private practice oral maxillofacial surgeon, in Richmond, Virginia. I have no financial interest in the company. I have been asked by TMJ Implants to relate my experience with their fossa-eminence product, and I have been reimbursed for my expenses from Richmond to Washington.

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Basically, there is no perfect device out there for temporomandibular joint disorders. If you look around this room on both sides, there are a lot of very eminent people here academically that have a lot of experience with this. As a practitioner in private practice looking for solutions, you can go around the country and you can talk to some of these very important people and you hear always do this; never do this -- there really is not one thing to do, and some things work real great in some people's hands and other things don't work well in other people's hands and there is a quandary.

We have a lot of patients. There are ten million patients that have TMJ problems and five percent of these patients will eventually be surgical candidates, and we don't have a lot of solutions; we don't have a lot of devices.

We have certainly learned lessons in the past from the Teflon Proplast, and there have been mistakes. But, basically, I want to just relate, firstly, my experience in the private practice trenches using the fossa-eminence system, not the total joint; not the condyle but the fossa-eminence. I have placed about a hundred of these and, basically, I have been in practice for almost twenty years and I have counted about fifteen

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materials that I have put in the joint because at any given point in time that was something that was purported as good, or the next best thing, or what was going to help patients, and it has been a confusing situation.

I can only say that about a decade ago I was told by some of my friends that were using the fossa-eminence system that it was a viable alternative, and they were seeing good results in their patients. And, I started using this. The first one I put in was in about 1991. This patient is doing well. I can't say that none of these patients has ever had problems because there are a lot of variables when you put anything in or operate on any patient.

As a surgeon, when you choose to operate on somebody, anybody who is honest will admit that they have done possibly the wrong operation; they have chosen the wrong patient; they have not put the device in correctly. In my home town, I say, you know, I have had good experience with this. There are other surgeons who have used this product and they haven't had good experience. I think a lot of it has to do with the learning curve and putting it in right, just like any device.

But when patients come to you, and if you see a lot of TMJ patients, by the time they get to you as a surgeon they are at the end of their rope. They are at

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their wits end. They have these horror stories. Some of these people want to kill themselves and, you know, they look you in the eye and they say, "what can you do for me? How can you help me?" And, there are just not a lot of alternatives.

I have used this fossa-eminence system. I have had good results with it. It has been an alternative. These patients have been able to open and close. It has helped their pain. Nobody is going to get cured. These people aren't going to get cured. They are going to have problems all their life because that is the nature of TMJ problems. But, I have not had to take these out. I have taken a few out and some of those may have been my fault. I may have technically not done it right and I may have put the wrong joint in the wrong patient -- the wrong eminence, but basically I have never had a loose screw from this fossa. I have never had a failure because of material. I have gone back and had to open up these joints to clean them out from time to time. I have never seen any significant resorption, and I have not seen significant condylar resorption that some people state that they have seen.

Basically, in my hands this has worked well and it has been a good alternative, but I will tell you that for the last year and a half I have been kind of

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stonewalled because I have patients that I can't offer this to, and I would ask you to consider seriously about putting the fossa-eminence back on the market. I basically have people waiting because I don't really know what to do.

Again, I think a lot of it boils down to what works well in your hands as a surgeon, and probably you could bring fifty people in here and talk about something, whether it was cartilage or repositioning of the disk, or this joint or that joint and, you know, it may work well in their hands and it may really serve their patient population without any bad situations. Basically, I just want to relate to you that, by and large -- and I try to follow my patients very closely, they have had good experiences with this and, obviously, I wouldn't still be using it if I didn't have good experiences. Again, it is really important and I don't think anybody that can come up to this microphone that operates on people can say that everything always works well and they don't have problems because this is a confusing disease process.

If you look at the National Institute of Health Technical Assessment Conference data, there are a lot of people out there with TMJ problems. We have all learned that you don't operate on people unless they have

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significant joint pathology, but there are a lot of people that come to me and other oral surgeons and they do have significant joint pathology, and what are our choices? You can't just tell these people -- you know, some people you can just tell them, "hey, if you just wait twenty years it's going to go away," but there are people -- like you heard today, their jobs are affected; their marriages are affected; their whole life is affected by this chronic pain and I think that I have been able to help a considerable population of these patients by using this device. So, I am just here to say that that has been my experience. I have not seen these negative effects that I have heard today, and this patient population has done well with this device. Thank you.

DR. HEFFEZ: Thank you. The next speaker invited is James Bergeron.

MR. BERGERON: My name is James Bergeron. I have no financial interest in the company. I have no support from them.

I want to thank you for giving me the opportunity to present before you on the review of the premarket approval application of the TMJ Fossa-Eminence Prosthesis, manufactured by TMJ Implants, Inc., by the Food and Drug Administration.

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My name is James Bergeron and I am the legislative director for Congressman Tom Tancredo. Congressman Tancredo represents the sixth congressional district of Colorado, which includes the southern and western suburbs of Denver, including Golden, Colorado, the headquarters of TMJ Implants. All of the current employees of TMJ Implants are constituents of the Congressman, and most of the employees who have been laid off by the company since this lurid tale began, more than a year ago, are constituents as well.

Now, the Congressman apologizes for the fact that he cannot be in attendance today because of legislative business on the floor. He, nonetheless, has taken an active interest and an active role in monitoring the progress of TMJ's implants application.

On numerous occasions he has met with Dr. Christensen, president of TMJ Implants, to find out information about the approval of the partial and total joint, and has personally talked to Commissioner Jane Henney and to members of the agency about the status of the company's applications. Congressman Tancredo has also been in contact with the House Commerce Subcommittee on Oversight which has sole jurisdiction over the FDA and issues relating to abuse and the internal operations of the agency.

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Specifically, the Congressman has been closely following this case since our office's first contact with Dr. Christensen and TMJ Implants in May of 1999. Incidentally, it was at this time that a meeting of the FDA's Dental Products Panel was held to review the company's PMA, and recommended approval of the PMA by a 9-0 vote. However, in spite of this action, it has not been lost on the Congressman that TMJ Implants finds itself in roughly the same spot today due to the actions or inactions of the agency. As such, I want to not only express Congressman Tancredo's support for the approval of TMJ Implants' partial PMA -- that is, after all, why we are here, and his desire that the Dental Products Panel approve the PMA much the same as it did in the 1990 panel, but also to express his concerns publicly about the process, and public health issues which accompany this application.

First and foremost, it is the Congressman's hope that the advisory panel will keep an open mind and listen carefully to the data that the company is presenting for the partial, for it meets the standard for reasonable assumptions for safety and effectiveness.

Next, the Congressman believes that the process has gone awry, and is concerned about the public health with the partial joint being withdrawn from the market.

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On the process, I am sure you will hear the problems that the company has experienced from those after me. It is no secret from all involved that there have been significant questions raised about the process, the sluggish pace of the review of the engineering data for both the total and partial joint and, more importantly, the constant moving of the goal posts during the review of both PMAs.

I sincerely believe that most of the frustration that has been expressed here could have been avoided had everyone sat down and laid everything out on the table in the spirit of what was fought for under the FDA Modernization Act. Unfortunately, the agency has been unwilling to do so, and it seems like these problems will continue into the foreseeable future. Thus, I will raise a question that others will raise as well as to why a new panel was needed. The May 1990 panel knew exactly what it was voting for. In fact, the panel was specifically told that it was voting whether to approve the PMA before it.

Now the public health concerns -- it appears that in an effort to address safety, and I am told that in this case the bar has been raised to a level significantly out of the ordinary, well beyond the statutory standard of reasonable assurance of safety and

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effectiveness. Because of this, the agency has done nothing more than cause harm to patients. It has failed to address the needs of the special patient population that is now suffering from the disorder and logically can be remedied without waiting until degeneration of the total joint calling for irreversible surgery. Based upon history and data provided by the company, the device, which has a thirty-year clinical history, should not have been removed from the market. The fact is that the safety concerns are suspect and a health hazard has been created by the removal of the partial joint from the market.

You should know that the FDA, in August of 1998, made a finding of public health necessary for this partial device and, mysteriously, nine months later threatened denial of the company's PMA unless the partial was withdrawn from the market and in spite of receipt of significant additional data supporting FDA's own findings.

Over the last year and a half, our office has received numerous letters from physicians all across the country, from the Mayo Clinic to the University of Maryland, each relating to us the benefits of the partial joint and the fact that the partial and total joint results in immediate and dramatic decrease in pain, an

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increase in range of motion and increased function. Surely, the thoughts of these esteemed surgeons cannot be ignored, cannot be swept under the table.

The Congressman is concerned about what has happened here for this device is not available to clinicians that have made it clear that it is helpful. All of this calls into question the integrity of the agency, something that the Congressman finds very disturbing.

Dr. Christensen is a true professional and a pioneer in his field and holder of the first patents. His implants are widely acceptable as effective and safe throughout the dental and surgery community. Indeed, several of my constituents have literally had their lives changed by the procedure. Congressman Tancredo is convinced that the work of the TMJ is based on solid scientific principles, and removal of the implants from the market has been, and continues to be, erroneous, contrary to the agency's earlier findings and the standard that should be applied. This has been devastating to thousands of people in the general public. This disaster must be remedied as soon as possible. Thank you.

DR. HEFFEZ: Thank you. At this time, I would like to ask if there are any other speakers who didn't

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sign in or signed in, in a delayed fashion and would like to present? No response from the floor.

At this time, I will ask panel members if they have any specific questions they would like to direct to one of the presenters. State your name.

DR. BERTRAND: I am Peter Bertrand, from the Navy. For the gentleman from Richmond, I was curious about your patient selection. Are these patients with fully degenerated joints, or are these patients with internal derangements who have not responded to so-called conservative therapy?

DR. HEFFEZ: Please restate your name.

DR. NIAMTU: Dr. Joe Niamtu, private practice oral maxillofacial surgery, Richmond, Virginia. Basically, I think the standard of care that exist for temporomandibular joint disorders -- I think anybody who treats TMJ patients has a responsibility, before you lay a scalpel on a joint, to make sure that you have done everything for that patient because of what can happen from surgery -- any surgery. Basically, you know, most of the time by the time the patients get to many oral maxillofacial surgeons like myself, they have gone through all the conservative therapy with their primary treating physician and/or dentist.

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I believe what you are asking me is what pathology I am looking for, or am I just using internal derangement. Internal derangement means a lot of different things to a lot of different people. When I explain it to patients I tell them that the innards of their joint are just not working in harmony; they are not working well. And, you can argue all day about what it is and what it isn't but, to finally answer your question, basically I look for the clinical signs. Most of the patients that I am operating on require a diskectomy. The far majority of them either have significant perforations, or very significant areas of thinning that will eventually be a perforation, of the disk is just very hypertrophic and in some cases hypoplastic. These people open and close and it sounds like they have gravel in their joint. I mean, to me, this has been a pretty consistent clinical sign. When they open and close, it kind of gives you goose bumps -- "I'm glad my jaw doesn't hurt like that."

One of the big indicators I think is the position of the disk on MRI, although we all know that that is not a sole indicator but certainly these other clinical symptoms, this type of pain, limited opening, the crepitus and joint noise, and displaced disk or perforated disk -- all these things add up.

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I think the biggest mistake a surgeon can make is just operate on somebody because the patient wants an operation or because nothing else works. I think people who do TMJ surgery -- you know, you come to a point where you learn who not to operate on and that is a significant thing. So, I think the presence of demonstrable pathology clinically and on imaging studies, and/or from previous invasive procedures like arthroscopy. Sometimes you will look in a joint and it is just beat up badly. So, this is what I use personally to make my decision, and I can honestly say that these people have been marched through a progressive cascade of conservative treatments before becoming surgical candidates.

DR. HEFFEZ: Thank you.

DR. NIAMTU: Did I answer your question?

DR. BERTRAND: For the most part. Do you ever anesthetize the joint before you do your surgery to verify, other than the patient's opinion, that it is actually the pain source?

DR. NIAMTU: Yes, diagnostic blocking is a significant part of our situation. Again, I think most surgeons look for an excuse not to operate on somebody. I really do because, you know, you can really help somebody and you can open a can of worms. On almost all of these patients we will do arthrocentesis, usually in

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the office where we will use Marcaine to anesthetize this joint. We will place two needles in to rinse out this joint, and we will frequently put some type of corticosteroid in there. You know, doing the diagnostic block -- for the people who are non-clinicians here, one of the hardest things for a surgeon is to understand is this a muscle problem, is it a neurologic problem, or is it actually a joint problem. That is the confusing diagnosis here. I think that this has brought light to this situation. I don't think it is a hundred percent effective but I certainly think it gives you information on which to choose to operate or not operate.

DR. BERTRAND: Thank you.

DR. HEFFEZ: Any other questions from the panel?

DR. STEPHENS: I am Willie Stephens. I have a question I would like to pose to Dr. Ryan. I was wondering if you might speak for a moment about your thoughts about treating patients who have failed previous alloplastic surgery, and whether you have concerns about putting another prosthesis in that has a plastic wear debris.

DR. RYAN: Well, as we know and it has been published, after two and a half surgeries or two to three surgeries, most of these patients are going to fail any procedure we do. It is unfortunate that we don't have a

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better way to treat those patients. So, the patient who has had multiple surgeries many times have central pain. They really don't have peripheral pain that you can operate on. So, those patients are essentially chronic pain patients from that moment on.

What we try to do on those patients is reestablish function for that patient. Essentially there are two components we have to deal with, one is pain and one is function. Many times we cannot help their pain because it is now central pain and has to be treated medically. So, now we have to deal with the functional component of their problem, which is getting back to where they can at least chew and talk normally. In that case, we need some type of alloplastic material in order to treat these patients.

Patients who have had multiple surgeries end up with very poor blood supply to the joint. So, autogenous material or natural tissues don't heal well in that joint. So, we need some type of alloplastic material. I think the thing that we need to look at is what is the best material to put in that joint that will cause the least wear debris -- everything is going to wear that we put in the joint. What material can we put in there that will cause the least amount of wear debris? Of that wear

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debris, which one of those particles that are produced will cause the least amount of reaction in the body?

So, I certainly think there is a place for an alloplastic material in the joint, but we certainly need one that has very little wear debris and one that does not cause further damage after it does wear. The problem in the past has been that we have not come across that. Acrylic in the past has been shown to be a problem in the hip joint, and that is a concern. Metalosis is certainly a problem, and you put metal-on-metal and you are going to end up with some problems because it wears, and it wears down fairly rapidly if it has point contact. So, I hope that answers your question.

DR. STEPHENS: If you have to do a joint replacement in a patient with a failed Vitek now, what would you use at this point?

DR. RYAN: I am using TMJ total joint prosthesis which, as you know, is high molecular polyethylene and metal condyle against that, similar to the other joints in the body.

DR. HEFFEZ: Dr. Patters?

DR. PATTERS: Mark Patters. A question for Dr. Ryan and perhaps any of the other surgeons that spoke. I perceive that the patients and their representatives are implying that patients who are not successful lose

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confidence in their surgeon; lose confidence in the system; and are lost to follow-up and therefore, the success data is skewed because those patients returning for follow-up are happy and those are not returning are very unhappy. What is your personal experience and would you agree that that is a concern?

DR. HEFFEZ: State your name, Dr. Ryan.

DR. RYAN: Yes, I am Dr. Doran Ryan, from Oshkosh, private practitioner. I think that is probably true. I think what happens is there is frustration on both sides. The patients become frustrated with the fact that they still have pain and still have trouble with function, and the surgeon who placed the implants becomes very frustrated because the patient has not done well also. So, at some point that bond is broken between the surgeon and the patient, and the patient wanders off to look for some other source of help. That has happened to me. I have patients that have wandered off, and I think I try to treat my patients very well but there is a certain frustration that everyone develops and, therefore, that bond is broken. They do. Patients do wander off and for that reason it is very difficult to track these patients and find out exactly the success rate, and we have proven that over and over again when we have looked in the literature and we find that in the

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temporomandibular joint everything had a 90 percent success rate, yet, we know that is not a fact. As time went on, we found out that many of those procedures had much less than that, sometimes less than 50 percent. So, they do get lost to follow-up for that reason.

DR. BILLINGSLEY: I would like to address one point, if I may.

DR. HEFFEZ: Restate your name in the microphone.

DR. BILLINGSLEY: Dr. Mike Billingsley, Colorado Springs, private practice of oral maxillofacial surgery. Our experience with Proplast Teflon patients has been limited but we have about a dozen patients in our follow-up group who had Vitek implants at one time. We did see some destructive changes in these patients, and followed them and recommended that they be removed, and we did replace them, all but one who refuses surgery, with the Fossa-Eminence Prosthesis and they have uniformly done well without further decline of their condyles.

One thing that is extremely important is proper debridement of the joint in that situation because any particles left will continue to propagate the giant cell reaction against the particles of the Teflon. So, we think not every joint that needs to be opened that has a disk removed needs a total joint. This is an extremely

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expensive undertaking and fraught with many hazards, much less predictable, and in most cases it can be managed with the Fossa-Eminence Prosthesis.

DR. PATTERS: Thank you.

DR. COCHRAN: David Cochran. I would like to know from the physicians that have spoken what the percentage -- realizing that this is a cascade for many of these patients to get to the point they are at, what is the percentage of patients that you actually operate that have a condyle that is still intact enough to not use a total joint replacement and only the fossa?

DR. HEFFEZ: Specifically who are you addressing the question to?

DR. COCHRAN: Any of the oral maxillofacial surgeons who have spoken.

DR. HEFFEZ: So, Dr. Niamtu is the closest.

DR. NIAMTU: Dr. Joe Niamtu, Richmond, Virginia. Can I answer the second half of his question or just the question that is on the floor?

DR. HEFFEZ: Answer the question on the floor, please.

DR. NIAMTU: Okay. Basically, what percentage of these joints have condylar damage? In my experience, very few of them. This is mostly for a disk problem. As I stated earlier, I can't say that none of these joints

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don't have some arthritic change on the condyle or an occasional osteophyte but, by and large, the vast majority of these that I have placed have been for a perceived situation with the disk. You know, the eternal question is when you get in that joint, what are you going to do with this disk? There are people today that will sit there and tell you that you can fix a hole in a disk, and orthopedic surgeons who will tell you that you can't do that because there is no vascularity. But right now we have well-known people fixing holes in disks. We have people that reposition disks, and there are people that still do it and say that they get good results but we know from the experience in the '70s that it didn't appear to work across the board.

So, to answer your question, when I get in that joint I am usually expecting to find a significant disk problem and the diskectomy or meniscectomy, taking that disk out, has worked well in my hands. The question again is do you put something in there; do you not put something in there? And, the condyle is usually in good shape, and I have had better experience putting something in there, and that something is the fossa. If the condyle is in very bad shape, then possibly you do need a total joint.

DR. HEFFEZ: Thank you.

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DR. BILLINGSLEY: Dr. Mike Billingsley, Colorado Springs. In terms of the numbers that you asked about, in our series of 80 implants, only 5 of those have required the total joint, and they were not generally related to disk disease; they were related to rheumatoid arthritic problems, sequelae of trauma and tumors in 2 cases.

DR. RYAN: Doran Ryan. I think we do total joints only as a last resort. So, we don't want to replace the condyle if we don't have to. I think in the case of ankylosis or severe rheumatoid arthritis a total joint is indicated but, short of that, I think we need to try to do something other than replacing the total joint itself.

DR. HEWLETT: I am Edmond Hewlett. I have a question for Dr. Billingsley. Dr. Billingsley, you indicated that in the 80 or so fossa-eminence implants that you placed you have observed some cases of condylar remodeling without condylar degradation or deterioration. I believe that is what you indicated. I am curious what criteria you are using to distinguish one instance from the other, and also what is the longest time span that you have had to observe these cases?

DR. BILLINGSLEY: Dr. Mike Billingsley, Colorado Springs. The longest time span is nine years in our

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practice. Most of these joints we don't have to reopen. We have only reopened two or three and, at that point where the fossa has been in place for, I think, at least two you ears in each case we went back in. When we first started doing these fossa-eminence prostheses there was some controversy about whether or not to leave a healthy appearing disk in place. In a couple of places we left the disk in place with the fossa above it in the sphere joint compartment and we end up having to go back because of decreased range of motion in these patients and removing the disk. The patients subsequently did fine. The observation of the condyle at that point was that it was smooth. It had some eburnation with remodeling surface changes, but no cortical collapse; no sub-condylar necrosis.

I think it is very important in these cases to identify whether there is any evidence of avascular necrosis in the head of the condyle at the time that you make the decision to do this. If you have evidence on MRI or other means that there is avascular necrosis, you are probably looking for trouble and you may eventually have to replace the condyle at that point. But we have not generally seen anything like that in the use of these fossas.

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DR. BERTRAND: Dr. Billingsley, I am Peter Bertrand and I have another question for you, Dr. Billingsley. When you are screening patients for a surgical procedure, does the role of an SSSRI have any impact on your decision tree in deciding to do surgery, and how do you assess whether parafunction is still existing in that patient?

DR. BILLINGSLEY: We try to treat our patients with a team approach. We think it is wrong for patients to be shuttled from non-surgical care to surgical care and then not followed up. So, we insist on good control of parafunctional habits under the care of a non-surgical practitioner -- good splint therapy, physical therapy, management of the medications by a physiatrist, a physical medicine specialist. We try to sole-source the medication. All of those things are part of our team approach -- psychological evaluation and management if necessary.

So, if I understand your question, we think it is extremely important to manage the occlusion in these patients. In terms of parafunctional habits, we think that it is very difficult to control in some cases. We think most of the trauma to the disk apparatus and the condyle are probably related to this phenomenon than any other factor.

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DR. BERTRAND: So, the decision tree is based on the collateral providers that you work with and whether the parafunction is judged to be under control or not.

