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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
 FOOD AND DRUG ADMINISTRATION  
 CENTER FOR DEVICES AND RADIOLOGICAL HEALTH  
 OFFICE OF DEVICE EVALUATION

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**MEETING OF THE DENTAL PRODUCTS PANEL**

**OPEN SESSION - VOLUME II**

Tuesday, May 11, 1999

8:00 a.m.

Holiday Inn Gaithersburg  
 Walker Whetstone Room  
 Two Montgomery Village  
 Gaithersburg, Maryland

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Pamela D. Scott, Executive Secretary

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Mark Patters, DDS, Ph.D.

CONSUMER REPRESENTATIVE

Donald S. Altman, DDS

INDUSTRY REPRESENTATIVE

Alton Floyd, Ph.D.

PATIENT REPRESENTATIVE

Theresa Cowley

TEMPORARY VOTING MEMBERS

Peter Bertrand, DDS  
Richard Burton, DDS  
Gilbert Gonzales, MD  
Leslie Heffez, DMD, MS  
Stephen Li, Ph.D.  
E. Diane Rekow, DDS  
Harry Skinner, MD  
Willie Stephens, DDS

FDA

Timothy Ulatowski  
Dr. Susan Runner  
Angela Blackwell  
Dr. R. Murty Ponnappalli

at

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P R O C E E D I N G S

**Welcome and Introductory Remarks**

MS. SCOTT: Good morning. Welcome to the Dental Products Panel Meeting.

My name is Pamela Scott. I am the Executive Secretary for the Dental Products Panel. Before we get started today, I would like to read into the record our conflict of interest statement for May 11, 1999.

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 financial interests reported by the committee participants.

The agency 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 an interest but no financial involvement in a firm at issue.

The agency has determined that Dr. Stephens may participate fully in all deliberations. In the event that

1 the discussions involve any other products or firms not  
2 already on the agenda for which an FDA participant has a  
3 financial interest, the participants should excuse him or  
4 herself from such involvement and the exclusion will be  
5 noted for the record.

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

11 Also, I would just like to read, again, the  
12 appointment to temporary voting status. Pursuant to the  
13 authority granted under the Medical Devices Advisory  
14 Committee charter, dated October 27, 1990, as amended  
15 April 20, 1995, I appoint the following people as voting  
16 members of the Dental Products Panel for this meeting on May  
17 10 and 11, 1999; Dr. Leslie Heffez, Dr. Diane Rekow, Dr.  
18 Peter Bertrand, Dr. Richard Burton, Dr. Willie Stephens, Dr.  
19 Steven Li, Dr. Harry Skinner, Dr. Gilbert Gonzales.

20 For the record, these people are special  
21 government employees and are consultants to this panel under  
22 the Medical Devices Advisory Committee. They have undergone  
23 customary conflict of interest review. They have reviewed  
24 the material to be considered at this meeting. Signed Dr.  
25 Elizabeth Jacobson, Acting Director, Center for Devices and

1 Radiological Health, May 6, 1999.

2 One last item. I just would like to reintroduce  
3 our panel members for today. The panel members are listed  
4 in the back of the agenda booklet that you received.

5 We have Dr. Janine Janosky who is acting as our  
6 chair today. She is an assistant professor with the  
7 University of Pittsburgh. We also have Dr. Mark Patters who  
8 is the Chairman of the Department of Periodontology at the  
9 College of Dentistry at the University of Tennessee. Our  
10 consumer representative is Dr. Donald Altman who is the  
11 Chief of the Office of Oral Health with the Arizona  
12 Department of Health Services.

13 Dr. Alton Floyd is our industry representative.  
14 He is the President of Trigon Technology in Edwardsburg,  
15 Michigan. Our patient representative is Ms. Theresa Cowley  
16 who is the President of the TMJ Association.

17 We also have with us today Dr. Peter Bertrand who  
18 is the Director of the Orofacial Pain Clinic and a Specialty  
19 Advisor for Oral Facial Pain with the National Naval Medical  
20 Center and Dr. Richard Burton who is an assistant professor  
21 of oral and maxillofacial surgery at the University of Iowa  
22 Hospitals and Clinics.

23 We have Gilbert Gonzales who is associate  
24 professor of neurology at the Memorial Sloan Kettering  
25 Cancer Center with Cornell University and Dr. Leslie Heffez

1 who is the professor and Department Head of oral and  
2 maxillofacial surgery at the University of Illinois at  
3 Chicago.

4 We also have Dr. Stephen Li who is a senior  
5 scientist with the Department of Biomechanics and  
6 Biomaterials at the Hospital for Special Surgery and Dr.  
7 Diane Rekow who is the Chairperson of the Department of  
8 Orthodontics at the University of Medicine and Dentistry of  
9 New Jersey.

10 We have Dr. Harry Skinner also with us today who  
11 is professor and Chair of the Department of Orthopedic  
12 Surgery with the University of California at Irvine. And we  
13 have Dr. Willie Stephens who is an associate surgeon for the  
14 Division of Maxillofacial Surgery at Brigham and Women's  
15 Hospital.

16 Again, our FDA participants for today are Mr.  
17 Timothy Ulatowski who is the Director of the Division of  
18 Dental, Infection Control and General Hospital Devices with  
19 the Office of Device Evaluation. We also have Dr. Susan  
20 Runner who is the Branch Chief for the Dental Devices Branch  
21 within the Division of Dental, Infection Control and General  
22 Hospital Devices.