DR. BILLINGSLEY: And a sufficiently painful dysfunction and a positive clinical and imaging assessment.

DR. BERTRAND: And, do you have any data on the percentage of your patients that may be taking a selective serotonin reuptake inhibitor while they are having symptoms?

DR. BILLINGSLEY: It is very small. That is not used very much in our community. The physical medicine doctors do not use tricyclics to any great extent. I can recall three or four patients.

DR. BERTRAND: Thank you.

DR. HEFFEZ: Any further questions from the panel?

DR. BURTON: This can go to any of the surgeons. I would like to know what percentage of your patients come back on follow-up. There seems to be a very strong question about the number of people who have long-term follow-up and why they are lost to follow-up, and how long after surgery is their care covered under, let's say, a global fee or do they pay for follow-up, and are we losing a large number of patients, particularly the

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dissatisfied patients, because they have to pay for follow-up care? Not asking about their financial policies, but for non-study related patients, what are their financial costs?

DR. BILLINGSLEY: Dr. Billingsley again. This is a problem with all of these patients. It depends on the state that you are practicing in. For example, last time I checked there were about 19 states that have a right to treatment law or regulation within the state, and those that don't are poorly covered by insurance, for the most part, in my experience. At least in my state that is the case. This joint seems to be excluded from the realm of right to treatment in comparison to other joints in the body. We think that is a horrible disservice to the patients.

In terms of losing patients to follow-up, it is difficult to follow these patients. We live in a mobile society. I spent twenty years in the military and I moved thirteen times, and I don't think that is so unusual anymore. We have patients, I would say, in our community that move -- I would say the mean is probably every five years. In our area we have a high tech base --

DR. BURTON: I am sorry, my real question revolves around the fact are those patients, let's say,

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three months, six months a year after surgery -- do they have fees for postoperative visits in your practice?

DR. BILLINGSLEY: My group has never charged for follow-up evaluation.

DR. BURTON: So, if a patient came one or two years later, or three years later, they would not then again be charged an examination fee. Obviously, there might be radiographs and things like that which is a separate issue, but I am talking about a professional fee for follow-up.

DR. BILLINGSLEY: We have not charged that in our practice. We want to see these patients and we try not to discourage them.

DR. BURTON: Thank you.

DR. RYAN: Dr. Ryan again. Dr. Burton, most insurance companies have a global fee which covers ninety days post surgery. So, those patients are seen for free during that ninety-day period. I think all oral surgeons try to get their patients back. That is extremely difficult to do. I think most oral surgeons do charge a fee for follow-up evaluation. It would be foolish not to. I mean, that is how we make a living. Certainly, I am sure we make exceptions for patients who don't have insurance, and try to follow those patients, but I still believe that there is a high percentage of patients that

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are not followed long-term. We saw that in the Proplast Teflon when we went back to see what happened to those patients. There are still patients out there that haven't been contacted. So, we know these patients aren't followed that well, and that is certainly a concern and it is hard to put together a controlled study of patients because the follow-up is very difficult to do, again, because of the mobility already mentioned and the fact that cost does get in the way.

DR. HEFFEZ: Dr. Bertrand?

DR. BERTRAND: I have a question for Terrie Cowley, please.

MS. COWLEY: Yes?

DR. HEFFEZ: State your name, please.

MS. COWLEY: Terrie Cowley.

DR. BERTRAND: You mentioned that since the last panel meeting 34 patients with implants have come to your awareness with the TMJ Association. Do you have any way of verifying what type of implants those patients had received, and which company produced those implants?

MS. COWLEY: These were all implants produced by Christensen, TMJ Implants, Inc.

DR. BERTRAND: And how was that verified?

MS. COWLEY: We can't verify. We cannot have a registry that should be in existence for TMJ Implant

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patients. What we have is almost a complaint system. A patient calls us, a patient e-mails us, a patient writes to us and tells us, I have this device, or I have a device made by this company, or I have a titanium device. And, in a conversation with the patient or in correspondence with try to find out more specifics about what they have. For the most part, we do have accurate information -- I had a fossa; I had an all-metal total joint -- you know, whatever. We have those broad statistics, not scientifically validated. Some people send us their x-rays. Some people send us their medical records, probably just trying to have us help them find out what they have. But if you are asking right now for a breakdown, I don't have right now how many of the 34 were fossas. I believe I can have that by this afternoon for you.

DR. BERTRAND: If your group can identify the oral surgeon that placed the prosthesis and it happens to be associated with one company or another company, do the companies or the registries freely communicate with you or is there a problem with that type of communication?

MS. COWLEY: The companies do not freely communicate with us unless there is some benefit to that for them. We have a problem. We have TMJ Implants, Inc. out there; we have TMJ Concepts. TMJ Concepts happens to

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answer any phone call from any patient who calls them. We know that. The patients tell us, and they tell us what the company is telling them about their device. They shuffle them over to their web site. They appear to be a company that communicates with the patients. Obviously, in the last year TMJ Implants, Inc. has not had any communication with patients. The people who have asked us how to communicate with the company; who is the company; where are they located, and on an on -- we simply give them their address and phone numbers. We obviously frequently hear, and I brought this out at the last Dental Product Panel meeting, these patients are always told you have to talk to your surgeon. They do not communicate with the patient who has had any type of complaint or even question. So, this is what I am hearing. Is there a database registry of patients in the companies? We sure hope so because obviously we, the patients, are going to have to take control of a situation where there is an incredible discrepancy between what the patients are living, what they are telling us and each other, what the doctors are telling the patients, what the manufacturers are telling the surgeons and the patients. So, until and unless we are able to collaborate in some manner with an implant registry that is mandatory, not voluntary, that has an

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independent monitor, this database into which patient, direct patient information is given -- unless we have that we can't trust anyone.

DR. BERTRAND: Thank you.

DR. HEFFEZ: Any other questions from the panel? As chair, I have one question to Dr. Ryan. Many of your comments addressed metal-on-metal. Could you tell us if you feel there are any indications for the fossa-eminence alloplastic replacement.

DR. RYAN: I have not used the fossa-eminence implant, mainly because I think there are other procedures that can be accomplished, short of putting an alloplast in the joint, for the indications they have indicated for that particular product. So, I have really not used that implant myself. I think my concern with it is that you are putting bone against metal. You are rubbing bone against metal and that, to me, doesn't make a whole lot of sense. It seems to me that bone is going to wear down from a biological standpoint. I just think there are other procedures that can be used. Again, there is no other joint in the body that does hemiarthroplasties. That has pretty well failed in the past. Does that answer your question?

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DR. HEFFEZ: Yes, thank you. Any further questions from the panel? At this time, we will take a 15-minute break. We will reconvene at 10:45 exactly.

[Brief recess]

DR. HEFFEZ: We will proceed to the next part of this meeting, which is the industry presentation. I would like to announce for you that the sponsor we are going to be hearing from is TMJ Implants, Inc. Today we are reviewing premarket approval application specifically for the TMJ Fossa-Eminence Prosthesis. Without further ado, I again need you to state your name for the record.

Industry Presentation

TMJ Fossa-Eminence Prosthesis

MR. COLE: Than you, Mr. Chairman. My name is Michael Cole. I am an advisor to the company, but this morning I am functioning in the role of moderator for the company presentation.

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We have a lot of information to present in a relatively short period of time. So, without any further preamble, I would like to introduce to you Dr. Robert Christensen, the president of the company and the developer of the implant, who will describe the clinical situation he was confronted with in the early '60s that led him to the development of the device, and where he

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believes it fits in the regimen of treatment for the GMD patient.

DR. HEFFEZ: While we wait for him to come to the podium I will remind you, you have one hour for presentation. We are starting at 10:45.

DR. CHRISTENSEN: I am Dr. Bob Christensen. I am glad to be here again. I do have a financial interest in the company, in case anybody thought I didn't.

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Back in the 1950s I had done surgery on this joint, on the patients and so forth, and had done a great deal of surgery on fractures and what-have-you but also had done things such as meniscectomies and so forth for pain in this joint and some of the other things that some of the older gentlemen remember. Dr. Laskin, back here, I know he remembers it. But we did things that at the time seemed right, and they did do some good.

But I began to realize that something was needed to be placed in that joint. It was not any big study of mine to get there. I was driving down the road and it really hit me how I could do this, and that was the genesis of that in the 1960's, forty years ago.

A few months after that I operated on the first patient. This patient had had the meniscectomy and condylectomy done by another surgeon in the State of

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California, and she had a fibro-osseous fusion of the condylar neck to the articular eminence. I knew I needed to put something in there. So, I developed and put in the fossa-eminence implant on that patient.

There was a lot of discussion at that time on was this a viable procedure or not, and one of the things that really helped me at that time -- the two doctors that did the hip surgery, Dr. Smith Peterson and Otto Alfrank in Dr. Willie Stephens hospital, up there in Massachusetts, wrote a letter in '64 and said this is a real contribution to the surgery of a degenerative joint problem, and he knew what I had done. He had seen my first article in the American Journal of Orthopedics in 1963.

I began to realize that this thing was very useful in replacing that disk. So, that is how I did it and I began to do it, and I almost never had to reoperate on these patients. I had an extremely good fortune over many, many years with it. We keep much better tracking today than I did then, but I can tell you that I look back at that first surgery about twenty-five years later and, instead of losing bone off that condylar neck, she began to grow bone back around it, and I went ahead and took that ankylosis out and left the original plate in that was there twenty-five years before and put a condyle

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below it. Forty years later she is still functioning. We have many patients just like that.

And, for somebody to stand up here and say they don't know about hemiarthroplasty in a joint -- they just don't know what is going on because Otto Alfrank and Smith Peterson had done it in the hip; many of them have been done since that time and certainly the shoulder joint is one that is operated quite routinely that way. So, without saying more about it, I think our presentation will answer a lot of questions for you and I will step back for Mike Cole.

MR. COLE: Thank you, Dr. Christensen. The question has been raised is unnecessary surgery being performed? Has the applicant sufficiently identified a patient population for whom the use of this device is suitable? We will attempt to address that question in a number of presentations this morning, and we believe that in large measure the standard of care is a very important consideration here, as is the diagnosis of internal derangement. To address those subjects, I would like to present to you Dr. Rick Alexander, from St. Luke's Roosevelt New York, New York. Dr. Alexander is a recognized authority on the standard of care, having lectured, written and testified on the subject numerous

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times as it relates specifically to the oral maxillofacial surgery. Dr. Alexander?

DR. ALEXANDER: Thank you, Mr. Cole and panel members. I do not have any financial interest in TMJ Implants, Inc., and the expenses for my trip here -- the payment of those was assisted by TMJ Implants, Inc.

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I am the director of the Division of Oral -- let me say something in the beginning, we are going to use this term, OMS, instead of oral and maxillofacial surgery. So, when you see that term, that is what we are talking about. I am the director of the Division of Oral and Maxillofacial surgery at St. Luke's Roosevelt Hospital Center, in New York. St. Luke's is a major New York City teaching hospital and a level I trauma center. I am here primarily out of my interest in patient care and appropriate residency training for oral and maxillofacial surgery residents.

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CDHR has raised the question of whether there is unnecessary surgery being routinely performed for TMJ disorders. It has been estimated there are some ten million people out there that at some point in their life have some kind of temporomandibular disorder. Approximately five percent of these patients have

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potentially a surgical problem. If you look at that number and look at how many people have a problem out there, I can assure you that nowhere near five percent of ten million are getting operated on.

The other issue I think is if you look at the ten-year closed-claim liability losses by description of procedure for TMJ surgery, AAOMS national insurance company, which is the largest insurer of oral and maxillofacial surgeons -- and, again, you are going to see this term, AAOMS and that stands for American Association of Oral and Maxillofacial Surgeons. This is the largest insurer of people in our specialty. Their ten-year closed-claim liability loss by type of procedure is three percent for TMJ surgery. It is higher than that for almost every other thing that we do. It is higher, for instance, for infections; it is higher for fractures; it is higher for dental-facial deformities. It is three times higher for those things, between eight and ten percent. Of the major surgical procedures that we perform, this has the lowest liability loss and I submit to you that if this surgery was being performed unnecessarily and poorly those statistics would be much higher.

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The other question that the CDHR has raised is whether internal derangement is a specific diagnosis. Internal derangement -- I think I can show you that it is a very specific diagnosis. First of all, internal derangement has to do with disorders of the disk or meniscus in that joint. Now, the disk or meniscus is an anatomic structure made up of soft tissue that is interposed between the head of the joint and the fossa or the socket. This disk derangement has been classified and staged by a number of authors -- Wilkes, Bronstein and Merrill McCain. Wilkes is probably the best known, and his classification divides the displacement and/or damage to the disk into five categories, early, early-intermediate, intermediate, intermediate-late and late. And, that is very specific in my mind. The other authors have done the same thing but as related to arthroscopy.

In addition to that, the 1995 AAOMS parameters of care list internal derangement as a specific diagnosis. It is interesting to note that the 1995 NIH Technology Assessment statement recognized this publication as being an authority at this time.

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The 1995 AAOMS parameters of care, what it basically does is it presents accepted patient management strategies, in this case for TMJ surgery. It presents

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them for other types of surgery we do. Now, the standard of care is defined as what a reasonable and prudent oral maxillofacial surgeon would do under the conditions.

I submit to you that a reasonable and prudent oral maxillofacial surgeon is going to follow these accepted standards. I am familiar with a significant number of people in the United States that do a significant amount of joint surgery. I am familiar with their practices, and I can assure you that complying with the standard of care and these strategies is the norm.

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If you are going to follow the standard of care, the first thing you have to do is make a proper diagnosis. Now, this is really important because temporomandibular disorders are of two types. The first type is not a surgical problem and it is not joint disease. This is just something where the patient can have pain that gets referred to the joint. They may have dysfunction of the joint, but it is not coming from the joint.

In contrast, we have another group of patients that have TM disorders which are actual joint disease. This is just like the hip, the knee, all other joints. These patients are potential surgical problems. You have

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to separate these patients out if you are going to perform surgery and do it appropriately.

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The TM disorders that are not surgical or not joint disease -- the most common of these is muscle spasm. Now, muscle spasm can refer pain to the joint. It can also keep the patient from opening wide. So, you can get dysfunction and you can get limited opening and pain from muscle spasm. That is not joint disease, and those patients aren't going to be surgical candidates.

Now, these are actual joint diseases, and despite what anybody will tell you, these are the same diseases that occur in every other joint in the body. It is nothing, you know, magic. Now, ankylosis, infection, general anomalies, tumors and trauma -- except for those top two, I submit to you that those are unquestionably surgical problems. Wearing a splint isn't going to help any of those people.

Internal derangement or disk disorders and arthritis in the early stages -- and, when we talk about arthritis, there are all kinds of types of arthritis; the type that affects this joint most often is osteoarthritis or degenerative joint disease, however you like to call it. In any event, these two conditions will sometimes, depending on their state, respond to non-surgical

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measures early on. As the disease process progresses, they are pretty refractory to those non-surgical treatments.

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The way we decide whether we have a non-surgical versus a surgical disorder is through a comprehensive physical examination, and I think it goes without saying that if you think the patient has a neurological problem, they get a neurology consult. If you think they have diabetes, they get an internal medicine consult. That is how we are trained to work patients up, just like everybody else in medicine or dentistry. So, that goes without saying. If you think the patient has a psychological problem, they are going to get a psychiatric and psychologic consult.

The other thing we use is imaging. The gold standard for imaging right now is the MRI because with these other imaging methods you can't see soft tissue and the MRI shows soft tissue. Internal derangement is a disk or meniscus problem and it is soft tissue. And, before the advent of MRIs, I will agree with anybody who said that we don't understand what is going on with this joint. I will tell you that with MRIs in combination with arthroscopy where we can look into the joint, we do know what is going on in this joint.

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Again, these disorders right here, except for the top two, are without question surgical, and internal derangement and arthritis can become surgical problems. For instance, internal derangement -- we have heard a lot this morning about that, and the Wilkes classification, as I pointed out earlier, is a classification that ranges from a very limited displaced and damaged disk to one that is very displaced and damaged. And, patients that fall into the category of III through V frequently end up being surgical problems. Patients with long-term internal derangement frequently develop degenerative joint disease, and frequently become a surgical problem.

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Now, as far as non-surgical treatments go, there are tons of them out there. The ones that you are probably going to see the most attention paid to are splints, medications, physical therapy, TENS. Obviously diets and a number of other things play a role.

The splint thing has received a huge amount of attention. I will address that again in a second. Medications -- the things that are used most commonly are anti-inflammatories. Physical therapy can either be performed by the patient or they can be referred to a physical therapist. Then, transcutaneous

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neurostimulation, it is questionable whether that is valuable or not but there are people that use it and it certainly doesn't do any damage.

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Now, splints receive all kinds of attention. What I classically see is a patient that calls me up and says, "oh, I've got TMJ and I'm wearing a splint." Well, TMJ is not a disease. So, the first thing we have to find out is what is wrong with them. I already showed you how we determine that.

So, a lot of these patients get a splint, and I think what you need to understand about a splint is that the only thing it does is unload the joint. Okay? These disease processes, internal derangement and arthritis are caused by overloading of the joint. Somebody on the panel mentioned that earlier, parafunctional habits, chewing on, you know, bobby pins, fingernails, gritting your teeth, those are all things that overload the joint. A splint unloads that joint, but I will tell you what it doesn't do. If you have an anterior displaced disk and it is all plastered down from adhesions, wearing a splint is not going to recapture that disk. Wearing a splint is not going to make a hole in a disk repair itself.

So, there is a role for splints to play but I don't think wearing a splint indefinitely serves any

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useful purpose. So, then the question comes how long should non-invasive or conservative therapy go on? Well, I think it is reasonable to say that if conservative therapy, splints, medications etc. haven't decreased the pain, increased the opening and gotten rid of noises in one to six months, they probably aren't going to in one to six years. So, this is an individual judgment that has to be made between the patient and the surgeon. I think most people tend to be in this range, one to six months. Some tend to be closer to one or closer to six. I tend to be in the middle.

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All right, when do you operate on these patients? Well, we are back to the AAOMS parameters of care. The AAOMS parameters of care say that surgical intervention for internal derangement or degenerative joint disease is indicated only when non-surgical therapy has been ineffective, and when pain and/or dysfunction is moderate to severe in nature.

I will submit to you that Wilkes Class III through V fit most of the time in this category, pain and/or dysfunction which is moderate to severe in nature. Surgery is not indicated for asymptomatic patients. Pretreatment therapeutic goals are determined individually for each patient. I just mentioned that the

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patient and the doctor have to decide how long they are going to proceed with non-surgical treatment if the patient can't open their mouth, has pain and noises.

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Back to the parameters of care again. Parameters of care list a number of acceptable procedures for the treatment of internal derangement or degenerative joint disease, the first of which is arthrocentesis, which is just washing out the joint. Patients that have an inflammatory process in the joint are going to have a bunch of byproducts of inflammation and this, not uncommonly, gets rid of those and helps the patient for some period of time.

Arthroscopy, you do the same thing but you can actually look into the joint. It is a scope with a camera on the end. We look up on a monitor or television screen and we can actually see what is going on. So, the argument that we don't know what is going on in this joint doesn't fly. Between MRIs and arthroscopy, we do know what is going on.

Another treatment that they have listed as acceptably is arthroplasty with or without grafts. That can include meniscectomy or removal of the disk. They also list grafts as acceptable, autogenous or alloplastic. Autogenous are ones that come from the body

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and alloplastic are not. I submit to you that TMJ Implants, Inc. is an alloplastic graft.

We heard a little earlier from one of the speakers that hemiarthroplasty is not performed in any other joint. In St. Luke's Roosevelt Hospital Center at least two cases a week of hemiarthroplasty of the hip are performed by orthopedic surgeons, and they place metal-on-bone with that procedure.

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This is really important because I don't think anybody who hasn't seen and worked with these patients can make any kind of a judgment, and you have to see the actual patient. Again, the parameters of care say that the ultimate judgment regarding the appropriateness of any specific procedure must be made by the individual surgeons in light of the circumstances presented by each patient.

Now, I want you to understand one other thing if you don't get anything else out of this. TMJ surgery or joint surgery of the hip or the knee, or any other joint, is not a perfect procedure. If you have a problem with your knee and you go to the orthopedic surgeon and it hurts, and you can't move it and you have noise in it, he or she is not going to tell you that they are going to operate on that joint and it is going to be like before

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all this happened. It is the same with TMJ surgery. The goal is to decrease pain, increase range of motion, get rid of noises and, to that extent, if you look at statistics we are as good, or better, at doing that than the people who do hips, knees, shoulders, whatever. I thank you for your time.

MR. COLE: Thank you, Dr. Alexander. We would now like to turn to two very experienced surgeons, the first, Dr. Anthony Urbanek in private practice, in Nashville, Tennessee. Dr. Urbanek used the Fossa-Eminence Prosthesis when it was available as a pre-enactment device. He also participates in the ongoing prospective clinical investigation. We have asked Dr. Urbanek to describe to you how he applies these standards of care or how does he pick his patients, what result has he seen with the device, and describe to you any untoward events that he has experienced, particularly any effect on the natural condyle. Dr. Urbanek?

DR. URBANEK: Thank you very much, Mr. Cole.

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My name is Tony Urbanek. I am from Nashville, Tennessee. I am an oral and maxillofacial surgeon, and I have no financial connection with TMJ Implants, Inc. or any other implant company. TMJ Implants, Inc. did

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support my expenses for this trip from Nashville to Washington today.