23 We have Ms. Angela Blackwell who is a biomedical  
24 engineer also with the Dental Branch within the Division of  
25 Dental, Infection Control and General Hospital Devices and

1 Dr. Murty Ponnappalli who is a mathematical statistician with  
2 the Division of Biostatistics in the Office of Surveillance  
3 and Biometrics.

4 Thank you very much.

5 I will turn it back over to Dr. Janosky now.

6 **Open Public Hearing**

7 DR. JANOSKY: At this time I would like to open  
8 the public hearing. Are there any requests?

9 [No response.]

10 DR. JANOSKY: So, I am correct in assuming no one  
11 is requesting to speak during the open public hearing?

12 Okay. Given that the case, then, we will move on.

13 At issue today is a review of a premarket approval  
14 application by TMJ Implants, Incorporated.

15 First, we will have the industry presentation  
16 which is scheduled for one hour. Currently, I have 8:10, so  
17 it will go from 8:10 to--oh, excuse me, we do have letters,  
18 so let's continue then with the open public hearing.

19 We have two letters that were sent to the FDA  
20 which Ms. Scott will read into the record.

21 MS. SCOTT: A copy of these two letters are  
22 included in the folder that the panel received.

23 This was received by the Center and it states:  
24 "This brief document is in reference to the open public  
25 hearing testimony on temporomandibular joint prostheses. As

1 a surgeon who has devoted a significant percentage of my  
2 practice to the surgical management of organic  
3 temporomandibular joint disorders/diseases I can offer my  
4 humble opinion that one of the most successful and well-  
5 researched contributions to the surgical practice of  
6 rebuilding the severely diseased jaw joint has been the CAD-  
7 CAM technology to use a chrome cobalt implant to replace  
8 vital portions of the temporomandibular articulation.

9 "In my own experience the metal/metal (chrome-  
10 cobalt) custom TMJ prosthesis has been uniformly well  
11 tolerated by patients who have had multiple surgeries or  
12 arthroplasties with or without autogenous or other  
13 alloplastic devices to attempt to recreate a functioning jaw  
14 joint.

15 "The very nature of the custom joint eliminates  
16 attempting to modify autogenous or alloplastic (off the  
17 shelf) devices to fit a given patient. These implants  
18 simply are designed for the individual patient and must  
19 remain available to salvage the lives of patients who had  
20 lost jaw joint function for reasons of arthritis, ankylosis,  
21 trauma, or neoplastic disease.

22 "With the notable exception of the Christensen and  
23 custom-made total joint prosthetic devices, there simply is  
24 nothing available in the technical surgical marketplace to  
25 off the patient who has an "end-stage" jaw articulation.

1 Patients who have lost function and have severe pain  
2 syndromes can have a significant restoration of function and  
3 an amelioration of their pain by reconstructing their  
4 diseased jaw joints with the Christensen prosthesis.

5 "I am aware that the above information is  
6 anecdotal and my conclusions do represent the results of a  
7 formal scientific study. However, any hearing regarding the  
8 efficacy of a surgical device should at least reflect  
9 opinions of surgeons with some experience (in this case 30  
10 years) who must deal with the suffering of individual  
11 patients, not groups or populations in a laboratory  
12 environment. Both of these kinds of inquiry are necessarily  
13 important and each should have appropriate weight in any  
14 decision, which would change the availability of a surgical  
15 device.

16 "Kindest regards, Dr. Guy A. Catone, Associate  
17 Professor, Department of Surgery, Division of Oral and  
18 Maxillofacial Surgery, Allegheny University of the Health  
19 Sciences."

20 The second letter that we received that we were  
21 requested to read during the open public hearing is from Dr.  
22 William Buck. It reads as follows:

23 "This letter is for open public hearing testimony  
24 on temporomandibular joint prostheses. I have been exposed  
25 to the Christianson total and partial joint system for

1 approximately eleven years. The Christianson joint has had  
2 an excellent track record in a field of other total joints  
3 that have fallen out of favor because of chronic failure.

4 "I have used the Christianson total joint, partial  
5 joint, the stock joint, the custom made joint and the metal  
6 head to metal fossa joint with success. This procedure is  
7 always reserved to a last ditch effort to give the patient  
8 function of her jaw when all else has failed. It is used  
9 when a bone graft has failed and has no hope of future  
10 success. In my patients, there was no other alternative for  
11 them to have normal life function.

12 "The evidence is clear that the Christianson joint  
13 is proven successful over a period of greater than 25 years.  
14 Newer joints have come and gone, but the Christianson is a  
15 well proven device that is absolutely needed for severely  
16 damaged temporomandibular joint patients. There is no other  
17 reasonable alternative. Please let me know if I can answer  
18 any other questions."

19 Signed, Dr. William Buck.

20 Also, I would like to note that the Center did  
21 receive numerous other letters regarding this particular  
22 meeting, and if any of the panel members would like to see  
23 those letters, we have copies of those available. Some of  
24 them also have been copied for you and placed in your  
25 packet, but there is another stack that we have available

1 also. Those letters did not specifically request to be read  
2 into the record at the open public hearing, but they  
3 available if you would like to read them and if you would  
4 like to see them.

5 Thank you.

6 DR. JANOSKY: Are there any requests to speak  
7 during the open public hearing?

8 [No response.]

9 DR. JANOSKY: At this time, we will close the open  
10 public hearing.

11 It is my understanding that Dr. Runner has some  
12 comments for us before we move into the industry  
13 presentation.

14 DR. RUNNER: Good morning. Just a reminder from  
15 what we discussed yesterday, because of the terminology that  
16 is confusing with these devices, we have determined that TMJ  
17 implants will be the generic device type, TMJ Concepts is  
18 the device we considered yesterday, and the Christensen  
19 device is what we are discussing today, just to avoid  
20 confusion.

21 DR. JANOSKY: At this time, the industry  
22 presentation lasting for one hour. I have 8:20 on my watch,  
23 so until 9:20.

24 **Industry Presentation**

25 DR. CHRISTENSEN: I am Dr. Robert Christensen. I

1 do have financial interests in this company. I want to  
2 thank Dr. Runner and Dr. Janosky and Dr. Ulatowski, and all  
3 the panel members for this opportunity to come before you.

4 My beginning in oral surgery started about 50  
5 years ago, and that first 10 years was kind of an  
6 interesting time to do all sorts of surgery on that joint,  
7 from fracture repair, but also condylectomies and  
8 meniscectomies, and you name it.

9 During that time, I wrote several articles  
10 regarding arthroplasty of this joint, but about 1960, I  
11 realized that something better needed to happen, and I came  
12 up with the idea of replacing this joint, both in a partial  
13 way and in a total way, and began to see my patients do  
14 very, very well. As a matter of fact, a chapter written in  
15 a book called "Oral Implantology," which I wrote in 1967, I  
16 talked about the first five or six years of arthroplasty of  
17 this joint using this alloplast.

18 In that time, I had done about 60 partial joints  
19 and a number of total joints, and I talked about the 60  
20 partial joints as that I had not had to reoperate one of  
21 those during that period of time with the exception of one  
22 that overgrew bone.

23 I am not going to give you much of a story this  
24 morning because I have got a panel here that can do a better  
25 job than I can do, but I would like to read you part of a

1 couple letters that were sent to me at that time.

2 One was from the founder of arthroplasty of the  
3 hip. I think the doctors here of orthopedics would agree  
4 with this. It is from Dr. Otto Aufranc, and in May of '63  
5 said: "This is a real contribution to the art of surgery  
6 and the correction of disabled joints. I have no suggestion  
7 to add to this except to compliment you on your good work."

8 J. Vernon Luck, who the orthopedic hospital in Los  
9 Angeles is named after, in January of '64 said: "I learned  
10 a great deal about temporomandibular joint arthroplasty that  
11 I did not know before. This subject is dramatically  
12 presented in your film."

13 I think, having said that, I must say too that I  
14 feel the way the patient advocate groups do too. I have  
15 suffered with those people 50 years to see them get healed,  
16 and that is why I started to develop a technique that works.

17 I think as you see this information, you are going  
18 to see that there is some very good information along this  
19 line. Have we done everything? No, probably have not, but  
20 we have come a long way in the last 40 years.

21 I would like to introduce Mr. Jim Morgan.

22 MR. MORGAN: Thank you, Dr. Christensen.

23 [Slide.]

24 Good morning. My name is Jim Morgan. I am the  
25 Director of Quality Assurance and Regulatory Affairs for TMJ

1 Implants, Inc.

2           Before I get into my formal presentation, I would  
3 just like to echo some of the Dr. Christensen's words  
4 relative to what Dr. Zuckerman said yesterday along with Mr.  
5 Clark and Ms. Brown and Ms. Cowley.

6           We have heard and understand your concerns and we  
7 appreciate the need for prosthetic alternatives in the  
8 treatment of temporomandibular joint disease. Indeed, it  
9 was the recognition of this need which inspired Dr.  
10 Christensen's invention of the Fossa-Eminence and Condylar  
11 Prostheses in the 1960s.

12           It was his desire for a long-term solution that  
13 prompted the selection of the materials used in these  
14 prostheses, and while we don't claim to cure disease, you  
15 will see from our data that our devices can improve the  
16 patient's condition.

17           [Slide.]

18           Along with Dr. Christensen and our presenters and  
19 staff, we are grateful to have the opportunity to present  
20 our products to you today.

21           Permit me to introduce to you the remainder of our  
22 presenting staff: Dr. James Curry, clinician in private  
23 practice; Mr. Al Lippincott, biomaterials consultant for TMJ  
24 Implants, Inc.; Mr. Doug Albrecht, Manager of Clinical  
25 Affairs; Mr. John Durnell, Operations Manager; Ms. Candace

1 Cederman, regulatory consultant for TMJ Implants, Inc.; Dr.  
2 James Murphy, Professor of Biostatistics, University of  
3 Colorado Health Sciences Center, and consultant for TMJ  
4 Implants, Inc.; Dr. Subrata Saha, Professor, Department of  
5 Bioengineering, Clemson University, and consultant for TMJ  
6 Implants, Inc., and Dr. David Gerard, cell biologist and  
7 Director of Research, Department of Oral and Maxillofacial  
8 Surgery, University of Tennessee, and consultant for TMJ  
9 Implants, Inc.

10 [Slide.]

11 We are here today to consider the market  
12 continuation of a temporomandibular joint prostheses and  
13 accessories which have been in commercial distribution for  
14 over 35 years.