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First, I would like to go through briefly what I believe are my credentials to speak before this very august panel, and very well-experienced people here this morning. I have a dental degree which I got from Indiana; medical degree I received from Vanderbilt; went through my surgical training at Vanderbilt, and entered a Ph.D. program toward a Ph.D. in anatomy. At that point in time, I applied for and was given a grant to the NIH for study of intrauterine field surgery using a laser. This was in 1976 before almost anybody knew what a laser was. I bring that to your attention not to pat myself on the back but just to say that I am a scientist; I am not just an oral and maxillofacial surgeon who does surgery every day. But that is what I am very proud of doing, and that is what I do.

I have a lot of experience and, in 1981, after doing all of that training I decided, for various reasons, that I was going to come out into private practice and I wasn't going to be an academician. At that point in time, in 1981, I was confronted and needed to see many patients with temporomandibular joint complaints. Over a period of the next ten years, between

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1981 and 1991, I tried and utilized all modalities of treatment that were available for these patients, conservative, non-surgical, surgical -- all varieties. If it was written about, I tried it.

What I found out during many, many, hundreds of patient experiences, many, many surgeries is that without exception, especially for the surgical patients, I did meniscectomies without reconstruction. I did meniscus reconstruction. I used all kinds of alloplasts and other types of implants, and I found that consistently within six months or a year each and every one of those patients would return to my office and tell me that they had the symptoms that they originally came in with and the same complaints.

This was very disconcerting. It was very frustrating. As I believe was mentioned earlier, I was at the point where I had decided I just didn't want any more part of temporomandibular joint surgery. If there is anyone in the room who is concerned and worried about the use of alloplasts and the use of implants in temporomandibular joint surgery, it is me. Between 1983 and 1987 I placed 80 Proplast Teflon implants. I have now taken out 78 of them, and the two that are in, in the same patient, are in a good friend of mine and I can't convince her to get them out. I see her frequently and I

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will take them off for nothing. But I have experienced that problem. I have had to confront it and, believe me, I would be the last person to engage in any kind of activity that I did not believe was successful for my patients.

With my comments about my technical credentials, I would like to say that I am not representing myself at this point in time as a scientist. My experience -- 35 percent of my experience, 35 percent of my patients are represented in the study that TMJ Implant will present to you very briefly, and I let those facts speak for themselves. I don't speak to you as a clinical. But I speak to you today because I represent my patients. I represent those 351 joints and 217 patients that I have done, and I represent these 14 patients, now 16 because there are two added to this list as of Wednesday, my last day in the office before I came here -- I represent these 16 patients who were unable to get the partial joint prosthesis for the past 6 months because it has been taken off the market by the FDA.

I am the one who has to explain to these patients why it is taken off the market. I had a conversation about eight months ago, maybe nine months, with Dr. Runner who asked my opinion -- this was on the telephone -- asked my opinion of my experience with this

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implant system in patients. I went through in great detail what I thought of it; what my experience was; my indications for putting it in; how I handle my patients; and exactly what I thought of it. I also asked her, I said, you know, this is a very good prosthesis. It has been on the market for 35 years. I have not had any significant problem with it. I would like to know why it is being reviewed again. I mean, I understood all of the problems in the review process and I wanted to know exactly why it has taken so long to get this thing approved.

I didn't get any direct answers, but what Dr. Runner did ask me is, she said, Dr. Urbanek, what would you think if, in the next couple of months, we took this prosthesis off the market for a period of time while we reviewed it? Because, at that point in time, it was still on the market. And, I said, Dr. Runner, this is not a question you should ask of me. This is a question you should ask of my patients. I can tell you what my patients will say. My patients will say that they are having extreme pain and that they want relief.

Now, this lists 16 patients. It is available to you if you care to see it. I agree with everything that Dr. Alexander presented to you this morning as to how I select the patients, my criteria, the use of the American

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Association of Oral and Maxillofacial Surgeons criteria, but it is the patients I want to speak for.

Over the period of the last ten years, beginning in 1991, I began using the Christensen prosthesis very carefully at first -- very carefully at first. I did a patient. The patient came back in six months, doing well. The patient came back in a year, doing well. Well, I got a little bolder. I went and did another patient. Well, over the next ten-year period of time I found that with the Christensen prosthesis, without almost any exceptions, after six months, after a year, after two years and longer the patients would come back and respond that they are doing well. Their function was good. They could chew what they want. They were opening well and, most importantly, they were out of pain. This is what I am confronted with daily, to deal with patients with pain, not for weeks or months but patients who have had five years, ten years, fifteen years, twenty years of constant, consistent pain and I am the last guy that they come to. They have already been to dentists. They have already been to neurosurgeons. They have been called crazy. They have been to psychiatrists. They have been on drugs. They have had surgery done on their sinuses. They have had surgery done on their nose. They have had all kinds of other surgeries and finally somebody, you

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know, pushes on their joint, the joint is tender and they say maybe you ought to go and see Dr. Urbanek.

I have a referral practice. My results are somewhat skewed because I don't see many patients who have Wilkes class I and class II temporomandibular joint problems. I see patients who have been around the block lots and lots, and they come from all over the State of Tennessee and beyond. The reason that I have accumulated this many patients is because it is successful. I will present with all sincerity to this panel do you think that I would be doing a procedure this many times and having patients coming back to me, saying, "I have pain; it doesn't work. I'm in the same shape I was in before."

Since 1991, I gradually began getting bolder and bolder using the prosthesis more and more. It is my definite experience that it is a very, very successful prosthesis in the way that it handles patients' pain and in ability to open. I have not seen any patient go to fibrosis after the use of the prosthesis. I have been into approximately five joints two years or so, or more, after the prosthesis was placed, because of trauma. I have had several patients who have had accidents after the prosthesis was placed. The prosthesis was displaced and I had to go in and replace it, just literally take the loose one out, put the new one in and then they went

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along their way. But at that point in time I was able to see the condylar head. I was able to visualize the condyle when I went in. Visually, I have never seen any evidence of condylar degeneration of the mandible on a prosthesis that has been in anywhere between a year and five years.

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The patients' response goes back in my practice to 1991. I have a twenty-year experience, and utilized all types of treatment. My practice is a referral type of practice. I have used the indications from AAOMS. And, over that twenty-year period, it is my common, consistent action that after I do a maxillofacial case of any kind, after a year or so I ask the patient if they want to write a success story about what I did for them. I have accumulated, not only on temporomandibular joints but on all kinds of facial surgery many, many success stories. I have before me, in my hands, ten of those success stories on patients who had done temporomandibular joint glenoid fossa implants over the past ten years, with the earliest one in this pile going back to 1994. If you care to read them, I have brought copies. I have a hundred more back in the office, if you would like to see some more.

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But, I would like to read one, again, on behalf of my patients because that is who I am speaking for: For the past twenty years I have suffered with headaches, chronic neck pain, facial pain, earaches, toothaches, shoulder pain and clicking of the jaw. As my pain got worse, I began to mention it to different doctors. They all thought I had sinus problems. So, after a series of tests, medication and x-rays proved not to help it and the problem got worse, I went to an ear, nose and throat specialist. He said that he thought I had TMJ but he didn't think anything could be done. Then I checked with my dentist who gave me some jaw exercises to do which did not make any difference in my pain either. Then I remembered a friend who said that she had TMJ. I questioned her about the symptoms and she referred me to Dr. Urbanek. I had TMJ surgery and have not had one headache, period. All of the other pain is gone. Needless to say, I am thrilled and ever so thankful for my relief. I feel younger and alive again.

I have only read one to you but this is representative of what I am holding in my hand. It is also representative of the hundred I have in my office. I am not here to promote TMJ Implant, Inc. I am here as an advocate for my patients. I have found over the past

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ten years that there is a prosthesis that in my hands consistently works to the betterment of my patients.

You know, I take it as an insult that my results by some have been called anecdotal. You know, I want to make it clear that all of us -- everyone on the panel, everyone who is a professional in the room, and myself included -- our primary interest is in the treatment of patients. If we get lost in the science, which is important -- I am a scientist. I am the guy who did the earliest study on fetal surgery. But if lose point of the fact that we are treating patients and that is what we are here for, for their goodwill and to protect, then we are not doing our job.

Now, I also want to state that I have heard from others who preceded me negative comments. Dr. Ryan had negative comments. I want to say that he admitted in front of you he has never done a partial joint Christensen implant. I present only my experience in retort.

So in summary, I would like to ask the panel to carefully look at our presentation as to the effectiveness and safety of the glenoid fossa Christensen partial insert, which I think is what our charge is here at this meeting. In fact, I know that is what our charge is at this meeting -- the partial prosthesis.

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I would like you to look at the evidence presented, the scientific evidence presented. The scientific evidence that will be presented is very clear-cut. The scientific evidence are a part of in the study which I have entered as a participant in Christensen company backs up the science behind it. But I ask you most importantly to consider the patients who will benefit by having it available. When you make your decision at four o'clock or so, I ask you with all humility to approve or to make a recommendation, because I understand it is a recommendation panel, to make your recommendation for approval and, as human beings, add that we expect it to be approved. Thank you.

MR. COLE: Thank you, Dr. Urbanek. We need to move along now right to Dr. James Curry, in private practice in Colorado, who will talk about his selection criteria, results, and make some comments on the FDA review of a study that was submitted in the premarket approval application dealing with wear on the natural condyle. Dr. Curry?

DR. CURRY: Yes, I am Dr. James Curry. I have been doing temporomandibular joint surgery for upwards of about thirty years, and I have had about a twelve-year experience with the Christensen devices.

[Slide]

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I would just like to state up front that we use a very similar technique in making a diagnosis and treatment plan for patients who might be needing a hemiarthroplasty.

[Slide]

I would like to show you just a study of some patients that I did prior to the registry that TMJ Implants, Inc. was required to keep, beginning in 1993. I looked at patients that I had operated between 1988 and 1992. This study was subjected to statistical scrutiny and there is a significant decrease in the pain in this group of patients, 50 in this study.

[Slide]

We looked at opening in a similar group of patients, and it has already been commented on that we do have some problems getting all of these patients back. These patients were measured with a Therabite measuring device, and there is a significant increase in the patient's ability to open in this group of patients.

[Slide]

This group of patients then was compared with patients from the TMJ registry and patients from our ongoing prospective clinical trial. You can look at the numbers of patients in these various studies, but the thing that I want you to really see is the amazing

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similarities in the beginning pain levels, the postoperative pain levels, the beginning opening levels and the postoperative opening levels.

[Slide]

There have been a number of questions raised at this meeting and at other times about what is the condylar response to the hemiarthroplasty in this joint, what is the bone response. We have heard some anecdotal remarks and no one seems to have any science on this. We follow our patients clinically and radiographically to make a determination whether or not the condyle has pathologically degenerated following our procedures.

[Slide]

This is an example, and I will show you two or three cases to typify what I have seen in my clinical practice and in my study. This is a stage IV internal derangement patient preoperatively, immediately postoperatively and 11 years, 9 months postoperatively. This is pretty typical of the patients that we see, and we generally follow our patients with Panorex. I don't charge my patients for coming back and I don't even charge most of them for their follow-up x-rays.

One criticism of the model fossa liner has been that it obscures our ability to look at every detail of the condyle, but I submit to you that you can't see every

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detail of a condyle on a Panorex anyway. In this particular series you can see very clearly that there is very little, if any, pathological remodeling anyway.

[Slide]

Let's look at this slide. This is the opposite joint in the same patient. I submit to you that this one is obscured even a little bit more in all three views, but when we look at the clinical picture of a patient this long after surgery and their occlusion hasn't changed, and their pain level is practically nil, and they can eat almost anything they want and their maximal incisal opening is 42 mm -- you have to look at both the clinical as well as the radiographical to follow these patients along.

[Slide]

This is a stage III internal derangement. This is immediately postop, in 1989, and this is a 5 year, 1 month radiograph. There are no real changes between the two, but you can't see the actual edge of the condyle as the fossa liner obscures that a bit.

[Slide]

I decided sometime ago that to try and answer this question for myself and my patients I would do some CT scans on some of these patients where the condyle was not as visible as it might be. This is a CT scan of that

[--- Unable To Translate Box ---]

patient. This is 10 years, 1 month postop. Clinically she is doing as well as any patient that I have, and in the sagittal CT scan you can see a very nice cortical outline and a nice marrow space, and in the coronal view you also see that the condyle has not degenerated.

[Slide]

This is an example of a stage V internal derangement. This is a multiply operated joint patient. This is the presurgical Panorex. This is the immediate postsurgical Panorex -- no, 5 years, 1 month postop. Again, a little bit of distortion because you can't see through the metal fossa liner.

[Slide]

This is the opposite side of this same patient. Again, you can't see all of the condyle. So, we did a CT scan on this lady.

[Slide]

In the CT view you are able to see more of the condyle. This is the sagittal in three different levels. This is the coronal view, and there is no pathological condylar degeneration 9 years, 9 months postop.

[Slide]

This is the opposite side. This is the sagittal and the coronal view of the same patient.

[Slide]

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I would like to submit to the panel that this is an example of a patient, and this is a tomogram of a joint in 1983. This patient went through standard conventional treatment for temporomandibular disorders and temporomandibular joint pain and dysfunction. Over the course of time, when she got to my office in 1991, there was absolutely no condyle there. This patient has never had an alloplast in this joint. This is the opposite joint.

What I am trying to explain to you as well is that you can see these kinds of pathological deteriorations radiographically even with a metal fossa liner in place.

[Slide]

You also begin to see clinical evidence of severe degenerative joint disease with open bite deformities, and that is the way this lady presented.

[Slide]

I would like to comment briefly on the idea that every TMJ patient must go through an exhaustive non-surgical treatment regimen. I think Dr. Alexander stated this very clearly. This is a 16-year old girl, fractured condyle, ankylosis. This patient doesn't need psychological care; this patient doesn't need splints. This patient needs surgery, and the surgery that we did -

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- rather than do a total joint, or rather than put some kind of a ribgraft in here, we did a hemiarthroplasty. I submit to you that hemiarthroplasty is much, much better for some patients than subjecting patients to total joint procedures.

[Slide]

This is another example of a pathological condition. You can see the tumor. This is synovial chondromatosis. This patient needs an operation. So, this was done.

[Slide]

In conclusion, surgeons must exercise good medical judgment in deciding whether to place the partial joint. There is an abundance of clinical evidence to support the use of a partial joint replacement system in this joint. CDRH should not substitute its judgment for the years of clinical experience with this device. Thank you.

MR. COLE: Thank you, Dr. Curry. We are running out of time and we have two very important presentations to make so I would like to move right into the results of both the prospective clinical study and the registry data, which we believe demonstrate that we have identified the patient population and demonstrated that the device is safe and effective for use in that patient

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population. To make the presentation on the clinical results, Doug Albrecht, the manager of clinical affairs at TMJ.

MR. ALBRECHT: Hi.

[Slide]

Right now, we have two data sets of patients that we are going to report on. One is our prospective clinical study, for which you received all the data that we have collected so far in your packet. What I am going to present here today is data regarding the indications for use compiled from that data.

[Slide]

To date, we have 113 patients with a partial joint replacement enrolled in the clinical study, and 109 of those are evaluable at this point. There were 4 recently enrolled patients for whom the data has not been collected yet.

The demographics are typical for this population of partial joint replacement, and in this group of patients 75 percent of those patients have received stock implants.

[Slide]

Dr. Runner's question or statement that internal derangement was not a specific diagnosis was taken back to our investigators and we asked them, you know, can you

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give us some more specific information with regard to the diagnosis that was given. Originally they reported 81 percent of the patients enrolled with a partial joint had internal derangement.

Upon revisiting this with the investigators, we found that the majority of the patients still have a diagnosis of internal derangement, with about one-third with perforation, two-thirds without perforation, and about ten percent with inflammatory arthritis. The majority of those patients in the inflammatory arthritis group also had a secondary diagnosis of internal derangement. Therefore, we are looking at about 85 percent of the patients with a diagnosis of internal derangement that did receive a partial joint replacement.

[Slide]

Again, as Dr. Urbanek and the other surgeons have alluded to today, these patients exhaust most non-surgical modalities when they are indicated for the patient, and these can be any of these listed on this slide.

[Slide]

When they have exhausted the non-surgical modalities, we have found in this clinical study that for 82 percent of the patients this is their first TMJ

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surgery, and the rest have had between one and six previous TMJ surgeries before receiving the prosthesis.

[Slide]

This graph is a graph of the pain reduction from the prospective study from those patients with internal derangement and with fibrosis and ankylosis. As you can see, they all start out with a pain level of 1-10, 10 being the most pain imaginable and zero being no pain at all. They all start out at about a level of between 7 and 8 on this VAS scale, and within 3 months after surgery they have clinically significantly reduced their pain levels to about a 3 and this continues to go on for about 3 years post-implant.

[Slide]

The same is seen with the interincisal opening. Again, for those patients with internal derangements and fibrosis and ankylosis, they all begin about the same place, between 30-35 mm of opening, which is fairly acceptable for this group of patients. Immediately postop their opening does go down due to the postop complications, but then back up to about between 30-35 mm and this extends out to 3 years postop.

[Slide]

We have seen no unanticipated adverse device effects from this surgery. We have had one event that is

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related to catching of the joint, which may be attributed to the positioning of the implant by the surgeon, but everything else is associated with either surgical complications, disease progression or trauma.

[Slide]

We also track patients in our TMJ Implants registry. Upon registry, we ask physicians for historical information, as well as some diagnostic information but not as detailed as the prospective study. In the TMJ registry we have collected pain and opening data on over 1300 patients since 1993. In order to track as many patients with as complete data sets as possible, we have isolated a cohort of 88 subjects which have complete data from preop all the way out to 3 years of implant duration. That population, as stated here, is typical of the partial joint population as shown with the prospective study.

[Slide]

Again, we ask the physicians to provide us with the Wilkes classification upon registration of the device after surgery. These are the definitions, as we have alluded to before in presentations.

[Slide]

Out of the 88 patients, the surgeons for 46 patients did report the Wilkes classification of class

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III or higher. We had no reports of I or II in this cohort group. Additionally, 50 out of the 88 patients reported surgical history, 36 percent of those having their first surgery at this point, and the remaining two-thirds of the patients had anywhere between 1-9 surgical procedures.

[Slide]

In looking at the cohort of 88 patients and the 46 that did report the Wilkes classification, we see the same pain levels, starting at about 8 on a VAS scale of 1-10. Within a month after surgery the pain is clinically significantly reduced, and this continues on out to 3 years post-surgery.

[Slide]

We see the same information again with the interincisal opening for the same group in class III, class IV or class V Wilkes classification. They start out at about 30 mm postop and then improve out to 3 years implant duration.

[Slide]

As I said before, we do have data on over 1300 patients within the TMJ Implants registry. Out of those 1300, over 800 surgeons returned the Wilkes classifications for their patients, and this graph represents the cross-section of that population. Cross-

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section means that we don't have the same patients followed at every time period. Because of the ongoing follow-up, patients either have not met that follow-up period or have been lost to follow-up. However, the numbers are fairly significant within the three classes of class III, class IV or class V.

[Slide]

We do again see a significant decrease in pain within the first month of surgery and that continues out to almost five years in implant duration.

[Slide]

We see the same information with regard to the interincisal opening with the class III, IV and V, with again significant improvement in opening out to 5 years implant duration.

[Slide]

With regard to any adverse device effects within the registry cohort of 88 patients, we have seen no unanticipated adverse events for this group of patients, and 93 percent of these patients still have the original fossa-eminence implanted three years after surgery.

[Slide]

With the cross-section of the 1358 patients minus the cohort of 88 -- so, we have two separate

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populations, again, 93 percent still have their original prosthesis implanted after five years implant duration.

[Slide]

The big key here is reproducibility of the data. No matter how you cut the pie; no matter what population we have looked at, whether it is the prospective study, whether it is the registry or whether it is independent data from other surgeons, we see the same information time in, time out. Looking here at the prospective cross-section of the ongoing trial, I have also been able to isolate 21 patients in the prospective study with complete data through 2 years, as well as the registry cohort which is 88 patients out to 3 years, and we see the same information of a significant decrease in pain and that continues out long-term.

[Slide]

We see the same information from the same three groups of patients with regard to interincisal opening.

[Slide]

In conclusion, we believe that the Christensen partial joint replacement is effective for the indicated populations of internal derangement with and without perforation, and associated with inflammatory arthritis. These can be correlated to Wilkes class III, IV or V. We have shown that a small population of patients with

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fibrosis and ankylosis do improve with the implant, as well as patients that have failed previous TMJ surgery, either autograft or allograft.

[Slide]

Again, we believe that the device is safe for the indicated populations. The overwhelming majority still have the device implanted at least after three years after surgery and some out to five years. We have seen no unanticipated adverse device effects, and there is no evidence that has been presented that the device causes degeneration of the natural mandibular condyle. The clinical data do demonstrate that the metal-to-bone articulation will not cause degeneration to the natural mandibular condyle. Thank you.

MR. COLE: Thank you, Doug. I know, Mr. Chairman, that we are virtually out of time. We have one more presentation that we waned to make in response to comments made by the Food and Drug Administration in its submission to the panel that, in fact, no engineering data on the partial had been submitted. I don't know if you want to take two minutes to do that. I would like to confirm that, in fact, the report that we prepared in response to that statement was distributed to the panel. If so, that might suffice in place of the testimony.

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DR. HEFFEZ: You actually have three minutes left, if you can be concise.

MR. COLE: I would like to introduce you to Mr. Durnell, one of the fastest talkers in the company, who will now very quickly go through the data on the partial joint that was in the premarket approval application.

MR. DURNELL: Thank you.

[Slide]

Good morning. I am here to summarize the preclinical testing which has been submitted in the PMA. A small percentage of the testing submitted in the original PMA was pertinent to a total joint system. However, the majority of the testing is relevant to both a partial and a total joint system, and was conducted either on representative material samples and devices or on the actual devices themselves.

The justification for use of all of these various testing configurations was explained in the appropriate sections of the PMA, and there were four distinct testing configurations. One, we used the material sample of cobalt chrome. This we used for the tensile property testing and corrosion testing.

The second configuration was cast cobalt chrome condylar prosthesis. This is made from the same material, utilizing the same processing as the Fossa-

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Eminence Prosthesis, and for that we tested the perpendicular and 3-point bend testing, and the biocompatibility testing was conducted using an extraction from a condylar prosthesis. Those include the systemic tox, cytotox, mutagenicity, irritation and intracutaneous reactivity.

The actual fossa device against a condylar prosthesis as a worst case scenario -- the is justification for this as a worst case is that, number one, it represents a single point contact which concentrates the forces and, two, this configuration is a hard alloplast on a hard alloplast. For these tests, the following tests -- contact area, contact stress -- all of our wear testing was done using this worst case -- physiologic fatigue and, in response to discussions with the panel and the Center, we conducted an S/N curve fatigue testing with post-fatigue strength testing using this worst case scenario. In addition, static load was conducted using this configuration.

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

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

MR. COLE: Thank you, Mr. Durnell.

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

MS. SCOTT: While Mr. Ulatowski is coming to the podium, I would like to confirm that the engineering data that was submitted by the company is included in the packet that you received today. The additional engineering data that was submitted by the company is included in the panel packet for today.

FDA Presentation

MR. ULATOWSKI: We need a little time to set up here but I would like to take that moment just to thank and appreciate the attendance of the panel today to discuss this topic, and recognize all the speakers this morning in regard to their presentation. FDA considers

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all of the information presented, both pro and con, and the presenters this morning have been very helpful.

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

[Slide]

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

[Slide]

My goal today in discussion with the panel is to respond to the panel's request to revisit the data for TMJ Implants, Inc. in regard to the fossa-eminence device. We want to obtain today the panel's vote based on the current set of data for the Fossa-Eminence Prosthesis. We want to obtain the panel's comments on labeling for the metal-on-metal total joint. So, there is a difference between our discussion today on the Fossa-Eminence Prosthesis compared to the metal-on-metal

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total joint. Time permitting, we will see how we proceed with the comment period on labeling this afternoon.

[Slide]

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

[Slide]

We are discussing today a type of device FDA called pre-1976 class III device, otherwise known as 515(b) type devices. As we all know, certain devices were on the market prior to when FDA started regulating medical devices in the premarket fashion, and we classified those devices. Some devices were ultimately classified as class III, which means they require a premarket approval by the agency, submission of a premarket approval application to the agency, and this is the type of device we are discussing today.

Now, the timing of when FDA required premarket approval applications has played out since 1976 for various types of devices. For this particular type of device, TMJ Implants, it has been relatively recent when

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we asked for submission of premarket approval applications for one reason or another. FDA has its priorities; there are other issues going on. That is just the way it plays out.

[Slide]

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

In May or 1999 a prior panel discussed the partial implant, and from the public discussion and disclosures in the press and elsewhere, it is self-evident that the outcome was that FDA did not move to approve that product after the panel discussion.

Let me clarify one respect, as speakers have already discussed, but let me just reemphasize that the panel around the table, here today, makes recommendations to the agency, and those are recommendations. Food and

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Drug Administration makes the final determination whether to approve or disapprove. We consider what you say. We consider what everyone has to say on the public record and make our decisions based upon the criteria that our Congress has outlined to us for making those decisions of reasonable assurance of safety and effectiveness.

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

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

[Slide]

We are going to proceed with a discussion of the engineering review, Angela Blackwell, the chief reviewer for this application from the engineering point of view. I might add that Ms. Blackwell was superbly supported in the engineering review and analysis by our Office of

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Science and Technology, Dr. Gary Fishman assisting us in the evaluation and I appreciate that assistance.

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

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

[Slide]

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

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

[Slide]

I am going to give you brief information about four different types of testing that were provided. Finite element analysis, fatigue tests, wear tests and metallurgical analysis.

[Slide]

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

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

[Slide]

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

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

[Slide]

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

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Taken all together, the tests conclude that the fatigue limit of the device is approximately 130 lbs. If a 3 times safety factor is used, the maximum load would

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be 43 lbs. Some patients, such as unilateral patients, could have a TMJ load larger than 43 lbs.

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

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

[Slide]

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

[Slide]

Metallurgical analysis -- analysis showed that the heat treatment used to dissolve secondary carbides does not always work. Gas porosity was shown to be on the surface of the implants. We have concerns about the

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effect of carbides or gas porosity in the fossa on the condyle whether it is natural or metal.

[Slide]

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

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

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

[Slide]

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

[Slide]

The patient specific Fossa-Eminence Prosthesis and the Stock Prosthesis are used for the partial reconstruction of the temporomandibular joint. The

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indications for use proposed by the applicant are for one or more of the following conditions:

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

[Slide]

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

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

Almost every term that we use here at FDA has a regulatory definition. Some are quite complicated. Quote, safety and effectiveness are defined by

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regulation, specifically in 21 CFR, 860.7. Pam Scott will go over these later today as we get to the end of the day. But one of the points that is very important is that we must consider in our review, number one, the persons for whom the device is represented or intended; the conditions of use for the device, including conditions of use prescribed, recommended or suggested in the labeling; the probable benefit to health from the use of the device weighted against any probable injury or illness from such use; and, the reliability of the device.

[Slide]

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

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

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

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

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

The applicant also presents data from a prospective study that is ongoing. This is a multi-center, open-label, single-arm study to evaluate the safety and effectiveness of the TMJ Fossa-Eminence Prosthesis. The primary objective of this study is to

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determine the reduction of pain as recorded by the patient. Secondary objectives include assessment of adverse events, improvement in diet and improvement in interincisal opening.

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

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

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

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

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

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

The results, as you see on the screen, indicate that at 12 months 29 patients have a reduction in pain from a mean of 7.5 to a mean of 2 on the VAS scale; 15 patients out to 24 months reveal a reduction to a mean of 1.0 on the VAS scale; and 2 patients out to 36 months have a mean pain score of 0. Similar reductions were

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noted in the VAS score for reduction in diet restriction. Note that these are mean values and standard deviations are reported.

Finally, the sponsor has also provided information from a patient set that indicates that patients who receive the partial joint prosthesis do not have clinical evidence of increased wear on the natural mandibular condyle, and you hear that information from Dr. Curry previously.

[Slide]

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

The preliminary data presented from the prospective study indicates that the use of the Fossa-Eminence Prosthesis may result in a decrease in pain and

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a reduction in dietary restrictions in certain patients. The applicant's most frequent preop diagnostic category is internal derangement. FDA has concerns about the adequacy of the characterization of this patient population. This category of patients may not be sufficiently precise to be able to identify the target population for this device.

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

During the May, 1999 panel meeting, the panel asked questions in reference to indications for use of these implants. Specifically, they questioned characterization of the pain prior to surgery, the heterogeneous nature of the population, the nature of indications for the Fossa-Eminence Prosthesis, and the need to accurately look at the indications and diagnosis.

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The panel also stated that the use of these devices should no be a primary modality but used as a salvage modality.

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

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

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

MR. ALBRECHT: The 93 percent reflects that patient population, the cohort of 88 patients. Out of that cohort of 88 patients, 93 percent of those 88 were

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still functioning after 3 years, as well as in the cross-section, if you look at the 1350-some odd patients that initially gave us preoperative data, out of those 1300 patients, 93 percent of them still had the device functioning at 5 years.

DR. PATTERS: Those available to follow-up?

MR. ALBRECHT: Yes, sir.

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

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

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

DR. HEFFEZ: State your name again.

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

These data were presented to support the data that is being presented for the prospective clinical study, which is a controlled study followed by a clinical protocol. As I indicated at the end of my presentation, no matter how you slice the pie, either from the registry or from the prospective study, we are seeing the same results out to at least three years after implant.

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

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

DR. BURTON: Yes, that would be fine.

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

DR. BURTON: Out of?

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

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

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

DR. HEFFEZ: Dr. Patters?

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

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

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

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

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percent of the patients with partial joints are still being followed.

DR. HEFFEZ: Dr. Bertrand?

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

DR. ALEXANDER: Rick Alexander. Again, I think I said that this has to be a decision that is made between the patient and the surgeon. If you have a surgeon that has a closed lock and can only open their mouth 10-15 mm, has pain -- you know, are you going to wait 18 months before you do anything? You know, I don't have too many patients that want to do that, and you start with some of the other procedures. Arthroscopy would be a start. But, you know, the goal here is to decrease pain, increase opening or do away with

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dysfunction and do away with noises. I mean, there are patients out there that have an internal derangement that have no pain, open to 42 or 50 mm, hyper-mobile patients, where the noise is so loud that they can't sit in a restaurant and eat. Are you going to wait around 18 months? Most of these patients are just dying to have this taken care of.

So, you know, I think it is a decision that has to be made between the surgeon and the patient, and if a pat wants to wait 18 months, then that is a reason to wait but I think you will find that patients that have serious internal derangement problems, by the time I see them, generally speaking are looking for something to solve the problem and they have already been through probably, some of them, years. I have a patient right now who has gone through three years of conservative therapy, has spent $22,000 on conservative therapy, and has a Wilkes class V internal derangement.

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

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

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

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

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

DR. BERTRAND: Probably greater than that.

DR. ALEXANDER: And that ranges to studies where they show 50 percent. Am I going to operate on those patients? No. But I will tell you one thing I am going to tell those patients, that it is crystal-clear that long-term internal derangement leads to degenerative joint disease, and if they start to have pain, and they start to have noise, and they start to have dysfunction they need to be reevaluated. But I am not going to operate on asymptomatic patients.

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

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

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

DR. ALEXANDER: Degenerative joint disease can burn out and never require any treatment but, again, I think that is something that the patient and the surgeon have to decide on an individual basis.

DR. BERTRAND: Thank you.

DR. HEFFEZ: Dr. Besser?

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

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DR. URBANEK: Tony Urbanek, Nashville, Tennessee.

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

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

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

DR. URBANEK: That is correct. Actually, I believe it was 345 joints, 217 patients.

DR. BESSER: So, that is even better then. I have a question as to how many of those were sort of more

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recent. You said you started very slow. You did one; you waited six months; you did a second one.

DR. URBANEK: Right.

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

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

DR. BESSER: So, give or take 120.

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

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

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

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

DR. URBANEK: I have seen no problems associated directly with the device. I have seen no device fractures. After opening, as I said, four or five joints

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for traumatic reasons, I have seen no giant cell formation, degenerative change of the tissue surrounding the implant in the glenoid fossa or degenerative change of the condyle itself by visualization. I follow the patients along with Panorex on a yearly basis for several years after surgery. I have seen no gross degenerative change of the condyle on Panorex, on x-ray examination.

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

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

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

DR. BESSER: Thank you.

DR. URBANEK: Certainly.

DR. HEFFEZ: Go ahead.

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

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DR. URBANEK: Yes, I have given it lots of consideration, especially recently once I became, let me say, embroiled in these discussions. In fact, I will do that.

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

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

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

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DR. URBANEK: In my own patient pool?

DR. BURTON: Yes, sir.

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

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

DR. URBANEK: Let me answer the second question first. A meniscectomy I have lots of experience with. Between 1981 and 1993 or 1994 I did lots of meniscectomies. Meniscectomy trailed off between 1991 and 1994 when I found that meniscectomy was consistently not working; patients were returning. Meniscectomy alone does not work because, whether it encourages fibrosis, it allows fibrosis to occur within the joint space, and when you reoperate a patient that has had only meniscectomy, that is what you will find visually, fibrosis scarring

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within the joint space. On the other hand, with the Christensen prosthesis, on opening several of these cases, I see no fibrosis at all. None.

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

DR. URBANEK: In the operated joint?

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

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

DR. HEFFEZ: Dr. Janosky?

DR. URBANEK: Excuse me, could I just add to answer the question specifically, the reason I think that the prosthesis works, in my opinion, is that it is extremely inert. I see no reaction of soft tissue, hard

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tissue. I do not see any bone resorption whatsoever clinically, visually or radiographically.

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

DR. HEFFEZ: In the interim, is there another question? Yes, Dr. Besser?

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

DR. CURRY: Jim Curry, from Colorado.

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

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

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

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DR. CURRY: What I am referring to there is I have had one occasion to reoperate a joint that had a total joint prosthesis in place where actually the phalange of the condylar element fractured after about eleven years. So, when I went in to replace the prosthesis, and when I took the glenoid fossa prosthesis out to replace it, I took some photographs of the base of the skull and it was my clinical observation at that point in time that if I had brought a person into the operating room to look at the glenoid fossa of this patient, and they didn't have any clinical history or anything of what was going on there, they would not be able to distinguish that fossa from one that had never been operated before.

The observation that I have is very similar to Dr. Urbanek's. In the very few number of cases that I have had the occasion to reoperate, either from trauma or whatever, I have not seen a single case of severe condylar degeneration. I just haven't seen that happen and we have, of course, seen that with other cases. I have seen it with people who have had surgery that had never had anything but just a standard placation, for example, or something of that nature, and I just haven't been able to see that in any of the several hundred patients that I have dealt with personally, and it leads

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me to -- I mean, God gave me a mind and I have just common sense and I make a statement like that just based on pure clinical observation.

DR. BESSER: Thank you very much.

DR. CURRY: Yes, sir.

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

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DR. JANOSKY: I want to just spend some time looking at your prospective study and your registry data. You presented two graphs, one from each of those. They are very similar. One was the pain score. This is a follow-up on some other questions that were asked and then sort of looking at it a different way.

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

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

DR. JANOSKY: Okay, 113, and if we just use the estimate, let's say, of 70 percent rate of return, what time point would that classify as? If we just say 70 percent of the patients, where do we have the point at which we have 70 percent of the data still available?

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What is the time point that that would classify? Would that be three months worth of data?

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

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

DR. JANOSKY: Right. So, you have 2 within the first group out of a start of 25. So, you have approximately 10 percent of your patients remaining at 36 months within that first group.

MR. ALBRECHT: Right.

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

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

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

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

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

MR. ALBRECHT: For the registry?

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

MR. ALBRECHT: I do.

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

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

[Slide]

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

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

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

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

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

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

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In the registry cross-section, with internal derangement anywhere between class V and class III we have over 800 patients to begin with.

DR. JANOSKY: And were using 70 percent again?

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

DR. JANOSKY: No, that is 30 percent.

MR. ALBRECHT: I am sorry.

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

MR. ALBRECHT: Right.

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

MR. ALBRECHT: Yes.

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

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

DR. JANOSKY: Thank you. I have some more questions later but I think I will stop for now.

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

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

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

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

DR. HEFFEZ: Answer for both.

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

In the registry, if we go back and look at what the physicians have provided us, the overwhelming majority provided class III, IV and V. Only 21 out of the 800-some odd returns gave us a class I and II. I think, to answer the question, we are looking for an indication of Wilkes class III, IV and V.

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

DR. BURTON: Yes, for Dr. Curry.

DR. CURRY: Jim Curry, from Denver.

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

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

DR. BURTON: I guess what I am getting at is what were your selection criteria? To me at least, it wasn't completely clear. Was it strictly the fact that you had three-year follow-up records on this particular group of patients?

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

DR. BURTON: And, from 1992 on, you do not have any patients that are more current -- let's say who were

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done in 1994 and three years would have been 1997, that would have met that criteria? I guess I am curious why the last patient falls in the '92 time frame.

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

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

DR. BURTON: No, not at this time.

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

DR. ANSETH: Kristi Anseth, from the University of Colorado. I have a question for Dr. Durnell regarding some of the dynamic material testing data that you have. Is there any information available on now the fossa-eminence interacts with a material other than just the cobalt chrome head or the polymethylmethacrylate head?

MR. DURNELL: John Durnell. To bench test an alloplast against bone doesn't really make sense. We chose the articulation of the metal-on-metal as the worst case because it was single point contact and it was hard

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alloplast on hard alloplast. It is difficult to reproduce either cadaver bone or anything with kind of a cartilage covering to articulate that and get any kind of meaningful test results.

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

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

DR. ANSETH: Thank you.

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

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

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

MR. ALBRECHT: Doug Albrecht, TMJ Implants. The data we were talking about, Dr. Janosky, was to response to Dr. Runner's comments regarding what type of internal derangements do we want to indicate this for, and I agree with you, the numbers are small. But if you look at the clinical report that I believe the panel was given prior

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to this meeting, on page 6 of that clinical report the numbers are much larger. Again, we have a cohort of 88 patients that are followed from preop all the way out to 3 years, the same group of patients, which is very revealing as far as pain reduction.

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

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

DR. HEFFEZ: At this time, I would like to break for lunch. The lunch will only be 20 minutes, giving new

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meaning to the word indigestion. At 2:10 we will reconvene.

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

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AFTERNOON PROCEEDINGS

[2:30 p.m.]

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?

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

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

MS. BLACKWELL: Yes.

DR. BURTON: Thank you.

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

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

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

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

DR. HEFFEZ: Thank you. Yes?

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

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

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

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

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

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[No response]

Thank you, Miss Blackwell. I would like to proceed with Dr. Besser's presentation.

Presentation by Panel Members

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

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

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

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Also, in one of the presentations they presented data from, I guess, 6/10 prostheses that have been tested and concluded that only 2 of these 10 had failed. They excluded 4 from the regression analysis that failed at very low numbers of cycles. I would like to hear some more from the company as far as why those 4 were excluded, leaving only the 2 that scored the best. In the material presented it was difficult to determine exactly what the criteria were for excluding those failed specimens from their regression analysis.

I also have concerns as to the wear testing. All the wear testing was done for the total joint prosthesis, nothing for the partial. I am not sure I have a solution to how best to look at wear on the intact condyle, which is what I would expect to show the wear as opposed to the metal prosthesis, but possibly some long-term postmarket surveillance, where an active effect was made to retrieve these prostheses further down the road to wee whether, in fact, some of the things that have been presented by a couple of the doctors who spoke -- their suspicions that this protects the mandibular condyle and it actually is better than not replacing the joint are, in fact true, or whether there is wear of the bone at the condyles that we are not seeing either because the data that you presented is too new or because

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it can't be seen on radiographs when you have the prosthesis in place.

I did have a question about the carbides. However, I will defer to Miss Blackwell if that has been handled as far as the manufacturing process is proprietary, and possibly someone from the company can talk to me in one of the breaks. Is that allowed?

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

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

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

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

DR. HEFFEZ: Mr. Ulatowski?

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

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

DR. BESSER: Somewhere between 250-500 lbs.

DR. HEFFEZ: You raised the question of criteria for excluding certain failed specimens from the regression analysis.

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

DR. HEFFEZ: And, handling of the carbides.

DR. BESSER: Carbide products. That is right.

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

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

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

DR. ANSETH: I am Kristi Anseth, and I sort of have dual affiliations. I am at the University of Colorado at Boulder, at the Chemical Engineering

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Department, and I am also associated with Howard Hughes Medical Institute.

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Again, without being too redundant about some of the issues that have already been raised, I wanted to focus mainly on two main points, the first being whether the data that is presented is relevant to both the total versus partial joint prostheses, and then special issues associated with specifically the partial joint prosthesis, and then some of the information that is difficult to get from the engineering data and can we draw any inferences from the clinical data set.

[Slide]

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

The tests that have some unique aspects are related to those that are the dynamic testing, and you are looking at motion and movement of the fossa elements against another material. As has already been iterated this morning, the worst-case scenario was selected as the

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highly polished head where you can get a single point contact on the fossa-eminence, the idea being that you will get the highest load at this point, the highest wear at this point. I think that is relevant for many cases, but I think there are also some issues that I would like to bring up.

There was a lot of finite element analysis done to address and get at loads and stresses that the implant would experience and, again, I think this is reasonable for looking at general material properties. Some of the issues come in when you are trying to look at the bone-on-metal type of interactions because finite element analysis, or at least what was presented, doesn't take into account any of the interactions at the interface or compliance of the bone, and what-not. But I do think it is relevant in terms of the bulk properties of the implant.

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

One of the issues I had was with the wear testing, and I just threw up this example from the data

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set which showed wear of the metal-on-metal versus the metal-on-polymethylmethacrylate head, and just to bring out the point that when you have two dissimilar materials you are going to get very different wear rates, which makes it more complicated when you want to look at the fossa-eminence on the bone. I would agree that the fossa-eminence worst wear rate is probably predicted by the studies that were done for the metal-on-metal. But when you look at the perspective of the bone or the native tissue, that may be where the concern lies, and that is not the case.

[Slide]

So, from the partial joint prosthesis, from the data that I just discussed briefly, when I say no additional tests I mean no additional tests that were just specific to the partial joint in terms of that dynamic environment. In particular, I was curious and would like to hear more about what the company thinks in terms of any potential issues or new issues that might result when you only have the fossa-eminence in place. And, I alluded to the perspective that you are looking at. Are you looking at the mechanical performance of the fossa-eminence? Are you looking at the wear of the fossa-eminence? Are you looking at what is happening to the condyle or if the disk is in place? And, wear is a

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very complicated process that is influenced by your number of contact points, the roughness, whether there is a third body present from wear debris and what-not. So, I think for the worst-case situation you need to be careful in terms of what perspective you are looking at.

So, because the company iterates that it is difficult to do this in vitro experiment with living bone against their fossa-eminence, there wasn't any data to try to extrapolate or compare to other systems, I looked a little bit at the clinical data to see if we could find if there was evidence for this occurring or should it be an issue. I think we heard about the clinical data already today and I just wrote down some of the basic numbers.