15 The TMJ Fossa-Eminence prosthesis may be implanted  
16 as a partial joint replacement, and the TMJ Fossa-Eminence  
17 prosthesis and TMJ Condylar prosthesis may be implanted  
18 together as a total joint replacement.

19 [Slide.]

20 We will demonstrate the safety and effectiveness  
21 of our devices when used in accordance with their labeling  
22 by introducing you to non-clinical test data presented by  
23 Mr. Al Lippincott, and clinical data presented by Mr. Doug  
24 Albrecht and Dr. James Curry.

25 I believe that Mr. Ulatowski has advised you

1 regarding valid scientific evidence. As you know, valid  
2 scientific evidence includes evidence from well-controlled  
3 investigations, partially controlled studies, studies and  
4 objective trials without matched controls, well-documented  
5 case histories conducted by qualified experts, and reports  
6 of significant human clinical experience with the marketed  
7 device. Our sources of data to be presented qualify as  
8 valid scientific evidence.

9 [Slide.]

10 The TMJ Fossa-Eminence Prosthesis may be indicated  
11 for use in cases of internal derangement, meniscal  
12 perforation, adhesions, or ankylosis of the  
13 temporomandibular joint where conservative therapies and  
14 treatment plans are not, or are no longer, indicated.

15 The TMJ Fossa-Eminence Prosthesis may be used in a  
16 partial joint replacement or with a TMJ Condylar Prosthesis  
17 in a total joint replacement procedure.

18 [Slide.]

19 The TMJ Condylar Prosthesis may be intended for us  
20 in conjunction with the TMJ Fossa-Eminence Prosthesis  
21 whenever total joint reconstruction is indicated or  
22 conservative therapies and treatment plans are not, or are  
23 no longer, indicated.

24 Such indications for total joint reconstruction  
25 could include correction of deficiencies in the natural

1 condyle in cases of serious adhesion, condylar destruction,  
2 ankylosis, avascular necrosis, intrinsic bone disease,  
3 congenital disease involving the temporomandibular joint,  
4 rheumatoid arthritis, osteoarthritis, foreign body giant  
5 cell reaction, previous failed implant surgery, or other  
6 pathology with resultant occlusal or function deficiency.

7 [Slide.]

8 The Fossa-Eminence and Condylar Prostheses are  
9 preamendment devices which have been manufactured and sold  
10 in commercial distribution since 1961 and 1965 respectively.

11 Our products are marketed in the United States,  
12 Canada, and the European Union, with a Notice of Compliance  
13 from Health Canada, and CE Marking Authorization from KEMA,  
14 a notified body in the European Union.

15 In addition, our facility is ISO 9001 and EN 46001  
16 certified.

17 [Slide.]

18 It is estimated that over 14,000 devices have been  
19 implanted in approximately 6,700 patients over the past 38  
20 years. Since 1993, when TMJ Implants implemented device  
21 tracking, 4,156 patients have received 9,152 implants.

22 [Slide.]

23 The TMJ Fossa-Eminence Prosthesis System are  
24 offered in 44 left and 44 right sizes to allow the surgeon  
25 to choose the device which most closely fits the individual

1 patient's anatomy.

2 It is designed to provide a smooth surface for  
3 articulation with either the natural condyle in a partial  
4 joint replacement or with a TMJ Condylar Prosthesis in a  
5 total joint replacement procedure.

6 The prosthesis is manufactured from cobalt-chrome  
7 molybdenum alloy and is secured to the zygomatic arch using  
8 cobalt-chrome screws.

9 [Slide.]

10 The TMJ Condylar Prosthesis Systems, Universal and  
11 Christensen/Chase, with three lengths available, 45, 50, and  
12 55 mm, are designed to seat against the TMJ Fossa-Eminence  
13 Prosthesis.

14 The Universal Prosthesis is designed to be used on  
15 either the right or left side. The Christensen/Chase  
16 Condylar Prosthesis is manufactured specifically for either  
17 the right or left side. Note the angled extension on the  
18 distal portion of the flange, allowing the physician to more  
19 closely follow the patient's natural mandibular structure  
20 and to provide anchoring options in the absence of bone.

21 The body of the Condylar Prosthesis is  
22 manufactured from cast cobalt-chrome molybdenum alloy while  
23 the head of the Condylar Prosthesis may be either cast  
24 cobalt-chrome molybdenum alloy or polymethylmethacrylate  
25 PMMA. These materials are commonly used in orthopedic

1 implants and PMMA is also used in intraocular lenses.

2           The prosthesis is secured to the ramus of the  
3 mandible with cobalt-chrome bone screws. The Fossa-Eminence  
4 Prosthesis and all models of the Condylar Prostheses are  
5 supplied to the user in kit form.

6           [Slide.]

7           These kits consist of sterilized prostheses,  
8 screws, and drill bits. Separate sterilizable sizing  
9 systems are available to aid the surgeon in the selection of  
10 the appropriate size and shape of Fossa-Eminence and  
11 Condylar Prostheses. A sterilizable instrument kit  
12 consisting of screwdrivers and holders is also part of the  
13 system.

14           [Slide.]

15           If there are significant bone loss, trauma, or  
16 other special circumstances whereby the standard stock sizes  
17 and shapes of prostheses are not suitable, a surgeon may  
18 request that the Fossa-Eminence Prosthesis or Condylar  
19 Prosthesis, or both, be cast to fit the patient's specific  
20 anatomical structure.

21           [Slide.]

22           In the case of the TMJ patient-specific condylar  
23 prosthesis, only the flange portion is adapted to the  
24 patient's anatomy. The articulating surface, either PMMA or  
25 metal, is identical to the standard condylar prosthesis.

1 [Slide.]

2 We believe that you will agree with us that the  
3 TMJ Implants, Inc., Fossa-Eminence and Condylar Prosthesis  
4 are safe and effective when used in accordance with their  
5 labeling.

6 Permit me to introduce Mr. Al Lippincott, who will  
7 discuss the results of our non-clinical testing.

8 MR. LIPPINCOTT: Thank you for the introduction,  
9 Jim.

10 [Slide.]

11 Again, I am Al Lippincott of Engineering  
12 Consulting Services, Inc., from Minneapolis, Minnesota. I  
13 am here as a representative for TMJ Implants, Inc., and have  
14 been asked to present the non-clinical testing of the  
15 Christensen TMJ device.

16 I have no financial interest in the company, and  
17 act as a paid consultant on the company's behalf. My  
18 experience is in the manufacture, design, and research of  
19 orthopedic implant devices, and since these TMJ devices are  
20 comparable in materials and also function as a load-bearing  
21 joint, the company has requested my services as a  
22 bioengineer adviser.

23 [Slide.]

24 I will present to you today the following four  
25 areas of nonclinical testing for the safe use of the

1 Christensen PMMA on metal, and metal on metal, TMJ devices.  
2 These four areas, as you see, are materials, device design,  
3 mechanical testing, device retrievals with various  
4 subtopics.

5 Due to time constraints and to move quickly  
6 through the presentation, I will only describe the purpose  
7 of each subtopic test and follow with a short summary of the  
8 test result.

9 [Slide.]

10 For the majority of the mechanical testing, TMJ  
11 Implants, Inc., chose to use the Christensen/Chase condylar  
12 prosthesis mated with a TMJ fossa-eminence prosthesis. The  
13 55 mm Christensen/Chase prosthesis provides the longest  
14 moment arm and is the thinnest in standard thickness of the  
15 stock devices.

16 For the fossa component, a larger size was chosen  
17 to provide a single point contact representing the highest  
18 load, whereas, the majority of the fossas used in vivo are  
19 multiple point contact.

20 For the patient-specific devices, the condyle and  
21 fossa thickness is the same as, or greater than, and screw  
22 hole placement and dimension is the same, or greater than,  
23 the stock devices. The condylar head geometries of both the  
24 patient-specific and stock components are identical.

25 This Christensen/Chase and large fossa component

1 represent a worst case condition applicable to all implant  
2 versions.

3 [Slide.]

4 The purpose of the biocompatibility test is to  
5 confirm that the materials cobalt-chrome moly and PMMA used  
6 to produce the TMJ devices by TMJ Implants, Inc., will meet  
7 biocompatibility standards according to ISO 10993. These  
8 materials have greater than 50 years of medical implant use  
9 as supported by laboratory testing and extensive literature  
10 documentation.

11 The following tests were run to support the  
12 material biocompatibility. The results of the testing show  
13 no unanticipated findings and supports the biocompatibility  
14 of the implant materials as manufactured by TMJ Implants,  
15 Inc.

16 [Slide.]

17 The purpose of this animal test was to determine  
18 the host tissues and blood effect of cobalt-chrome moly and  
19 PMMA particulate when injected into animal TMJ joints.  
20 Parameters of the testing are shown. Wear particles used in  
21 this animal test were generated from pin-on-disk testing.

22 [Slide.]

23 The results show a mild to moderate early reaction  
24 to the particles where the particle-injected joint was  
25 indistinguishable from the opposite side, a saline-control

1 joint, at greater than three months for PMMA and at greater  
2 than six months for cobalt-chrome moly.

3           There was no evidence of foreign body reaction or  
4 giant cells in either material in both blood chemistries and  
5 histology of organs were observed as normal with no  
6 pathology of sequestration of PMMA or cobalt-chrome moly  
7 materials.

8           [Slide.]

9           The PMMA acrylic and cobalt-chrome moly metal  
10 materials are received from raw material vendor sources as  
11 certified to ASTM and ISO medical standards. These  
12 standards are validated with the additional testing as  
13 shown.

14           All materials produced by TMJ Implants, Inc., have  
15 met the specific medical industry standards.

16           [Slide.]

17           The purpose of this next test was to examine and  
18 evaluate the metal microstructure and polished articular  
19 surfaces. Metallography analysis shows that the  
20 microstructure is a dendritic structure with minor porosity,  
21 which is typical of a manufactured cast alloy process.  
22 Also, random minute scratches, as detected under  
23 magnification, are observed on the articular mirrored  
24 polished surfaces, again representing the manufacturing  
25 polished process and is typical of a highly polished

1 surface.

2 [Slide.]

3 The purpose of the FEA analysis was to model  
4 stress distribution within a condyle and fossa component.  
5 The following implant type combinations were modeled. The  
6 results of the modeling with the condyle show maximum  
7 stresses at the uppermost screw holes, while maximum  
8 stresses in the fossa decrease with increased use in the  
9 number of screws.

10 [Slide.]