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

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

Again, these are just excerpts and I don't feel the need to read them all, but I think there is also a point of view, in the last quote, where Dr. Garrett says that in cases where you do see resorption of the condyle, he points out that it is not the fault of the prosthesis as surgeons may think who are not clinically experienced. Other surgeons may call this a failure of the Fossa-Eminence Prosthesis even though there is absolutely no evidence of reaction to the prosthesis. I think to some extent we have to also assess where the burden lies. Is it up to us to find whether the implant is causing

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negative impact or resorption of the condyle, or does the company need to provide more quantitative data on that?

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

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Again related to this issue, it wasn't clear to me either whether the disk should be removed or left in place, and whether this mattered at all with the Fossa-Eminence Prosthesis. There was one study of 17 patients and 10 of the patients did not have the disk removed when they were implanted, but subsequently 4 of these had to have their disk removed to treat their symptoms. I think it at least brings up a question. If there is wear of the fossa-eminence, what happens to the debris? Does the debris get into the disk or not? I mean, that is one common thing in terns of polishing things or looking at different kinds of grinding wheels, you put particles in a soft adhesive and you use that as a means to polish

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something. So, I think this might be one issue I would like to hear more about.

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

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I guess the last is that clearly one of the benefits of this device, as stated, is to salvage the natural condyle, and are there benefits associated with that early surgical intervention, and the clinical study that is ongoing to evaluate primarily the pain and to assess different safety issues and opening issues, but are there things associated with the study where we can better quantify these effects on the natural tissues? Thank you.

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

DR. BURTON: Thank you. Dr. Richard Burton, University of Iowa. My review personally led more to some of the clinical issues, and I will try to be brief

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in covering those as I think we need to carefully assess them as we move through the deliberation process.

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

Again, a number of the papers and presentations -- there is never a clear delineation of how you determine adaptive bone changes in the condyle versus degenerative bone changes. In all the cases, they keep going back to the fact that none of these seemed to be implant related. I guess it is very unclear to me how that is being determined. There may be some changes and I think that may eve be acceptable. The question is, can they be implant related or are they normal adaptive changes, and I don't feel that that has been addressed, candidly, on any level.

We have large numbers of letters of support that were part of our packages. In reading through those, unfortunately, most of those didn't provide any good,

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hard data that was, again, normally just related to clinical observation, both pro and con.

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

Another issue that runs through all this is the question of internal derangement and whether the fossa implant should be a primary treatment for that. It seems to me that as a means of preventing further treatment -- we did have the letter from Dr. Keller which the company presented as support, with some other questions from Dr.

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Curry. In Dr. Keller's letter, he asks us to consider the fact that that particular case was more of a salvage procedure versus a treatment, and he actually said not for internal derangement.

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

In looking at some of the materials that were presented to us, I have some concerns regarding the informed consent process and I think that Dr. Anseth provided a quotation from Dr. Garry about the failure of the implant versus a progression of disease, and I have concerns that in each of the things that were presented to us, every time there seemed to be anything that was either adverse or could be interpreted as adverse, it always seems to be either operator or patient dependent

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and at no time shows any correlation with the implant itself and I think, you know, that after all a bad result with proper consultation, informed consent is not a surgical failure or failure of the prosthesis, it becomes an indication for the next procedure which has already been discussed as a possibility with the patient.

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

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

Unfortunately, it appears from what I can see in the data that the majority of the patients who are receiving these are receiving these for internal derangement -- the great majority for that, and that seems to be the primary indication for its utilization.

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Certainly the other ones fall into that but the majority of the patients being selected for this particular implant are due to internal derangement. So, we have a question of safety, and it appears, at least from the metallurgical standpoint and possibly from some of the engineering standpoints that that may be resolved. The question then secondarily is, is it an efficacious treatment for internal derangement?

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

So, like I said, I think we need to look at the safety and the efficacy and, most importantly, what are

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the clinical indications for the utilization of the implant.

DR. HEFFEZ: Thank you very much.

Open Committee Discussion

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

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

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

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

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

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

DR. HEFFEZ: I believe to avoid some difficulty in interpreting this question, I think we should clarify internal derangement because people have been using the Wilkes classification -- there are several classifications available, but if we go through the Wilkes classification since its name has been evoked here several times, it has grade I through V. So, one could easily say grade V internal derangement, but I don't want

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to preempt it. But the second question is going to refer to degenerative processes. So, I believe that if we, as a committee, look at this question indicating earlier internal derangement problems rather than the later one, which are usually in relationship to a degenerative process, we may be able to answer this question easier. So, I would like to hear from the committee how they feel about that -- the term internal derangement not referring to the degenerative process and, therefore, it would be earlier stages of internal derangement. How does this committee feel about that?

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

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

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

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

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

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

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

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

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

So I am at a loss, then, to find the valid scientific data to even answer this question since I

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don't believe the registry study is a true clinical study and the prospective study is not complete at this time.

DR. HEFFEZ: Mr. Ulatowski?

MR. ULATOWSKI: The panel is considering valid scientific evidence which is a range of possibilities, not necessarily consisting of a prospective study. So you need to assess and find the merits of the elements of the data presented and whether it is supportive or not supportive. Registries are, I won't say often used, but for 515(b) devices, these pre-'76 devices, that sort of information is more common in regard to supportive data, data over the years, where you necessarily have to go back and look back at what has been going on rather that what we traditionally do now with the newer devices.

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

MR. ALBRECHT: Doug Albrecht, TMJ-Implants.

[Slide.]

This is the slide with basically the symptoms that a patient would experience with Wilkes clarification. Radiologically, for class I, you may see a slight forward displacement with good anatomic contour of the disc. For class II, you will see, again, a slight forward displacement, some deformity of the disc that is

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beginning and some thickening of the posterior edge of the disc.

Class III is where you will see an anterior disc displacement with significant deformity, prolapse of the disc and increased thickening, again, of the posterior edge. Stage IV, you will see an increase in severity of the symptoms over class III with positive tomograms showing early to moderate degenerative changes, flattening of the eminence and deformed condylar head sclerosis.

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

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

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

Does the committee feel that there is scientific evidence to warrant the use of the Fossa-Eminence Prothesis in that situation? Let me stimulate some

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discussion, then. Dr. Besser, do you have something to say?

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

It is presented as a yes/no question and the answer is not yes or no. I think I have seen evidence presented today that, for patients in category IV where there is significant joint degeneration going on, and these are obviously candidates for both surgery and for an implant, in these cases, I think, you can see some indication for the Fossa-Eminence Prosthesis.

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

Somewhere in the middle, we may cross that line. So possibly, if we can look at--unless there is a need to

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only use the two words "internal derangement--to look at indications or subheadings of internal derangement that might be easier to say yes or no to when asked the question.

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

You raised one point regarding loading. You felt that loading wasn't satisfactory. One could raise the question whether, in the early problem when there is mild clicking, for example, that the loads across that joint might be greater than later on in the cycle of the disease and that might help you in your thinking process.

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

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

Published in the Annals of Internal Medicine in January, 2000, less than--about 15 percent of patients

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with continuous pain, crepitus, painful function, 83 percent of them have a comorbidity of many other factors. My concern about doing something surgically to this group of patients, how well have those comorbid factors been included in the documentation and treated right from the onset.

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

With the emerging evidence that, perhaps, bruxism is a serotoninerically effect, has that been addressed? What are the medications that might be contributing to the factors that are producing this type of presentation to start?

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

DR. HEFFEZ: Thank you.

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Dr. Burton?

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

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

So I guess I have concerns about utilizing the indication of internal derangement as an indication for the fossa prosthesis. We can discuss whether or not we should try to quantify it and that, obviously, will become much more difficult.

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

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

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

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

Dr. Stephens, did you have a comment?

DR. STEPHENS: I think that makes sense because, even though internal derangement is a broad term, I think that when you open this up and start to define what areas of internal derangement that we are going to use, it starts to move toward clinical decision making. These patients, I don't there is any way to take a lot of the decision making out of the surgeon's hand at the time

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that he is evaluating the patients because they really do present very differently.

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

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

I am talking about what we might call the scientifically valid data from the prospective clinical trial. I think that the very small amount of data and the length of time that we have a substantial number of subjects from whom data have been collected is a significant issue here and it makes it difficult for me to be able to answer this question in the affirmative.

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

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

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

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

DR. CHRISTENSEN: You may not. This may be an internal internal-derangement process. The only way you are going to know on that is a biopsy of that tissue.

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The symptoms may be exactly the same or they could be slightly different.

DR. HEFFEZ: Thank you.

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

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

DR. HEFFEZ: Dr. Hewlett?

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

Clearly, in what has already been characterized as a subject pool at a very preliminary stage of data collection, I would submit that we really don't have a strong enough sample size of these various conditions to really answer question No. 2.

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

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

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

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

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

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

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

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

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

DR. BURTON: Temporary interpositional graft.

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

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

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

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

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

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

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DR. BURTON: Richard Burton. I guess I would also like, from industry, a little clarification on what the last one is. It says, "failed alloplastic partial joint reconstruction." Was that one of these particular ones that needed to be replaced? Is this an indication for its replacement or--I guess I am not currently aware that there is or has been another alloplastic partial joint system on the market.

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

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

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

We have used the Fossa-Eminence Prosthesis on a number of occasions for just bony ankylosis. I wrote

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papers on that back in the '60's. So if you want to look it up, it's there.

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

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

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

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

MR. ALBRECHT: Doug Albrecht, TMJ Implants.

[Slide.]

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On the screen now is the breakdown of the different indications that we did present data on, as I said. Nearly 90 percent include internal derangement, either with perforation or without perforation or associated with arthritis. In the prospective study, itself, 3 percent of the patients had a previously failed tissue graft or alloplast before receiving our device again.

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

[Slide.]

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

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

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

DR. HEFFEZ: I would like to move on to question No. 2--well, question No. 3, really. I will read question No. 2; has the sponsor provided valid scientific data to support effective use of the Fossa-Eminence

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Prosthesis for those indications that we had listed before. We will be having to look at; if not, which indications are appropriate for use of the partial joint prosthesis and what additional data, if any, are required to support the particular indication?

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

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

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

DR. CHRISTENSEN: Bob Christensen. A screw, in a bone plate or an implant, can certainly loosen. It depends on the type of bone you have got there and the problems there. If you have a problem with the screw,

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you are going to see evidence of a pattern of loosening of screws in the ramose area or in the base of the skull.

Screw loosening is really extremely small considering the great number, or the fair number, of these that we have out there. We pulled up some information on that. I don't think it necessarily shows all of them. So, when we see it, it is either--we consider it a surgical entity because of the bone of that patient, or it can be the way the doctor puts it in.

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

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

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

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

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

DR. HEFFEZ: Thank you.

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

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

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

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

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

Another way to describe that would be that I think that someone who does this work, inserts this prosthesis, needs to have experience gained from others, whether it be in a training program or whether it be mentoring or whether it be in a clinical program where he is exposed to others who have more experience putting this in.

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

I would hope that, in surgeons who apply this technology to the temporomandibular joint, that they don't do that. How much mentoring they would need? On a relative scale, not that much. If I was starting off from scratch, I would feel very comfortable watching and

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participating in three, four, five of these before I felt comfortable enough where I would do it, myself, considering I had the broad, general surgical experience and the specific surgical experience of other types of maxillofacial reconstruction.

DR. HEFFEZ: Were you mentored?

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

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

DR. URBANEK: I felt very comfortable.

DR. HEFFEZ: Okay. Thank you very much.

DR. URBANEK: You are very welcome.

DR. STEPHENS: Just one follow-up question. I am Willie Stephens. Do you know if there have been any differences in screw loosening between the stock prosthesis and the patient-specific patient because I am

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wondering if the screw problems may not the screw as much as it is the fit of the prosthesis.

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

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

DR. HEFFEZ: Thank you very much.

DR. URBANEK: Thank you.

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

DR. URBANEK: That is correct.

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

DR. URBANEK: That's correct.

DR. BERTRAND: As for the more severe joint problems, of severe fibrous ankylosis, bony ankylosis, or

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failed other implants, can you give us some numbers on your experience with that group of patients?

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

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

I have heard from TMJ Implant, Inc. and they submitted to you that their proposal is to draw that line at internal derangements at Wilkes classification III, IV and V to be indicated and degenerative joint disease and fibrosis. I would agree with that, by my experience. My diagnosis of internal derangement--when I say I diagnose 75, or 80, percent of my patients that I operate by internal derangement, those are Wilkes classification III, IV and V, not I and II.

Patients I and II get evaluated, get a pat on the head and I say, "Come back and see me when you have a

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problem. This is what you do; diet, antiinflammatories." But when they come to you with an internal derangement, by definition, as you saw up there, by Wilkes, and I would present to you that it is not a wrong tack to actually--it is a very commonly accepted--in our profession, it is totally accepted, Wilkes classification is the classification how you classify internal derangements of the temporomandibular joint.

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

There is no cut-and-dried answer. It is a very gray area. You didn't ask the question, but I have the opportunity to answer it. The relationship that you see between your patient, what they present with and their degree of pain, and the objective findings you see on physical examination, on the MRI, is what makes you

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determine that this patient is going to need surgery and this patient is not.

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

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

DR. HEFFEZ: Thank you very much.

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

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

But he or she may or may not be capable of doing that safely and competently. In a couple of the letters that came in to you sort of said, well, you know, the stupidity--I believe one of them stated that--of the practitioner. But the thing is that when we put this product out there, I guess I still feel we have to look at what the least common denominator that is going to be utilizing it is because that is where the danger may lie.

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

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Unfortunately, the patient doesn't know that.

DR. URBANEK: That is correct.

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

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

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

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

But when it came to putting this out where a larger number of people could be helped, I was concerned about that also. Fairly early, we started a teaching course, and we put on maybe three or four or five or six, sometimes, per year. We did that up until a year and a half ago when this was taken off the market, which has been a shame because there is a core of people out there

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that need to be taught and can be taught, and we had the opportunity to be able to teach them.

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

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

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

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

So we would put it on with, sometimes, live surgeries but always with a multidisciplinary approach to the thing, not just this technique but what else might

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help that patient. So we try to cover quite a few things.

DR. HEFFEZ: Thank you.

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

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

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

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

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

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

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

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

DR. BURTON: Dr. Burton. This would probably best addressed to industry and, perhaps, Dr. Christensen. But when we looked previously at the total joint, there were a number of questions raised about heterotopic bone formation around that. What have been your observations in terms of the difference in this formation or--and I know that, in some of the readings that we had this time, it talked about going back and either changing the implant or removing bone around it and sometimes I

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believe putting some fat, various things like that, around it.

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

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

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

That is not the experience that I have had for fifty years of operating on that joint. When you know that the disease process is involved and the degenerative process of that joint and there would be severe enough internal derangement or you get some bony changes in

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there, your best operation is that first operation for carrying that out.

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

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

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

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We can help that by moving that back a bit. I am not saying do it injudiciously. Hear me on that. But do it correctly and I think we can stop that.

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

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

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

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

DR. HEFFEZ: I would like to know what specific data do you think you could provide, in addition to what you have, or do you feel that there are certain weaknesses in some of the data that you have been provided that you would like to provide, if you had the

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opportunity, more data in that area that would support the use of the device.

DR. CHRISTENSEN: I think we have given you about all the data we have. It is amazing how many ways we have looked at this thing. In the area of the internal derangement, in the upper ends of that, III, IV and V, I think that there is more than enough indication there for it. Ankylosis is a smaller group so it takes you longer to get a long group of people in that area. But the results are very good.

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

DR. CHRISTENSEN: I see.

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

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

So when you see this thing level off at a year, they pretty well stay there. So I think your first few

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months, and that first month or two after surgery, is when I would say you are going to see the biggest problem, 28 days later, 30 days later, two weeks later.

If that is the case, then we have gone out. Even if it is, as a statistician, your type of look at this, we have gone out, probably, far enough to get a pretty good look at it. But we have looked at a lot of them a lot longer.

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

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

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

We are not seeing any changes as far as noise in the joint. Muscle tenderness decreases tremendously as

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the patient goes out. So all this will be included when the study is completed and the final report is issued but just eyeballing the data right now, the patients are doing terrific postoperatively.

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

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

So I would be hesitant to suggest to patients that you go through a meniscectomy and do nothing in there. We have had such remarkable luck with--I shouldn't say luck; that is not the word--success with this fossa on putting in there, on joints that had fibrous fusion and so forth--they have done extremely well and I don't know that I--I wouldn't want to put my wife or sister or me through a discectomy and not put a

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good device in there when we have got so much evidence that shows it going out forty years.

MR. ALBRECHT: Doug Albrecht, TMJ Implants. I think this question was also posed to Dr. Urbanek who very clearly stated that he initially did meniscectomies and he found that he had to go back in and do surgeries again and then put the alloplast in.

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

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

So again it is sort of--I would agree. I think that your success has been very good. Conversely, there also have been other groups who have not utilized that in

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their hands that have had very good success with the other treatment.

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

MR. ALBRECHT: I would like to yield to Dr. Curry but I would like to say that we are not saying that this is not the only treatment available. We are saying it is a treatment that does work very well.

DR. HEFFEZ: Dr. Curry?

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

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

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

DR. BERTRAND: Peter Bertrand. I do think, when we are talking about invasive procedures, we need to keep in mind the thirty-year Dutch literature that has looked at many patients, long-term, supportive therapy, we are looking at close to 90 percent of those patients with abnormal imaging findings doing rather well thirty years later.

The indication is that whatever type of physiologic stressors that caused the changes arthritically may well be self-limited. The question becomes, do we need to do a surgical procedure to get the same results long-term that the support therapy does.

We don't really know, thirty years, if that is the case unless I have not seen that literature from Dr. Christensen or a longitudinal cohort of patients over thirty years exists. That would be an important thing to see.

DR. HEFFEZ: Dr. Christensen, do you wish to address the panel?

DR. CHRISTENSEN: I think of many cases. But I go back to the very first one I operated. And this is not against what you are saying, Richard, but this is the

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lady that had a meniscectomy. Then she had a condylectomy and she ended up with a fibrous ankylosis.

She was going down hill. There was no way that she was going to get any better. Putting in that implant in there, forty years later, she has--other than I finally had to put in a condyle on one side, but the other side, thirty-eight years, a year later than that first, I did a fossa-eminence implant for a perforation, she has never had another surgery there.

So if you add up those two sides, I have got about eighty years history on that one patient. She wasn't doing that well when she had a meniscectomy. She got three or four years before she began to fuse up again. I have seen many like that, plus a lot of our SLA models. I could show you one after another of these things fusing up, where they have taken the disc out and done meniscectomies, and we have to go into a total-joint--many, many of them. Some of them don't.

DR. HEFFEZ: Dr. Patters?

DR. PATTERS: Mark Patters. Dr. Heffez, I think the panel is struggling here because it is very difficult to deal with these questions that FDA has posed without first dealing with the overriding question as to whether this is an approvable PMA and whether there is the

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existence of satisfactory valid scientific data to be reasonably assured of safety and effectiveness.

All of these questions, as I see them, look at possible indications of which indications are proven or not proven, but I don't really know that we can answer this question without having some feeling where the panel stands on the overriding issue of the PMA, itself.

So I am suggesting that we are going in circles and, without dealing with the PMA, itself, and whether it is approvable, can we, then, look at what indications may be appropriate and what are not.

DR. HEFFEZ: I agree with you, but I have found that sometimes if we go through the questions and we are raising certain questions, it helps come to that--answer that question. So if we can go to question 4 and then question 5, and then--

DR. BESSER: Can we stop at question 3 on the way?

DR. HEFFEZ: Sure. We were on question 3. Let me just finish my point. Once we finish doing that, we will return and ask that global question. It might bring us some data. Dr. Besser?

DR. BESSER: Dr. Besser. Back to question 3, one of the contraindications. There was a vague statement in one of the physician things about excluding

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patients with high loads, or susceptible to high joint loads. I would like that quantified. Current data supports loads up to about 50 pounds, so if there are patients whose disease or presentation would cause them to load the joint at greater than 50 pounds, I would consider them contraindicated.

DR. STEPHENS: How would we know that? How would we get that information?

DR. HEFFEZ: Dr. Stephens has a question. Repeat the question again.

DR. STEPHENS: The question is how would we get that information?

DR. BESSER: Dr. Besser. I am not sure that people have done either modeling studies of the TM joint or have actually instrumented the TM joint to look at what forces at the TM joint are normal or with certain activities.

I know that, in one of the findings, I think it was from the FDA, they printed the normal forces of the joint were 80 pounds for chewing, I think, and up to 300 pounds for clenching of teeth. I am not sure if that was at the tooth interface or at the joint. Perhaps, someone can give an indication for this.

DR. HEFFEZ: Dr. Christensen?

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DR. CHRISTENSEN: I think we are the only company in the nation or the world that has done a so-called kinematic study of a normal joint, a partial fossa-eminence joint and a total joint of our system on fifteen subjects and came up with the figures.

And then we had that backed up by another study done at Clemson University, where I happen to be on the faculty at the Engineering School, on that, too. The total-joint patient is only generating about 20 pounds or less of force in that joint. The partial joint is going up to 35 to 45.

We don't see these 300-pound bites and all this stuff. We measured it with transducers and fluoroscopy and everything that goes with it, and all the scientific and engineering data that goes with it, and you are not seeing that kind of thing in this type of patient.

So when you are trying to start limiting, then you put that alongside of our clinical experience, I have not seen a total joint fall apart, or a partial joint fall apart because of that type of pressure. I have seen a few of them where they have been hit in motor accidents or somebody has come in with a sledgehammer and hit them and that does change things a little bit.

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But, in the overall thing, the science is there that this thing does stand up to the pressure that we expect in that joint.