11 The purpose of this next study in design is to  
12 assess in-vivo kinematics and kinetics of the TMJ by  
13 computer analysis, fluoroscopic videos, and bite force.  
14 Fifteen patient subjects, there were 5 normal TMJs, 5 fossa-  
15 only TMJs, and 5 total TMJs were evaluated.

16 The results from the study show that the relative  
17 applied force and average applied torque at the TMJ for  
18 normal subjects was greater than that of patients with  
19 either a partial or total TMJ joint replacement, and four of  
20 those subjects with total TMJ joint replacements, minimal  
21 translation occurred, indicating that these total joint  
22 replacements only rotate and do not translate.

23 This study also demonstrates the significant  
24 decrease in TMJ joint loading from a normal subject to a  
25 diseased partial/total joint subject by almost a factor of 4

1 times. This study is also the only documented source that I  
2 know of comparing normal TMJ subjects to diseased/implant  
3 replacement subjects.

4 [Slide.]

5 The purpose of this final study in design was to  
6 demonstrate the point contact interface and stress between  
7 condyle and fossa components. The results of the study  
8 confirm that contact areas increase in size with increasing  
9 loads. The average measured contact stress was well within  
10 each respective material's yield strength.

11 This average point contact stress in the TMJ metal  
12 components is comparable to contact stresses measured in  
13 orthopedic mating congruent hip prosthesis.

14 [Slide.]

15 The purpose of this first study under mechanical  
16 testing was to determine the maximum load to failure of the  
17 TMJ implants as a static load to failure with 3 point  
18 bending across the laser mark section.

19 In the PMMA on metal testing, an average failure  
20 load of 365 pounds was recorded at test completion with  
21 fracture of the cobalt-chrome moly fossa component in three  
22 of the five tests.

23 In the metal-on-metal testing, an average failure  
24 load of 465 pounds was recorded with stopping the test due  
25 to screw pullout and bending of the condylar device. Three

1 point bending across the condyle laser marking resulted in  
2 failure at an average load of 217 pounds.

3 Note that the above failure loads on all TMJ  
4 devices are values well above TMJ condyle loads observed in  
5 vivo as documented in the literature. I will discuss  
6 typical in-vivo TMJ loading conditions in the following  
7 testing.

8 [Slide.]

9 The mechanical testing of dynamic fatigue under  
10 physiological in-vivo type conditions was conducted for 5  
11 million cycles. A loading condition of 2 to 35 pound cyclic  
12 load was used for the test. This loading condition is  
13 supported by the work of Brennon, et al., in laboratory  
14 testing measuring direct loads on the TMJ condyles of  
15 primates and adjusted to human levels following the work by  
16 Smith.

17 These loading conditions are comparable to various  
18 mathematical calculations as determined from the literature.

19 [Slide.]

20 Results of the dynamic fatigue show that no test  
21 units fractured or showed signs of fatigue failure under  
22 these physiological conditions after 5 million cycles. All  
23 components maintained mechanical stability and rigidity  
24 throughout testing.

25 This dynamic fatigue testing is intended to

1 characterize physiological performance in chewing forces of  
2 hard foods. It was felt that there was no need to generate  
3 a stress to failure to number of cycles or S-N curve due to  
4 the low forces exhibits in painful diseased and/or  
5 prosthetic TMJ joint in comparison to the high static load  
6 to failure values as previously reported.

7 [Slide.]

8 The final mechanical testing with cyclic wear was  
9 performed under similar physiological conditions as the  
10 dynamic fatigue testing. Parameters for the testing are  
11 based on FDA guideline documents.

12 As discussed at yesterday's panel meeting, where a  
13 20-pound constant load was used for wear testing, cyclic  
14 loading in our test was adjusted to attend a 35-pound load  
15 range again supported by the work of Brennon and Smith with  
16 a jaw movement at a 30-degree, single axis arc motion for a  
17 test duration of 2 million cycles.

18 Particulate wear volume was measured using a  
19 profile analysis system taking measurements of the articular  
20 wear surfaces at the beginning and conclusion of the test.  
21 Completed wear measurements of the metal-on-metal result in  
22 a 0.194 mm<sup>3</sup>/million cycles, volume material loss as compared  
23 to a greater wear loss on the PMMA-on-metal of 1.64<sup>3</sup>/million  
24 cycles.

25 All test units showing wear had a striated

1 uniaxial wear pattern surface with no wear through of any of  
2 the components. As a comparison, the wear of orthopedic hip  
3 implants of a metal polyethylene combination yield volume  
4 material losses anywhere from 40 to 130 mm<sup>3</sup>/million cycles.  
5 This is a factor of 24 to 80 times the amount of hip implant  
6 particulate wear generated over these TMJ devices.

7 [Slide.]

8 This is a photo of the wear test station with the  
9 outer container removed for viewing purposes. The TMJ  
10 implant devices are placed and loaded anatomically, here  
11 with the condylar unit, and here with the fossa unit  
12 superior to the condylar head.

13 The fossa rotates in the 30-degree arc motion in  
14 relation to the stationary condyle. Cyclic load is  
15 transmitted vertically throughout the condyle. The testing  
16 protocol is more physiological and more representative of  
17 in-vivo conditions than pin-on-disk testing.

18 [Slide.]

19 This last slide on the retrieval analysis will  
20 describe the wear zones and surfaces of explanted devices.  
21 Examination was conducted on metal-on-metal specimens up to  
22 a five-year in-vivo duration and with PMMA-on-metal up to  
23 11-year duration.