DR. BESSER: Dr. Besser. Then I am wondering why, in the Physician's Guide, in your submission, you have a phrase here; "Those patients which create abnormal forces within the joint need to be alerted to possible injury or fracture of the prosthesis due to increased force placed on the implant."

DR. CHRISTENSEN: We did that to help compromise and satisfy the FDA.

DR. BESSER: It leads me to the question of how big is too big.

DR. CHRISTENSEN: We measured it. So, since we have measured it, we know that these things fit in that area. If they don't, you go to a custom implant. If you have some big-jowled individual with acromegaly or something else, you can go to a custom implant and fortify the whole thing more than that if you need to.

But we have not seen that happen. So, to try and restrict Dr. Urbanek and Curry and all these other doctors and say, "You can't do this on a patient that might have some weird pressure," gets to be a bit academic.

DR. HEFFEZ: Dr. Hewlett?

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DR. HEWLETT: Ed Hewlett. Dr. Christensen, is it, then, your contention that all of the incidences in the clinical situation of fractured fossa-eminence implants have occurred through means other than the shear biting force of the patient?

DR. CHRISTENSEN: They have occurred--I don't recall anything that I think fits into the shear biting force of the patient. I have seen doctors, and I have done it, myself, in years past, try to bend the fossa-eminence implant in a pair of pliers and crack it or break it. We warn against things like that.

But there have been a few cases where they have been in motor-vehicle accidents, where they have been hit. There has been a case or two where somebody--and this was in years before--somebody kept cranking the jaw open when bone grew up around this thing and they should have gone in and taken out the bone around it.

If you crank it enough, you are going to break something. You either break right through the base of the skull, you break the jaw, or you break the implant. I have seen other motor-vehicle accidents where the jaw breaks and the implant stays intact. So you have got a number of things to think about.

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DR. BESSER: Just to follow up, the study that you quoted from Clemson, is that included in here somewhere?

DR. CHRISTENSEN: Yes. It is in the PMA.

DR. BESSER: You wouldn't know where, would you?

DR. CHRISTENSEN: No; I don't. Brian May--when I was a reviewer on the program.

DR. HEFFEZ: Dr. Curry?

DR. CURRY: Dr. Curry from Denver. I would like to respond, and I don't know who asked the question about have we ever seen biting force cause a fracture of the Fossa-Eminence Prosthesis. I think the only Fossa-Eminence Prostheses that have been reported fractured were combined as a total joint prosthesis.

I have never heard of, and personally never seen, a Fossa-Eminence Prosthesis fracture in clinical use as a partial joint replacement.

MR. ALBRECHT: May I make one comment, Dr. Heffez?

DR. HEFFEZ: Yes.

MR. ALBRECHT: Doug Albrecht, TMJ Implants. In the clinical report that the panel was given, page 26, we do have a summary of our NDRs and it does refer to fractures of the Fossa-Eminence Prosthesis and we would like to review that.

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DR. HEFFEZ: I would like to go to question 4 so we can get some global understanding of this PMA and then revisit the questions. Question 4, this partial joint prosthesis, the Fossa-Eminence Prosthesis, is designed to articulate on the natural condyle, mandibular condyle, which raises concern regarding the potential for degeneration of the natural condyle.

The first question, do the engineering data, based on the total joint prosthesis, provide adequate support for use of the Fossa-Eminence Prosthesis as a partial joint prosthesis? If not, what additional data is necessary? Are the inferences in the engineering data, basically, from the total joint adequate to be applied to the Fossa-Eminence Prosthesis?

How do people feel about that?

DR. ANSETH: Kristi Anseth. I think, in part, a bulk of the data that represents just the basic material properties, biocompatability, are very similar for the two joints and show a reasonable degree of safety of the material, itself. I think there is still a little bit of the issue of the load that is experienced, which we just talked about, whether there should be any restrictions on that.

And then, related to part 2 of this question, from the non-clinical data, there really is no

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engineering evidence about the metal-to-bone that I thought supported that it would not cause degeneration. So I thought there was lack of evidence from that perspective.

The clinical data, again, the N is very small. So there is a little bit of uncertainty in terms of what we are looking at, but there is some clinical evidence that there is not as much degeneration. But, from my perspective, that information is lacking.

DR. HEFFEZ: So the second part of the question is, do the engineering and clinical data demonstrate that the metal-to-bone articulation will not cause degeneration to the natural mandibular condyle, and you feel that there is not enough data to support--

DR. ANSETH: I don't believe there is enough evidence--the engineering data, I don't think, supports that. The clinical, I will defer to some comments from the clinicians.

DR. HEFFEZ: Dr. Cochran?

DR. COCHRAN: As regards the clinical data, we saw some nice radiographs that showed that there was not much condylar change. But I feel like, a little bit, we are going down the path that endosseous dental implants went down where the data you are looking at or the cases that have been successful and that you can follow.

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Without prospective data, we don't know if the ones that are dropping out, the patients that are dropping out, maybe they are having problems in that area so I don't feel like we really have sufficient data and we won't have it until you do a prospective trial and follow the patients and look for changes on radiographs over time.

DR. HEFFEZ: How would you suggest evaluating the changes in the condyle? We already note there is some difficulty sometimes in evaluating it through CT. You are relying mostly--in most cases, it would relying on linear or polytomograms or panoramic radiographs.

DR. COCHRAN: I acknowledge the fact that it is not an easy thing to measure, but I would like to see some sort of measure of that in a prospective fashion, be it on whatever radiograph you could find. But it would be on all the patients and not only on the patients that are just successfully treated.

DR. HEFFEZ: In a qualitative fashion, in other words.

DR. COCHRAN: Some sort of qualitative--whatever you can do.

MR. ALBRECHT: May I respond, please?

DR. HEFFEZ: Who said that? Yes.

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MR. ALBRECHT: Doug Albrecht, TMJ Implants. That is part of the prospective study. We do collect radiographs, panorex radiographs, on all patients at every follow-up visit. It will be evaluated at the conclusion of the study.

DR. HEFFEZ: How are you evaluating them? What is the scale that you use to evaluate the changes on the radiographs?

MR. ALBRECHT: We don't have a scale. We are going to have them reviewed by a radiologist and provide the results at that point.

DR. HEFFEZ: My suggestion is that you should have a well-defined scale.

MR. ALBRECHT: I am sure the radiologist has a scale of disease process that he looks for when he does examine these. I am not familiar with that type of scale but they will be evaluated.

DR. HEFFEZ: Okay.

DR. BERTRAND: Peter Bertrand, question.

DR. HEFFEZ: Can you wait one moment, Dr. Bertrand? Does somebody from industry want to--

DR. CHRISTENSEN: I would like to answer that in another way. You know, Dr. Urbanek, back here, has had 351 partial joints out there going back ten years, or whatever the number is. Any of us that are clinicians in

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here realize particularly that, if you have a bilateral or a unilateral in which that condyle is shrinking away, that jaw tends to move that direction.

That jaw tends to slide and you get an anterior bit. You don't have to be a rocket scientist in radiology--I am not saying that we don't do that, but you don't have to be a rocket scientist in radiology to determine these condyles are not melting away.

Otherwise, this occlusion is not staying there. I am sure you are just as familiar with that as I am. I know Dr. Curry and Dr. Urbanek both can speak very well to it.

DR. LIPPINCOTT: I am Al Lippincott. I am the bioengineer consultant to TMJ implants. I don't have any financial obligation to the company. But, to answer your question, Dr. Anseth, about any studies that have been done of the metal against bone, there are three articles that I am aware of in the orthopedic literature where they have done animal studies regarding cobalt chrome as one of the materials.

But, in many cases in the orthopedic literature, they are also evaluating cartilage degeneration as well. So whether it would be in reference to actual bone that you would see in the TM joint, that is what would have to be reviewed.

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DR. HEFFEZ: I think Dr. Bertrand had a question, initially.

DR. BERTRAND: If we are trying to three-dimensionalize whether there is loss of condylar formation, and these patients have CAT scans, why not three-dimensionalize the CAT scan, make a model down the line, take another CAT scan and three-dimensionalize it, and compare over time. That technology is readily available now.

DR. HEFFEZ: Dr. Hewlett?

DR. HEWLETT: Actually, I would like to pose a question to, is it Dr. Lippincott? In your manuscript of your wear study that was included in the materials, you described a gross examination of three explanted polymethylmethacrylate condyles and described visible to the naked eye wear on those condyles.

One, I believe it had been in for eleven years, went to extent that the plastic had worn away down to the metal core that serves to hold the polymethylmethacrylate in place. Albeit it is a very small sample of these, I found it somewhat interesting in that, in this entire body of information, it is the only example of two dissimilar materials functioning in vivo in the TMJ implant situation.

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I would be interested to hear your opinion on how the wear of the polymethylmethacrylate might be extrapolated towards our concerns about the wear, understanding, of course, that polymethylmethacrylate can't regenerate itself.

But I guess my ultimate question is is there possibly a subset of patients out there whose regenerative capability might be exceeded by some abrasive wear that would occur between the bone and the fossa-eminence implant.

DR. LIPPINCOTT: Al Lippincott, to answer your question. Understand that in those retrieved devices, we did not see any foreign-body reaction, or none was reported. In many cases, we didn't receive any histology sections of tissue to identify that, but identification by the surgeon, there was no inflammatory reaction. I wanted to make that clear with the methylmethacrylate.

Granted, there is more extensive wear regarding the comparison of bone against cobalt chrome. All you can take is, really, the clinical data and what you are seeing. In many cases, if there was a retrieval or there was a need to go back into that joint, my understanding, from the clinical side, they didn't see any staining of the tissue that would make one think that there was wear

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from the fossa component as far as identifying where, from bony erosion of the bone.

Again, it all depends if histologies were taken. Really, even that would be subjective as to whether you could identify that or not.

DR. HEFFEZ: Dr. Besser did you have a question?

DR. BESSER: I wanted to--sorry; doing three things at once.

DR. HEFFEZ: Dr. Curry?

DR. CURRY: Jim Curry from Denver. I don't know of a clinician that is doing this type of surgery that is not also somewhat concerned about the response of the natural mandibular condyle of our patients to the use of an alloplast in the joint. We are all concerned about that.

My approach to this, a little bit, has been I don't know of a test that you can do preclinical to help us with that understanding because, as you well know, if you put a splint on a patient for any length of time, you are likely to get some changes, radiographically, in a mandibular condyle with no surgery at all.

Or, in the case that I showed earlier, if a patient goes through standard other kinds of surgery, the entire condyle may fall away and melt away. And so we don't have any real understanding of what the process is

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that makes progression of disease. To blame it on the Fossa-Eminence Prosthesis, when we have, literally, thousands of patients out there that we can look at clinically.

If the natural mandibular condyle was going to wear away because of the metal, it ought to be happening most of the time. You may find an occasional case where, as you have suggested, there may be some odd-ball physiological reason why that patient it didn't happen to. But the majority of patients ought to have that condyle melting away in front of our eyes and I am telling you that simply is not happening.

It doesn't happen with anybody that I know that uses this. And we all follow our patients both clinically and radiographically.

DR. COCHRAN: This is David Cochran. I don't think the intention of the question was that we were blaming the implant. It was simply that the only way to determine if there is a relationship or an association with success or, in fact, you can prove that there is no change is to do it prospectively and look in the different patient groups, the ones that are successful and the ones that are not successful, and show whatever changes occur.

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It is just going to document the changes. It is not saying that necessarily there is something wrong. But you have got to do the study. You have got to do the prospective study and follow all the patients and make that determination. It is the only way you are going to do it.

DR. CURRY: Dr. Curry from Denver. In response to that, I agree with that. But I also agree that there is some validity to retrospective analysis looking at people who have been around for ten or fifteen years that we have access to. You may not have a presurgical CT scan on a patient that has been out there ten or fifteen years.

We didn't know to do it then. But we can get some of those patients, and that is what I tried to do, and look at what their condyles look like and what their bite looks like and what their clinical picture looks like and extrapolate from that what is going on.

DR. COCHRAN: I agree with you, but I think you are missing the point. The point is the cohort that was followed longitudinally, where you have it, are the ones that have been successful. The interesting group is the ones that were not successful and to show that maybe there weren't bone changes in that group either.

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That is the group that is most interesting. Then you have got a comparison and you have got an association.

DR. CURRY: Dr. Curry from Denver. I think I understand your point but, as a clinician, I see various kinds of patients who have varying degrees of disease in their joints and I have not ever been able to correlate one specific treatment to bringing on a more rapid progression of disease except in the case of teflon and proplast, which I did very few of, and silastic.

I have seen those joints melt away within just a few months. And so we made a natural correlation to that and we are having to do the same thing with this prosthesis.

MR. ALBRECHT: Doug Albrecht, TMJ Implants. One other way to look at it is in our cross-section data, of the 1270 patients for which we did have clinical data on preoperatively, and I grant you, yes, some of those patients are not followed up totally out to the five years, but I did look at all 1270 patients.

We would know if they progressed from a partial joint to a total joint because we would have to supply them with the total joint. Out of 1270 patients, only 25 patients have progressed to a total joint from a partial

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joint. If I do the math right, that is less than 1 percent.

That pretty much is for either iatrogenic placement, infection, loose screws. Unfortunately, in 19 cases, the physician did not provide us any information why they went from partial to total. But, still, it is less than 1 percent out of all those patients with partial joints that have progressed, for some reason or another.

DR. HEFFEZ: Dr. Besser?

DR. BESSER: Mark Besser. I found the reference in the original PMA for the TMJ joint loads. They are a little bit higher than what Dr. Christensen had stated. He stated it for, if you will pardon the expression, the normal group. Average values were 388 Newtons. That is about 75 pound. The maximum value for a subject was 621 Newtons, 130, 140 pounds.

The lower values given for the Fossa-Eminence only in the total TMJ groups were 200 Newtons, about 50 pounds, and 91 Newtons for the total joint group. But, again, even for the Fossa-Eminence group, the maximum value for a subject in that group was 536 Newtons, about 120 pounds.

Therefore, my concern still stands when looking at this population as to whether a contraindication for

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people with high TMJ joint loads exists and whether some determination of that joint load--and this modeling was done from a bite load through some anatomical modeling to get a joint load.

So it is possible that minimum values for bite load, or maximum values for bite load, should be determined and used as a criteria for acceptability of this prosthesis.

DR. CHRISTENSEN: This is a good point. But you have to take into consideration about 10,000 fossa-eminence implants out there in people, maybe 11,000. Half, or a certain figure of that, maybe 4,000 or 5,000, are total joints. The rest of them are partial joints. Out of all of that, as Dr. Curry said, I don't know that I remember anybody fracturing that fossa in the normal situation.

Am I wrong?

DR. HEFFEZ: Thank you, Dr. Christensen.

DR. BESSER: Dr. Besser. To follow up, I think that--I agree with what you are saying and understand what you are pointing out. I am answering the question that was asked of me, which talked about the engineering data. I think there is a 30-year history of clinical data that cannot be ignored, especially when looking at some of the questions we have been asked about condylar-

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joint degeneration where it is very difficult to simulate in a lab, and you can't ignore the fact that you have an awful lot of data from the clinic that may make working very hard to simulate it in the lab unnecessary or irrelevant.

However, I am concerned by some of the engineering data that has been presented, looking at it as an engineer, and would like to see additional data.

DR. LIPPINCOTT: May I comment on that?

DR. HEFFEZ: Identify yourself.

DR. LIPPINCOTT: Al Lippincott from TMJ Implants. I understand, and it was identified by FDA, that the metal-on-metal represented the worst-case condition which represented point contact. Understand, with point contact, you have higher stresses.

If we talk about only a hemiarthroplasty only with bone with a broader surface onto the implant surface, your contact stresses will be substantially reduced.

DR. BESSER: I am assuming that the loading that was put in here for the normal group assumed bone-on-bone interface if you have a better model or, I guess, a better method for measuring what that joint contact force is. When we are looking at fatigue and the wear values and the wear data that was generated was using a bearing

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force of 35 pounds, the fatigue data, again, using 130 pounds, I believe.

It would be nice to look at that at a higher force and see what additional wear or what the fatigue behavior of the prosthesis was.

DR. LIPPINCOTT: Al Lippincott, again. Just a comment on that, as well. We did look at much higher loads under a static condition. Really, understanding fatigue and its relationship to a static load, usually, it is, of course, a lower percentage that you will see as far as failure.

Basically, what we did, as well, is after fatiguing the device, we did a static load to failure and found that, even at the static load, we were at much higher forces, I think around the 650 pound, something like that.

DR. BESSER: Mark Besser. I have no problem with the static loads that you subjected this to and its yield strength. We have no argument there.

DR. HEFFEZ: I would like to move on. Question 5, I think, has been answered, really. We have been discussing if there are safety concerns, what measures can be taken to mitigate these concerns. We discussed loading. Were there any other safety concerns that panel members had?

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DR. BERTRAND: Peter Bertrand. Are we sure the quality-control modifications pointed out by the FDA, that the metallurgic problems are satisfied?

DR. HEFFEZ: Are we sure we have to rely--is that a question to me?

DR. BERTRAND: Sure; to anybody. There were some difficulties that the FDA had with interpreting whether the gas-carbide problem--they have made suggestions. My understanding is that those suggestions have been undertaken, but have the suggestions shown that, yes, the problem is indeed taken care of.

I am not aware that we know that it has been taken care of. Or am I misinterpreting?

DR. HEFFEZ: I believe Ms. Angela Blackwell--if you would like to come to the microphone just to clarify what you said before regarding the gas porosities in carbides.

MS. BLACKWELL: The questions about the carbides have not been answered specifically yet. There is a procedure in place to answer them. They can't be answered until the company is back into production. They don't have anything to test.

DR. HEFFEZ: Dr. Besser?

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DR. BESSER: Mark Besser. Are there criteria in place, once they are back into production and they have something to decide whether it passes or fails?

DR. HEFFEZ: Does industry want to reply to that question?

MR. DURNELL: This is John Durnell. Yes; quality-control measures are in place once normal production has resumed.

DR. HEFFEZ: Is this information that you feel is proprietary and that you don't wish to reveal at this meeting with the people present?

MR. DURNELL: Proprietary.

DR. HEFFEZ: Dr. Besser, do you feel that you want to hear this information? We would arrange for that.

DR. BESSER: No; Ms. Blackwell has indicated that the criteria were in place for success and failure when they go back into production and I am comfortable with that. Thank you.

DR. HEFFEZ: Yes?

MR. LARSON: Floyd Larson. I was just looking at that section. It is in binder 3, if you have it handy there. That section, or at least the FDA comments regarding that section, are addressed in binder 3 but it is not paginated.

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DR. BESSER: About how far in?

MR. LARSON: I only have a section of it scanned in here. I think it is near the front. It could even be about page 7.

DR. HEFFEZ: Any other questions? Comments?

MR. ALBRECHT: Doug Albrecht, TMJ Implants. May I respond to Dr. Burton's question early on regarding the registry not being a study and the prospective study being a study?

DR. HEFFEZ: Fine.

MR. ALBRECHT: I agree with you. It is not a controlled clinical study. But, for preamendment devices, again, the FDA has said it could be a prospectively controlled study, case histories or significant human experience. We believe that the registry is significant human experience. We are looking at thousands of patients, to begin with and, granted, the follow up is not ideal--

DR. HEFFEZ: I think Mr. Ulatowski indicated already that we should be using all data available including the registry.

MR. ALBRECHT: Okay.

DR. HEFFEZ: I would like to, at this time, move to the open public hearing.

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DR. HEFFEZ: Since we had an extended open public hearing in the morning, I would like to only reduce this to a total of fifteen minutes. If there are people that would like to address this panel, please identify yourself and we will bring you to the podium.

MS. LUCAS: Ellen Lucas. I have no financial anything. I was just listening here about a few people have had this, and very few people have had that. I must be very special because I was looking at some of my op reports and I have had--since I had the all-metal joint in, I had ankylosis on both the left and the right, and loose screws. And then--let's see, heterotopic bone on the right and metallosis and staining on the left.

So I have had all these different things in just two surgeries, they were discovered. That was since the metal joint was put in.

Thank you.

DR. HEFFEZ: Dr. Patters?

DR. PATTERS: Question for Ms. Lucas, if I could.

MS. LUCAS: Excuse me. I also forgot my pathology report that states I also had a giant-cell reaction.

DR. PATTERS: Mark Patters. If I could ask a question of you. One of the overriding concerns is the

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number of patients lost-to-follow-up. You have had a negative reaction. Was that reported by your implanting doctor to--in other words, are you one of the people lost-to-follow-up or are you in the data?

MS. LUCAS: I sent MedWatch forms in to FDA and I also tried to call the company but I never got a response.

DR. PATTERS: But did your implanting surgeon report to--

MS. LUCAS: I don't know that for sure. I don't know.

DR. PATTERS: So you could be someone lost-to-follow-up?

MS. LUCAS: I could be lost; yes.

DR. PATTERS: Thank you.

MS. LUCAS: Thank you.

DR. HEFFEZ: Is there anybody else who wishes to address the panel in the open public hearing? Ms. Cowley?

MS. COWLEY: Terrie Cowley with the TMJ Association. Just one thing which hits very hard to a patient listening to a learning curve of twelve patients and learning TMJ by trial by fire. All I could think of was what was the condition of those twelve patients while this person learned how to do the procedure.

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Another. Dr. Christensen is extremely proud of his fifty years of dealing with this joint. I kind of wish we had fifty-years worth of data on the screens today. I have not heard one mention of the immunological--not immunological, per se, but the allergic reaction to materials that we are hearing increasingly from the patients.

Another person talked about things happened in two months and then everything seems to be fine. I am talking to people who have broken devices in their heads now for three years. Their surgeon either will not take it out, they are waiting for something else, or they just don't want to get into surgery No. 22.

So whether it has happened in two years, whether it has happened in four, the devices are out there breaking. I feel compelled to reaffirm what I mentioned this morning and that is that this panel, should you choose to approve any of these devices, you must include in the labeling that an independently monitored TMJ Implant registry be established complete with the explanted device analysis and input from the patients.

Thank you.

MS. HOSFORD: Toni Hosford. I just wanted to say that you tend to hear, as far as for follow up, more complaints than people who are doing well with their

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implant. People that are doing well generally go on their merry way and they don't have any reason to go back to the doctor and complain.

I also believe that if the correct surgery is done in the first place, then there is no need for other surgeries. I have had no other surgeries, no allergic reactions, did all the conservative methods. I do believe in this product. I sympathize with people that have had multiple surgeries, but I do think, regarding data, it is hard for doctors to keep track of patients that are happy and don't come back.

It does take time to call the patients and try and talk them in to coming back to get an X-ray to see how they are doing.

Thank you.

MS. COWLEY: Is it possible for me to address the panel?

DR. HEFFEZ: Yes; you may.

MS. COWLEY: Terrie Cowley, TMJ. We hear this an awful lot from all different treating professionals, the splinters, the grinders, and so forth. All of these patients are doing so terrifically. My question is, without scientific data, how can you ethically subject a patient to either getting better or turning out so

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horrendously as the over 10,000 people who have called us?

DR. HEFFEZ: Anybody else wish to address in the open public hearing?

We are not going to have the break. We are going to move along and do the open committee discussion at this time.

Open Committee Discussion and Vote

DR. HEFFEZ: At this point in time, I would like to bring up Dr. Patters' point. If you could reiterate your point.

DR. PATTERS: Mark Patters--my point regarding dealing with the issues of safety and efficacy before we look at indications?

DR. HEFFEZ: Correct.

DR. PATTERS: Yes. I feel that we have to come to grips with whether, as defined by the law, that there is reasonable assurance of safety and efficacy based upon valid scientific data and deal with that issue. Once the committee has established its point of view, then to determine what possible indications or contraindications exist.

So I would recommend that is where the discussion be focussed.

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DR. HEFFEZ: At this point in time, I think it would be valuable to have Pamela Scott read out a definition of safety and a definition of effectiveness. We have it on a powerpoint slide.

MS. SCOTT: The definition of safety, and the reference for this is 21 CFR 860.7, section (d), subsection (1). "There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health under the conditions of use outweigh any probable risk. The valid scientific evidence shall adequately demonstrate the absence of unreasonable risk associated with use of the device under the conditions of use."

The definition for effectiveness; again, 21 CFR 860.7, section (e), subsection (1). "There is a reasonable assurance that a device is effective when, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when labeled, will provide clinically significant results."

DR. HEFFEZ: Thank you, Ms. Scott.

So, let's address the first issue of safety. I would like to hear from the committee whether they feel that there is enough scientific evidence including all

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the evidence that has been provided, including the registry.

MS. MORRIS: Could I make a comment?

DR. HEFFEZ: Yes.

MS. MORRIS: Lynn Morris. I am the consumer representative on the panel. I find today's discussion very difficult. On one hand, if I were a patient or a member of my family or a loved one had the pain and chronic conditions that TMJ causes, I would definitely be desperately seeking Dr. Christensen's or Dr. Urbanek's phone number to help me.

On the other hand, although I don't have any technical ability to assess the data here, I am concerned that--I know that the FDA is now looking at the least burdensome way to prove something. But I am concerned that the panel still has a responsibility to have the data in front of them to make the decision on safety and efficacy, and to make that decision based on scientific data, not on any data that is presented, either here or that you specifically know otherwise.

The other issue that concerns me is that it seems like, perhaps, you are using the registry as part of that decision. I guess I would like to be assured that you consider that scientific data because it doesn't

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appear, from my experience, to be that. That is one issue.

The other is while I don't have any experience on the technical end of this, I do have experience in the regulation of medical professions. When I walk away from an FDA meeting as a consumer representative, I want to be very assured that the product is clinically proven to be safe and effective, because if I have to rely on the learning curve of practitioners, which I see every day, I would be very nervous.

So I guess, basically, my two concerns are that we really have the scientific data to show it is safe and effective and that we take concern and really look at what the learning curve is and, if we are going to go forward with this, what we are going to require.

DR. HEFFEZ: If I may ask you a question. As a consumer, I would interpret it as saying that you would not want to see any device being used from a preventive point of view--in other words, to prevent more serious disease from occurring--is that correct? If I interpret what you are saying, you would rather have a device available as a salvage procedure.

MS. MORRIS: No; I am not saying that. Again, I think that that issue is more practice-related. I guess, just from a comfort level, and I think you talked earlier

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about the panel having a comfort level with safety and efficacy, because I am somewhat less comfortable with the practice end of it--I mean, the surgeons and the doctors that are here today are very distinguished, and I would put myself or my loved ones in their hands.

But I have seen many, many surgeons in the regulation of medical practice that I would feel much less comfortable with. So, starting out, I want to be really assured--and I think the consumers in the audience do as well--that the device really has a pretty significant level of safety and efficacy.

For me, that would be to have a good deal of scientific data to show that. I guess that comfort level has to be higher when there is a learning curve involved. The higher the learning curve, the more you would want to see--at least I would want to see on the safety and efficacy side.

DR. HEFFEZ: Thank you. Dr. Patters?

DR. PATTERS: Mark Patters. I have some serious concerns about using the registry data for safety because it requires an assumption be made about the patients that are not represented in the data. We know that the sponsor presented data of 1358 cases and, at one year, there were only 555 available.

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So, nearly 60 percent were lost-to-follow-up. To know whether their device is safe, I would have to know something about those 60 percent. One can argue that the most successful patients don't return to follow up. One can also argue that those who feel that they have been damaged don't return for follow up.

I don't know the answer, but I find the prospective study is the place where safety data should emerge that should be clear. Unfortunately, at this point, the prospective study is not far enough along to make any conclusions from, at least conclusions out to 24 and 36 months.

So I have some concern that the data is not available at this point, but should be available in future, to answer questions about safety.

DR. HEFFEZ: Do you feel the prospective study, as it is constructed, is adequate--will be adequate to answer those questions?

DR. PATTERS: I don't know that, but I know that the prospective study is a protocol which requires, to fulfill the protocol, that follow-up examinations be done on patients and patients know that entering the study. That is far different from the registry data which relied on whether implanting surgeons returned forms and were able to contact patients.

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So, certainly, as designed, if 60 or 70 percent of the patients can be retained in the study, it should provide that answer.

DR. HEFFEZ: But the study, as is constructed with inclusion criteria, exclusion criteria, those, you feel, would, once the study is completed, be able to answer those questions in your mind.

DR. PATTERS: With the caveat of being able to retain the majority of patients out to 36 months.

DR. HEFFEZ: Dr. Burton?

DR. BURTON: Dr. Heffez, and this is probably to Dr. Patters as well, and Dr. Janosky who has addressed these issues, too, I think that it probably is adequately constructed. The question is going to be, given the current input numbers that exist, whether the 36-month point, particularly in some of these subcategories which have extremely small numbers, whether we are going to have enough to have a reasonable correlation with those.

I guess the question, then, is the clinical trial correctly designed. The answer to that may be yes. The question is, is it large enough that, at 36 months, we are going to have an adequate number of patients and a significant percentage of the patients, enough to make a decision based upon that.

DR. HEFFEZ: Dr. Hewlett?

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DR. HEWLETT: One suggestion for the structure, the construction of the prospective study, in spite of the overwhelming empirical evidence, as Dr. Curry pointed out, that the fossa-eminence implant does not result in degenerative damage through abrasion to the natural condyle. I would urge for inclusion in the protocol of some standardization, probably in the radiographic follow up, that would facilitate, as close as we can get, to a quantitative assessment of changes in the condyle over time.

I would urge that some modification of this nature be added to the protocol to settle, once and for all, this question of condylar changes, if any, in the partial implant situation.

DR. HEFFEZ: Dr. Cochran?

DR. COCHRAN: I would reinforce what Dr. Hewlett has said. Any time you design a prospective trial, you should set the outcome variables in advance. In this case, I would use a blinded radiological assessment tool of some sort to make that.

My point I wanted to make was that, given the current design of the prospective trial, I am a little worried that, a year from now or two years from now or whenever it comes back to this panel, given the inclusion criteria without better definition, we are going to still

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be struggling with the same questions about which patients can be operated, how many had ankylosis, how many had prior alloplast, and if that number is still 3 percent or 4 or 5 percent, I just worry about what kind of conclusion you are going to be able to make for that particular indication.

DR. HEFFEZ: So if I had to summarize, the current protocol could be improved by looking back at the inclusion criteria, consolidating, defining them a little bit better, that we could look at establishing standard means of evaluating radiographs, define clear what the adverse effects are; for example, device-related, meaning implant loosening versus screw loosening. They are both in both different categories. Define better unanticipated chronic pain, for example.

In other words, provide a better, more objective means of evaluating the results that would improve the current protocol.

The reason why those items are brought up is to be efficient and provide a less cumbersome way of evaluating everything, we do wish to find an answer to these questions and we don't want to keep asking the same questions over and over again.

Other comments from committee members? Yes?

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MS. WARMON: Sue Warmon, patient representative. As a recovered TMJ patient, I would be extremely hard-pressed to bring a member of my family to face one of these procedures without some type of long-term study that would give me the information on the safety and the effectiveness of this product.

I don't think three years is enough to satisfy me. However, I do recognize the fact that there are TMJ patients out there who will grasp at anything to relieve their problems. I recently read an article in a local paper of a woman who had twelve separate surgeries and still was having problems.

So you have to understand that a TMJ patient, when faced with the tremendous pain and disability that they live with every day will go to any means and any doctor who promises to give them some relief.

I would hate to see these patients end up in the hands of someone who didn't have the skills to use this product compounded with no longitudinal data to support it.

DR. HEFFEZ: As a consumer, though, would you--I am trying to be as objective as possible--as a consumer who would be in tremendous pain, seeking some avenue of resolving your pain, do you think it is appropriate, at that time, to undergo an operation with a device that may

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not have the scientific background that you would like to have?

MS. WARMON: That is a real hard situation to answer. I know when I was faced with my surgery, there was a long process of thought that went into it before I agreed to it. I have no implants. I think I would really want to know what the long-term effect of something foreign in my body would be. I think I would look at other means before I would do that.

MS. MORRIS: Could I please answer the same question. Lynn Morris. I am the consumer representative. I truly understand that question and it is a struggle. It is a struggle in my mind, particularly after hearing everything today. But I think we need to be incredibly aware of the panel's responsibility.

As I understand it, and please correct me if I am wrong, it is not the panel's responsibility to do this balance that we are seeking. It is the panel's responsibility to insure safety and efficacy with scientific data.

DR. HEFFEZ: You are correct in knowing what the panel's goal is, but we have to evaluate everything in a very objective fashion and ask all the questions that we feel are related to the issue at hand.

Other questions?

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MR. ALBRECHT: Doug Albrecht, TMJ Implants. I would like to respond to the comments regarding the size of the studies and the validity of the studies that we presented, or the validity of the data that we presented.

As I stated before, for preamendment devices, the FDA has given us the opportunity to provide significant human experience as well as any controlled clinical trials and any case histories presented by physicians. I believe we have done that.

In our registry, granted, the follow up is not ideal, but if you look at the numbers that are in each follow-up period and the number of devices and number of patients, we are looking at 1300 partial-joint patients in almost 2000 devices, that we have available some data out to five years.

I can't imagine that all these patients are the good patients and we have not seen any of the bad patients. I am sure there is a mix in there. I cannot separate them out at this point. Regardless, the numbers speak for themselves. Out to 24 months, we have 286 patients reporting a pain level of 2.1. At 36 months, we have 166 patients reporting a pain level of 1.9.

We are doing the prospective study and we are correlating that with what we have seen, given us an idea of what we would expect to see in a prospective study.

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So we are doing the prospective study. We correlate that with what we see in the registry right now and the numbers are pretty much identical.

You overlay the grafts and the data, one on top of the other, they are almost exactly the same. Granted, we don't have the numbers long-term yet, but it would show me that the same trends are occurring. We may not have reached statistical significant, but I think there is clinical significance there that the device truly does work.

If we were to see some problems with the device, we would not see pain levels below 2.0 at three, four and five years from a group of 1900 patients.

Also, provided in the registry with regard to safety was our retrospective study in which we did look at safety issues, and we came up with only, out of over 300 patients, three device-relate issues that the physicians had indicated in that retrospective study.

If you look at our MDRs, we have less than a 0.2 percent MDR incident rate from every device that we manufacture. With regard to fossa fracture, we don't have any fractures from a partial joint alone. All fractures were with total joints and most of them with trauma associated with the fracture.

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So, with regard to the numbers; yes, I would agree with you. The numbers, long term, are not there yet. But if you look at all the data put together, I believe everything looked at together would provide reasonable assurance that the device is safe and effective at this point.

DR. HEFFEZ: I think the two biggest concerns that are coming out in the discussion are the evaluation of the failures and the longevity of the existing data in the prospective study. Those are the two issues, I think, that people are trying to grasp.

Dr. Patters?

DR. PATTERS: Two points. I may be mistaken, but in my previous experience on the panel, does not allow industry, the sponsor, at this point, to volunteer information when not sought by the chair. Am I wrong, Mr. Ulatowski, that this is a committee discussion?

MR. ULATOWSKI: That is correct. It is per the discretion of the chair to recognize any person at this time. But it primarily a panel discussion at this time.

DR. PATTERS: My second point is--

DR. HEFFEZ: I just want to say that I do feel that it is important, to try to come to an answer, to have industry give that data.

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DR. PATTERS: My second point is that I have no doubt that some patients have benefitted enormously from this device, but there appear to be some patients that have been injured by the device. I shouldn't say--they have been injured. Whether it is the device that injured them or the surgeon that injured them remains to be known.

But, certainly, we cannot discount that there are people here today who claim to have been injured. We really don't know as to what injured them. But that data needs to be available and I believe the prospective study has the best opportunity to provide it.

DR. HEFFEZ: Any other comments from the committee members? At this point in time, I would like to ask the sponsor to have an opportunity to make any final comments regarding the PMA. This will precede the voting regarding this PMA.

DR. CHRISTENSEN: I am not sure what else to comment about that we haven't commented about this time or last time. But, having been around surgery of this joint for fifty years, I can tell you that I know for sure this implant works. Some of you may not have that feeling, but I wish you could go into a surgery and watch these surgeons do it, and then watch these patients afterwards.

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We don't see patients being reoperated as--I forgot your name, but the person on the panel here that is a patient. I don't expect to. I didn't see it in my practice and I don't expect to see it in others providing it is done at the right time with the right disease.

So, having said that, we can try to compile data forever. We have got a lot of data. I don't know whether you have got it all. We have got an awful lot of data. I tell you--you may say, well, it is not structured just this way. Being an adjunct professor in bioengineering down at Clemson University, I know what studies are like.

But I also know that this is a preamendement device and if you look back at the hips and the knees, and so forth, some of them got through with 50 patients. One paper had no engineering. So I am saying that where we are, we have come a long way

I tell you, I am confident enough, myself, to have that implant put in me or my wife or my children--I have got ten children so I speak that with some trepidation--if that were the case. But I would have no problem putting this device in those children, or putting it in me.

MR. ROSEN: I am David Rosen. I am outside counsel to the company. I am also a former FDA employee.

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I just have a couple of other points I would like to make.

First of all, the prospective study is ongoing. It goes out to five years. The company has committed to completing that study and to appropriately monitor that study and to comply with our reporting requirements. So the company will see any additional adverse-event data and is under an obligation to report such data to the agency under strict reporting requirements.

Second, there are procedures in place for the company to review explanted devices so they can see what is going on with the explants. And they have also made arrangements with physicians to look at the condylar portions of those bones, if they from a partial to a total. They can examine those if they go back into the joints, and the company would certainly commit to have procedures in place to look at the condyles when additional surgeries are going into that joint.

I think you have heard a significant number of the arguments with respect to the totality of the data that are here. It is consistent with the standards that this committee and that the agency has used in approving other TMJ implant types of devices.

I think if you look at the totality of the data that was used to approve a previous device that it would

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be consistent with the data that has been presented here today. Lastly, the company does have this ongoing obligation to monitor adverse events whether the products are through the registry. As they become aware of those types of things, they have an obligation to investigate and to report those things if there is an increased trend in adverse device events or defects that are associated with the device.

Thank you.

DR. HEFFEZ: At this time, I will ask all industry representatives if they could leave that area. I would appreciate it.

I would like to ask if the industry representative has any comments on the panel regarding--Floyd?

MR. LARSON: Just one comment about the numbers. There is a lot of concern about the numbers, especially as the data are stratified. If you look at the protocol, the sample size that was calculated for the study was not based on stratification to those specific indications.

So question 2 is really dealing with indications that just were part of the "or" list of inclusion criteria. So, as I read the protocol, there wasn't any intention that each of those be indicated separately. So that is where the numbers look back when you look at them

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that way, but I think if you have a more general indication, obviously, the numbers still are not wonderful, but at least they are better than what they looked like when everything was stratified down so deeply.

That is just a comment on the protocol and on the numbers and how it relates to question 2 in particular.

DR. HEFFEZ: But regardless of whether they were stratified, they still had only data, really, up to six months, basically.

MR. LARSON: Right. It was about six months, was the 70 or 75 percent, not three months. Yes.

DR. HEFFEZ: At this time, I will ask Ms. Scott to read panel recommendations, options for the premarket approval applications.

MS. SCOTT: The Medical Device Amendments to the Federal Food, Drug and Cosmetic Act require that the Food and drug Administration obtain a recommendation from an outside expert advisory panel on designated medical device premarket approval applications that are filed with the agency.

The PMA, or premarket approval application, must stand on its own merits and your recommendation must be supported by safety and effectiveness data in the

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application or by applicably, publicly available, information. Safety, again, is defined in the Act as reasonable assurance based on valid scientific evidence that the probable benefits to health under the conditions of use outweigh any probable risk.

Effectiveness is defined as reasonable assurance that, in a significant portion of the population, the use of the device for its intended uses and conditions of use, when labeled, will provide clinically significant results.

Your recommendation options for the vote are as follows; approval. Approval; there are no conditions attached. Agency action; if the agency agrees with the panel recommendation, an approval letter will be sent to the applicant. The second option for the vote is approval with conditions. Under this particular option, you may recommend that the PMA be found approvable subject to specified conditions such as resolution of clearly identified deficiencies which have been cited by you or by FDA staff.

Prior to voting, all of the conditions are discussed by the panel and listed by the panel chair. You may specify what type of follow up to the applicant's response to the conditions of your approvable recommendation you want; for example, FDA follow up or

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panel follow up. Panel follow up is usually done through homework assignments to the primary reviewers of the application or to other specified members of the panel. A formal discussion of the application at a future panel meeting is not usually held.

If you recommend postapproval requirements to be imposed as a condition of approval, then your recommendation should address the following points; the purpose of the requirement, the number of subjects to be evaluated, and the reports that should be required to be submitted. Agency action; if FDA agrees with the panel recommendation, an "approvable with conditions" letter will be sent.

The third option is not approvable. Of the five reasons that the Act specifies for denial of approval, the following three reasons are applicable to panel deliberations. The data do not provide reasonable assurance that the device is safe under the conditions of use prescribed, recommended or suggested in the proposed labeling; reasonable assurance has not been given that the device is effective under the conditions of use prescribed, recommended or suggested in the labeling; and, lastly, based on a fair evaluation of all the material facts in your discussions, you believe the proposed labeling to be false or misleading.

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If you recommend that the application is not approvable for any of these stated reasons, then we ask that you identify the measures that you think are necessary for the application to be placed in an approvable form. Agency action; if FDA agrees with the panel's "not approvable recommendation," we will not send a "not approvable" letter. This is not a final agency action on the PMA.

The applicant has the opportunity to amend the PMA to supply the requested information. The panel recommendation will be reviewed by the panel at a future meeting unless the panel requests otherwise.

The last option is tabling. In rare circumstances, the panel may decide to table an application. Tabling an application does not give specific guidance from the panel to FDA or the applicant, thereby creating ambiguity and delay in the process of the application. Therefore, we discourage tabling of an application.

The panel should consider a nonapprovable or approvable-with-conditions recommendation that gives clearly described corrective steps. If the panel does vote to table a PMA, the panel will be asked to describe which information is missing and what prevents an alternative recommendation.

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Following the voting, the chair will ask each panel member to present a brief statement outlining the reasons for their vote.

DR. HEFFEZ: At this time, I would like to entertain a motion to proceed with the PMA. I am looking for a motion from the panel regarding this PMA. If one of the primary reviewers of this PMA--maybe they can assist us with a motion. Dr. Burton?

DR. BURTON: Richard Burton, University of Iowa. I move that it be placed in a not-approved status due to inconclusive safety and efficacy with the return to the company that, with completion of the existing IDE to completion with an adequate retention of the patient population would then allow return to the panel for approval.

DR. HEFFEZ: Any panel members wish to second this?

DR. BESSER: Mark Besser. I will second.

DR. HEFFEZ: Any further discussion? Dr. Patters?

DR. PATTERS: Question to FDA. I somehow missed, or failed to understand, why the device is off the market at present. Could you elaborate on that?

DR. HEFFEZ: Mr. Ulatowski?

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MR. ULATOWSKI: Tim Ulatowski. Well, the term "off the market" isn't entirely accurate in a regulatory sense. The investigational program continues as a possibility for availability, albeit under investigational limitations. We have entertained, from time to time, requests for expansion of that investigation, given a firm justification and a good idea of what number of investigators are requested, and so on and so forth.