24 Removal of the devices was due to pain resulting  
25 from fibrous adhesions or ectopic bone formation. The wear

1 zone on the PMMA acrylic heads was larger than that of the  
2 metal-on-metal wear zones as is to be expected with the  
3 softer material and as what is shown by laboratory testing  
4 simulator wear studies.

5           The surface finish of the retrieval zones on both  
6 the PMMA condyle head and metal-on-metal surfaces was smooth  
7 and polished to the naked eye. Under magnification, the  
8 wear surfaces had multi-directional scratches representing  
9 multi-axial movement as a result of abrasive wear. No wear-  
10 through of the retrievals was observed.

11           [Slide.]

12           A similar size wear zone area of both retrievals  
13 and laboratory test acrylic condylar heads were observed.  
14 Comparable acrylic material height loss of both the  
15 retrievals and test specimens were measured.

16           In the retrieval components, no major surface  
17 irregularities were noticed with this being the retrieval,  
18 whereas, material yielding was noted in the laboratory test  
19 components. These major surface irregularities on the test  
20 units show a comparable or higher load condition used in the  
21 testing than that shown on the PMMA materials.

22           Comparison of metal-on-metal retrievals to  
23 laboratory testing units show less wear with the retrieval  
24 implants.

25           [Slide.]

1 In summary, materials manufactured for the  
2 Christensen TMJ devices are biocompatible and conform to  
3 medical implant material standards:

4 2. Animal testing indicates the materials elicit  
5 no foreign body reaction to tissue.

6 3. The design of the Christensen TMJ devices were  
7 analyzed using FEA kinematic/kinetic modeling and contact  
8 stress analysis yielding commonly expected and safe results.

9 4. Load-to-failure testing shows a 6 to 10 times  
10 safety factor in Christensen TMJ device survival over in-  
11 vivo physiological loading for dynamic and cyclic wear  
12 laboratory testing.

13 5. Particulate wear volume of the Christensen TMJ  
14 implants are a factor of 24 to 80 times lower than wear  
15 volumes as generated in orthopedic hip implants.

16 6. No device failures were observed in the  
17 dynamic fatigue or cyclic wear testing. Finally, because we  
18 chose the worst case combination of representative implant  
19 test devices, all testing is applicable to all implant  
20 types, specifically, the fossa only, the PMMA-on-metal, the  
21 metal-on-metal, and the patient-specific of the Christensen  
22 TMJ system.

23 Now, I would like to introduce Mr. Doug Albrecht,  
24 Manager of Clinical Affairs of TMJ Implants, who will  
25 present the various clinical studies.

1 MR. ALBRECHT: Thank you, Al.

2 [Slide.]

3 As Al said, I am Doug Albrecht. I am Manager of  
4 Clinical Affairs for TMJ Implants, Inc.

5 Today, I will be presenting a compilation of data  
6 from a variety of data sources that we believe to be valid  
7 scientific evidence supporting the reasonable assurance of  
8 safety and efficacy of the Christensen designed TMJ  
9 prostheses.

10 [Slide.]

11 Recognized sources of data for preamendments  
12 devices as defined by the FDA can be anywhere from well-  
13 controlled clinical studies to significant human experience  
14 including marketing and MDR history.

15 The Christensen prostheses have been available for  
16 over 35 years, and TMJ Implants has been manufacturing the  
17 Christensen prostheses for approximately 10 years. A  
18 significant portion of the data presented today will be from  
19 significant human experience, marketing and MDR history from  
20 TMJ implants obtained over the past 11 years. Additional  
21 data will be presented by a partially-controlled,  
22 retrospective study and an ongoing prospectively-controlled  
23 clinical trial.

24 [Slide.]

25 The objective of today's presentation is to

1 demonstrate that the Christensen designed TMJ prostheses are  
2 safe and effective in the majority of patients through the  
3 evaluation of pain reduction, improvement in interincisal  
4 opening, and the evaluation of adverse events.

5           The analyses presented today will be from patients  
6 who have supplied clinical data implanted with the  
7 Christensen prosthesis, those implanted with either a  
8 partial joint or total joint replacement, those implanted  
9 with either a metal head or PMMA head condylar prosthesis,  
10 or those implanted with a patient-specific total joint.

11           In most of these studies, data was also collected  
12 on diet restriction and interference with life. While  
13 analyzing the pain data along with the diet restriction and  
14 interference with life, we found that regardless of the  
15 source of data, the same pattern of improvement from all  
16 three parameters was seen.

17           Therefore, in consideration of time, the data  
18 presented today will be that of pain reduction and  
19 improvement in interincisal opening, with the understanding  
20 that similar patterns of improvement were seen with both  
21 diet restriction and interference with life.

22           [Slide.]

23           The measurement of TMJ pain, diet restriction, and  
24 interference with life were measured using a 10 cm visual  
25 analog scale. Ten cm was chosen based upon the results of

1 Seymour, et al., who determined that scales of 10 to 15 cm  
2 had the smallest measurement error.

3 With these scales, the left side represents either  
4 no pain, diet restriction, or interference with life, and  
5 the right side of the scale represents the most pain  
6 imaginable with the inability to eat solid food and the most  
7 severe interference with normal daily activities.