So it is certainly not commercially available because it is not approved, but the investigational program is still a viable situation with the product.

DR. PATTERS: Do I understand, then, it was withdrawn? It was commercially available and was withdrawn?

MR. ULATOWSKI: Once the PMAs were required, the product either had to be approved--when the 515(b) PMA requirement went into effect, you either had to have an IDE or some other authorization for distribution. So that is the only authorization available for these products at this point in time until they are otherwise approved.

DR. PATTERS: Thank you.

DR. HEFFEZ: Any further discussion? Dr. Besser?

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DR. BESSER: Mark Besser. In addition to the completion of the clinical trial, I would like to see some further preclinical testing, specifically fatigue analysis with a higher load; also, a more realistic, I guess, prosthesis underlying the substrate interface model, not the total contact embedded right now--I think it is some synthetic acrylic that was sort of embedded in so you had a total contact underneath the prosthesis.

But that is not, in fact, situation when the prosthesis is in the patient anchored with screws on the irregular substrate which was their former fossa.

DR. HEFFEZ: This is for both static and--

DR. BESSER: This is for the fatigue analysis and for the yield strength. I would like to see both of those. And some either retesting at higher loads or appropriate limitation as far as indications for use, especially since the data presented indicate that TMJ loads of 75 to 100 pounds are not uncommon, even if not the average for individuals with temporomandibular-joint disorder.

DR. HEFFEZ: Any other further discussion? Dr. Hewlett?

DR. HEWLETT: Edmond Hewlett. Just a little guidance from the chair, I guess. There are still remaining questions about the actual indications as far

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as how specific the indication of internal derangement should be. How should we address that? Is that addressed during discussion now or as an amendment to the motion?

DR. HEFFEZ: The PMA would be approved or disapproved. Under those circumstances, you would approve it but there would be certain conditions and we would then start talking about the specific indications and conditions. So that would be relevant if it was approved.

Am I right?

MR. ULATOWSKI: You are making a motion. I have heard a motion to disapprove. But you can't divorce the indications for use from your thought process here. You have made a motion, I suppose, and correct me if I am wrong, on the listing of indications in the data in hand. You can continue discussion along those lines and have an outcome.

However, you may also choose to come back to reconsider subsets of indications or other situations that may be more acceptable at this point in time in terms of the status of the product. So you have to consider what is given to you in the labeling.

DR. HEFFEZ: So I think it is best to revisit the motion by Dr. Burton and ask him to respecify his

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motion whether the disapproval was for the indications as they were listed.

MS. SCOTT: Can I make a clarification just before we move on that the panel's recommendation is not approvable, just in terms of the regulatory sense, we are very sensitive to the actual language that is used. The panel's recommendation is not approvable and the agency makes the decision of agreement with that to either disapprove or to make another finding.

So the correct terminology would be not approvable in terms of the motion and in terms of the vote.

DR. BURTON: Richard Burton. I stand corrected. It is based upon the existing indications as they have been formulated and presented thus far which, obviously, includes internal derangement as one of the primary indications which, at least in the datasets that were presented to us, represented greater than 80 percent of the patients for whom it had been indicated and utilized.

DR. HEFFEZ: So, could you restate the whole motion?

DR. BURTON: I move a recommendation that it be disapprovable--

DR. HEFFEZ: Not approvable.

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DR. BURTON: Not approvable; pardon me--not approvable based upon the lack of substantive safety and efficacy data for the given surgical indications as seen currently in the PMA. It could be reconsidered for approval with the completion of the existing IDE to term with adequate retention of the dataset, the following of all explanted devices and further clarification of the surgical indication and to--sorry.

DR. HEFFEZ: The motion should just stand alone and then, after that, we can qualify the motion to see what industry could do to reach a higher level of--to get an approval status.

DR. BURTON: I'm very sorry. I will shorten it back to, be not approvable based upon the lack of adequate safety and efficacy data as presented.

DR. HEFFEZ: With the indications.

DR. BURTON: Yes; with the indications as presented in the PMA.

DR. HEFFEZ: Dr. Besser, do you still second that motion?

DR. BESSER: Yes; I still second that motion.

DR. HEFFEZ: Is there any further discussion? Mr. Larson?

MR. LARSON: Just a thought. Having been recovering from surgery at the time of the last meeting

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and, therefore, not being here for that meeting, I am not sure whether this is appropriate but should we consider whether we are holding this device to a higher standard than has been done previously for similar devices, number one. Number two, are we being influenced substantially in terms of the interpretation of the clinical data by the very, very detailed list of indications and would both a less specific indication and maybe limitation to those III, IV and V, combined with a consideration of the level of support that has been required in the past, change our thinking on this?

DR. HEFFEZ: I think that, when we looked at the indications, we looked, basically, over approximately 80 percent was for one category; that was internal derangements.

MR. LARSON: If that was limited to III, IV and IV, you mean? Just III, IV and V?

DR. HEFFEZ: When we have understood the definition of inflammatory arthritis, meaning that that also included early internal derangements, it made it so fuzzy that, and correct me if I am not right, but the understanding was that this was referring to internal derangement, all categories. It wasn't clear.

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MR. LARSON: Would clarification by industry help that situation? Would limitation, I guess, help that situation?

DR. HEFFEZ: I will ask Dr. Burton if he feels comfortable with his motion or whether he wishes to withdraw it.

DR. BURTON: I still would feel that I am comfortable with the motion. I was present at the last meeting and I don't really feel that there is a change in standard from a clinical call of that. The reason that I feel that was that the other types of products that we have looked at have been oriented more toward a salvage or reconstructive approach whereas this, at least with the indications as they are currently presented, is indicated more as a first-line or an early treatment as opposed to the other.

Certainly, their support for that stems from the fact that they feel that that is an indicated type of procedure for the indications as--like I said, I guess I don't feel that there is a different standard because I think we are dealing with very, very different indications. My motion is based upon the indications as they have been presented and been followed within this PMA.

DR. HEFFEZ: Question?

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MR. LARSON: I do understand that point and I guess I am thinking salvage as well. If the sponsor was willing to rather dramatically change that approach, would that make a difference in the recommendations of this panel in terms of that early-intervention attitude?

DR. BURTON: I guess that is a hypothetical case, but I am not sure that we can really consider something that would be a relatively major change in what has been presented to us, consistently presented both in the last presentation, the last panel meeting, and what we have seen here thus far today.

MR. ULATOWSKI: Can I make a point?

DR. HEFFEZ: Yes. Mr. Ulatowski?

MR. ULATOWSKI: Mr. Ulatowski. I am looking at our voting expert in the audience. The question I would have is, with a nonapprovable on the table, considering the indications as listed, that is one sort of action. Another sort of action I seem to be hearing as an option or what other people may be thinking about is approvable, to entertain an approvable with the conditions of modifications to the labeling, or some such actions, which might be more amenable to some.

So we can consider both avenues, I suppose, but that is how I see it now.

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MR. DEMIAN: Haney Demian. I am exec sec for the Orthopedic and Rehabilitation Devices Panel. I think that you would have to first vote on this particular motion or have him withdraw it. Then you could go to another main motion of approvable with conditions, and state your conditions, that the indications for use are a salvage procedure and not this first-line sort of prevention.

So it is really up to the person that made the motion either to withdraw it, and if he doesn't wish to withdraw it, since you already have a second on the table, you can vote that down and see if the votes carry.

If it does carry the not approvable, then you can state how the sponsor can place it into approvable form, meaning that they would have to narrow their indication for use down. Does that clarify it?

DR. HEFFEZ: Yes; thank you.

Any other discussion?

DR. BESSER: Mark Besser. Can I have a definition of "salvage?"

DR. HEFFEZ: I could provide a definition from a surgeon's point of view, simply that the patient is last resort basically, that the patient, perhaps, is in terrible pain, there are no other avenues to explore and the question is whether the patient has to remain in pain

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or whether you will salvage the case by performing an operation, with this device, not having all the--

DR. BESSER: I understand that part. I am wondering whether there are objective criteria for a patient who has exhausted all other options. I am uncomfortable with my level of understanding of what that would entail, approving this as a salvage device.

DR. HEFFEZ: Since we have a motion of the floor and it has been seconded, we can deal with that issue following the voting of this motion. Okay? Mr. Ulatowski?

MR. ULATOWSKI: Looking back at the labeling for the Fossa-Eminence, I believe it is not labeled as a primary--if we could turn to that particular labeling, just make it clear to everyone.

DR. HEFFEZ: I will permit industry to make a brief statement to that effect, if you wish. Go to the podium, please.

DR. ROSEN: David Rosen. The indications statement, we have added a section to the warning which is bold. It says that, "This device is not intended as primary intervention in the case of internal derangement." That is in the proposed labeling that is front of the panel today. You can see we also have

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statements, "not responsive to other modalities of treatment."

In the design of this labeling, we were trying to fashion it as not being primary intervention, as being a salvage type of therapy. Thank you.

DR. HEFFEZ: Dr. Patters?

DR. PATTERS: Mark Patters. I would like to ask the chair to call the question. If this motion doesn't pass, then we can consider other options.

DR. HEFFEZ: I would call the question. I would like to go around the table for the vote. I would like to start with voting members. Just to let everybody know, those voting members with be Dr. Anseth, Dr. Hewlett, Dr. Patters, Dr. Janosky, Dr. Bertrand, Dr. Burton, Dr. Stephens, Dr. Besser and Dr. Cochran. The chair will only vote to break a tie.

So I would like to go around the table starting with Dr. Besser.

DR. PATTERS: Just to clarify, we are voting on calling the question?

DR. HEFFEZ: Hold on just for one moment, please. One correction. Dr. Cochran is not available for vote. Dr. Besser?

DR. BESSER: The same question; we are voting on the motion to make it not approvable.

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DR. HEFFEZ: That's correct, with the indications that are outlined.

DR. BESSER: I vote in favor of the motion.

DR. HEFFEZ: Following your vote, you can also state, at the same time, the reasons for that, if you can, Dr. Besser.

DR. BESSER: My reasons are as I stated earlier. I don't believe that the preclinical data adequately support safety and the clinical data, to date, also do not support safety and efficacy for the product yet.

DR. HEFFEZ: Dr. Bertrand?

DR. BERTRAND: Peter Bertrand. I vote not to approve based on the inclusions of internal derangements as part of the initial surgical procedures.

DR. HEFFEZ: So you vote in favor of the motion.

DR. BERTRAND: Right.

DR. HEFFEZ: Reasons? Would you like to state a reason?

DR. BERTRAND: I just stated the inclusion of internal derangements as an initial surgical procedure.

DR. HEFFEZ: Dr. Patters?

DR. PATTERS: I voted in favor of the motion and I feel it is not approvable at this time and that approval awaits completion of the prospective study.

DR. HEFFEZ: Dr. Janosky?

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DR. JANOSKY: I am in agreement with the motion and the data for safety and effectiveness are insufficient at this time.

DR. HEFFEZ: Dr. Stephens?

DR. STEPHENS: Willie Stephens. I vote for the motion. I believe that the safety and efficacy of the procedure of the device has not been established at this time.

DR. HEFFEZ: Dr. Burton?

DR. BESSER: I vote in favor of the motion and, as the maker of the motion, I think my reason has been previously stated.

DR. HEFFEZ: Dr. Hewlett?

DR. HEWLETT: I vote in favor of the motion citing inadequate safety and efficacy data from a controlled prospective trial.

DR. HEFFEZ: Dr. Anseth?

DR. ANSETH: I vote in favor of the motion, lack of substantive safety and efficacy data in the clinical set.

DR. HEFFEZ: As you know, if the recommendation is not approvable, then we need to identify some measures that we feel would be necessary to render this application approvable. So can we, at this time--we have mentioned a few and I am going to say them to be

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expedient. If there are others, or if you need to qualify what I say, please, committee members, feel free to speak up.

One item was that higher loads should be used in the fatigue analysis. Secondly, that there was some concern about testing for yield strength and fatigue analysis and the fact that the implant was placed against a substrate with multiple points of contact which may not correlate to the clinical situation.

We discussed the clinical device study protocol should clarify the inclusion criteria, clarify and define the inclusion criteria. It should clarify the specific radiographic means of evaluation of radiographs and should clarify the definition of adverse outcomes.

I will ask the committee to identify any other measures that would help or assist in rendering this PMA approvable. I should add that the data that is coming from the prospective study should make every attempt to evaluate those failures and those patients who do not follow through with a complete examination.

Do I have any other measures that the committee members feel that should be included? Mr. Larson?

MR. LARSON: Only reflecting what I think I heard earlier, did I hear anything in this discussion just now about labeling, about indications?

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DR. HEFFEZ: No.

MR. LARSON: I think that was one of the major issues as well, so I think that should be at least addressed.

DR. HEFFEZ: So we will add that the company should look carefully at the indications. The indications as they are stated seem to show some overlap, perhaps are poorly defined. If those can be more clearly defined, that would assist in rendering the PMA approvable.

Any other recommendations? Dr. Cochran?

DR. COCHRAN: Sort of as a follow up to that, we didn't hear anything, in the statistical review, about power analysis of any sort. I think if you are going to try to clarify the indications, you are going to want to have some sort of statistical input as to power analysis for indications.

DR. HEFFEZ: Could you define better for us what you mean by power analysis?

DR. COCHRAN: I would refer to the statistician for that.

DR. JANOSKY: I have in front of me this clinical study protocol, TMJ96-001. My understanding is that that is the protocol that they have started and need to continue. If you look through there, the issue is

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presented in terms of sample-size estimation and most of those issues that we are talking about. So I don't know if the data were available and we just weren't given the data or it is just not collected yet.

DR. HEFFEZ: Okay. Any other measures that need to be identified? Dr. Hewlett?

DR. HEWLETT: If I could just clarify, I think, the comment about the evaluation radiographs. It was to the extent that it is standardized in such a manner to facilitate the monitoring of condyle changes over time.

DR. HEFFEZ: Correct. Any other comments? So the motion passes. Do we need to vote on the measures? No? Okay. At this point in time, I want to thank everyone for their input, both from industry and panel members, and ask for a short break for ten minutes.

[Break.]

DR. HEFFEZ: We will ask Mr. Ulatowski to present on behalf of the FDA.

Discussion of Labeling for a Total Temporomandibular Joint

FDA Presentation

MR. ULATOWSKI: For closing today, we want to take just a few moments of your time, hopefully just a few moments, but that depends on you as much as me, for some comment, if any, on some aspects of the proposed

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labeling for the total joint, the metal-on-metal, total joint from TMJ Implants, Inc.

We are on a different track with the total joint. We are seeking only comments on labeling. Let me just preface by saying you heard some discussion this morning about the fatigue tests and the loading and the safety factors and the apparent low fatigue strength, perceived low fatigue strength.

We have a similar concern and we want to address that in the labeling for the total. We have been working with the company to provide some information for the surgeon to help him or her properly select patients for the total joint in view of the engineering data and results that we have.

[Slide.]

So if you examine just a couple of slides that I have in regard to those elements in the labeling that we have worked with them on, I would like to see if you have any other--or your reaction and any other comments to these in terms of contraindications as stated, the ability to exert significant postop masticatory muscle forces, or uncontrollable masticatory muscle hyperfunction, clenching or grinding, which may lead to overload and fracture of the device, or loosening of the screws.

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This is a contraindication, a contraindication, for the total joint.

[Slide.]

Precautions; dynamic fatigue tests were conducted on the TMJ Implant's metal-on-metal total joint replacement system with the force applied vertically to the device. No failures occurred at or below 130 pounds. Physicians should carefully consider the results of these fatigue tests when considering patients with particular anatomical considerations or with high-normal to unusually high masticatory forces.

[Slide.]

We also had the inclusion of some not only observable adverse events during the course of the investigation but also those sorts of recurring adverse events that one may typically see in implant surgery. We made suggestions regarding addition of those types of adverse events.

So, in brief, there you have it in regard to our response to the fatigue-test data and directions to the surgeon for proper selection and advice for selection of patients, given the fatigue-test results.

I ask simply if there are any comments or observations regarding what we have stated in the proposed labeling.

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DR. BURTON: Richard Burton. Mr. Ulatowski, one thing I was not clear about before--

MR. ULATOWSKI: Angela and Susan; could you join me?

DR. BURTON: I'm sorry; what is the--both as labeling exists, what is the obligation of the implanting surgeon and the company in recording adverse events or explanation. I guess that is one of the questions we have had going along, is what happens to these and why does it seem that you get what certainly is anecdotal reports from various groups that are there but we don't ever see those.

So, is there any way within the labeling structure, or whatever, that we can have it set out--I can't say making it mandatory, but that that is somehow encouraged within that such that when adverse events or explanation might occur, that the mechanism is better defined?

MR. ULATOWSKI: I am open to suggestions but, under the investigational regulations, there are reporting expectations and those occurrences and observations are under tighter control during the investigational stage. Once a product is approved, made commercially available, there are physician and

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healthcare facility reporting requirements that are in place.

Do those requirements play out in terms of the types of reports we ought to be seeing? No. The reporting system is there but we don't often see all the reports that should have been submitted. That is a recurring deficiency with manufacturers and with the physicians.

So the mechanisms are there. To require additional reporting mechanisms I think is a bit overkill with this type of problem that you are describing.

DR. BURTON: Thank you. I am sure, actually, that most of the problem lies with the physician and not the company.

MR. ULATOWSKI: Yes; we can regulate up to the top of our head, require this and that. It doesn't necessarily mean people will execute those regulations as expected. We have not seen that execution as expected with all the regulations we have.

DR. BURTON: Thank you.

DR. HEFFEZ: Any other questions for Mr. Ulatowski? Thank you very much.

MR. ULATOWSKI: Thank you.

DR. HEFFEZ: I would like to ask industry at this time to present.

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Industry Presentation

DR. ROSEN: David Rosen on behalf of the company. All I want to say is that we worked very closely with the division to fashion this labeling. We believe that it is appropriate labeling. It conveys the right message. It is consistent with the labeling that is with the approved product. It is modeled directly after the labeling with the approve product and it is what we consider to be in the mode of salvage therapy.

So thank you.

Open Committee Discussion

DR. HEFFEZ: We are just going to take a two-minute respiratory break while I wait for Pam Scott to come back with some of the actual labeling documents because I don't feel that everybody has it in front of them; is that correct? So, if you would wait two minutes. If I could have one to read out to them.

You have had an opportunity to review this before. Are there any comments regarding it? One comment would be the use of the screws, only those screws for the system should be utilized. I am asking industry if they can--you think on the Warnings, No. 4, if longer screws are necessary, do you feel that placing--in the document indicating specifically only those screws that come with the kit should be utilized.

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My point is that there should be, in the Warning, that you should not use screws from other kits. I am saying that that should be inside the Warning.

MR. DURNELL: This is John Durnell. I believe it is in there.

DR. HEFFEZ: Is it located in the Warning Section? I don't believe so. Could you please come to the podium and identify yourself and then make your statement?

DR. CHRISTENSEN: Bob Christensen. That has been in the Physician Guide or the Package Insert for the past ten or twelve years so I am sure it hasn't moved. It will be in there somewhere.

DR. HEFFEZ: Yes; but my point is that is should appear under the Warnings.

DR. CHRISTENSEN: It will be under Warning, but maybe not in the thing you are looking at.

DR. HEFFEZ: It is located under Precautions. Any comments from the committee? Dr. Patters?

DR. PATTERS: Mark Patters. Does FDA want a motion here?

DR. HEFFEZ: Yes.

MR. ULATOWSKI: No.

DR. HEFFEZ: Oh; it is just discussion and comments.

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MR. ULATOWSKI: Discussion and we are out of here.

DR. PATTERS: My comments are I strongly endorse the intended use as described in the document as negotiated between FDA and the sponsor.

DR. HEFFEZ: Any other comments from panel members?

DR. BESSER: Mark Besser. My only other comment has to do with the sort of nonspecified nature of uncontrollable masticatory muscle hyperfunction and then, later, when patients present with particular anatomical considerations are high-normal to unusually high masticatory forces.

I would ask whether clinicians at the table are able to ascertain this of their patients presurgery?

DR. HEFFEZ: The specific question is--

DR. BESSER: Is whether one can know presurgery whether someone has unusually high masticatory forces and how high is unusually high, what are those numbers? Are there any numbers on that at all, or is that just a clinical judgement.

DR. HEFFEZ: At this point in time, it is a clinical judgement. There is no routine testing of masticatory muscle forces prior to placement of the implants, or devices.

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Any other comments? With the failure to hear any other comments, I will move to closing comments. I would like to thank the members of the Food and Drug Administration, all the committee members, members from industry, many people who work behind the scenes whom I do not know their names, but without whom we would not be here.

I would specifically like to thank Ms. Scott, who has been very helpful in directing the meeting and keeping us on line. I hope that industry leaves here with some good recommendations so that, when it is brought again back to this panel, it will be easier to make it approvable, the PMA approvable.

At this point in time, I will turn the microphone to Ms. Pamela Scott.

MS. SCOTT: I would like to thank all of the panel members, consultants, representatives here today for attending the meeting and for your input into the issues at hand. I would like to thank you for your hard work.

I would also like to ask, just before we close, those who are voting members--Dr. Heffez, Dr. Anseth, Dr. Hewlett, Dr. Patters, Dr. Janosky--did I cover everyone? I am not sure if you all brought your calendars with you, because I was going to see if we could--maybe we can do

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it by E-mail. I just want to see if there are particular dates that would be good to set up our tentative meeting dates for the Year 2001.

If you prefer, I can do it by contacting--okay; we will do it that way. Then, again, I would like to thank you for everyone's participation. I would like to thank all of FDA staff that was supportive for putting this meeting together. If there are no further comments, the meeting is adjourned.

[Whereupon, at 5:05 p.m., the meeting was adjourned.]