8 Again, this terminology was chosen and shown to be  
9 the most suitable by Seymour, et al.

10 [Slide.]

11 These scales are marked by the patient and are a  
12 commonly accepted method of recording pain and other  
13 subjective parameters.

14 [Slide.]

15 Interincisal opening was measured using a  
16 Therabite scale, and these data are presented in  
17 millimeters.

18 [Slide.]

19 The data being presented today have come from the  
20 following sources of valid scientific evidence. This slide  
21 represents the baseline demographics from these sources. I  
22 will be focusing my presentation on the first three studies  
23 listed, as these provide the strongest evidence of safety  
24 and effectiveness.

25 As you can see from the baseline data, age,

1 gender, and pre-op pain and opening values are consistent  
2 across all studies.

3 [Slide.]

4 As the registry tracks all patients receiving the  
5 Christensen-designed prosthesis, patients from the other  
6 studies may appear in the registry, however, the data being  
7 presented from the other studies was collected and analyzed  
8 independent of the registry.

9 [Slide.]

10 The TMJ Implants registry began in September 1993  
11 in response to the device tracking regulations. A secondary  
12 function of the registry is to collect and store data on the  
13 progress of each patient implanted with the Christensen  
14 device. Baseline or preoperative assessments of pain, diet  
15 restriction, and interincisal opening are requested at the  
16 time of device registration.

17 On a monthly basis, additional requests are sent  
18 to either the implanting or following physicians to obtain  
19 the most current data related to the pain, diet restriction,  
20 and interincisal opening.

21 This is a voluntary system and physicians are not  
22 required to complete and return the forms. Since the same  
23 group of patients therefore is not represented at each time  
24 period within the registry, we conducted cohort analyses  
25 targeting patients who reported data at the same specified

1 time periods.

2           The goal of cohort analyses is to demonstrate  
3 similar patterns as seen with the cross-section data. For  
4 all subgroups of patients analyzed, cohort analyses for pain  
5 and opening were conducted, first, a repeated measures  
6 analysis of variance F test which tests for overall patterns  
7 and then repeated measures analysis of various tests of  
8 contrasts, which tests the difference between mean pairs  
9 were used for these cohort analyses.

10           For each subgroup of patients presented today,  
11 cross-section data will be overlaid with cohort data in  
12 order to demonstrate similar patterns of improvement.

13           The following slides are the results of our  
14 analysis of pain reduction.

15           [Slide.]

16           This first slide represented a cross-section  
17 analysis of the reduction in pain from the registry through  
18 five years implant duration. These data represent all  
19 patients who provided at least preoperative pain data.

20           A significant reduction in TMJ pain is  
21 demonstrated through five years, starting at one month post-  
22 op, and that pattern maintaining itself out to five years  
23 implant duration.

24           Although these data are cross-section  
25 representation, the mere numbers of patients reporting at

1 six months, which is well over 1,000, and at two years,  
2 which approaches 500, tells the story that patients do  
3 achieve a significant reduction in pain from the use of  
4 these prostheses.

5 [Slide.]

6 This cohort analysis includes 284 patients, each  
7 having preoperative, six-month, and two-year pain data. A  
8 significant pattern in the decrease in pain scores, as well  
9 as a significant decrease between pre-op to six months and  
10 pre-op to two years was demonstrated.

11 The difference in pain scores between six months  
12 and two years was also significant albeit the change was a  
13 slight increase of only 0.3 cm. It is not considered to be  
14 clinically significant.

15 [Slide.]

16 This slide compares the cohort data to the  
17 corresponding cross-section data with the number of patients  
18 in the cross-section indicated at each time period. As you  
19 can see, there is virtually no difference between the 284  
20 patients included in the cohort analysis and those from the  
21 cross-section analysis.

22 [Slide.]

23 A second cohort analysis included 60 patients each  
24 having pre-op, one month, six month, 12, 18, 24, and 36-  
25 month pain data, applying the same statistical methods, a

1 significant pattern in the decrease in pain scores, as well  
2 as a significant decrease between the pre-op and all other  
3 time periods was demonstrated.

4 A reduction in pain between the post-op period and  
5 all subsequent periods was also significant. Again, a  
6 comparison of the cohort and the cross-section data is  
7 presented, and again there is virtually no difference  
8 between the 60 patients included in the cohort analysis and  
9 those represented in the cross-section analysis.

10 [Slide.]

11 This slide represents the reduction in pain from  
12 patients implanted with a fossa-eminence prosthesis or  
13 partial joint replacement, and those implanted with a  
14 condylar prosthesis mated against a fossa-eminence  
15 prosthesis or total joint replacement.

16 The cross-section data, as demonstrated by the  
17 solid lines, demonstrates a pattern of pain reduction for  
18 both groups, similar to all patients presented earlier. The  
19 cohort data represented by the dotted lines includes 51  
20 patients with partial implants and 31 patients with total  
21 implants. The cohort data demonstrates a similar pattern of  
22 pain reduction through three years implant duration.

23 [Slide.]

24 This slide represents the reduction in pain from  
25 patients implanted with a condylar prosthesis with a metal

1 head mated against a fossa-eminence prosthesis or metal-  
2 metal total joint, and those implanted with condylar  
3 prosthesis with an acrylic head mated against a fossa-  
4 eminence prosthesis or a PMMA total joint.

5           The cross-section data are represented by solid  
6 lines, the cohort by dotted lines. The cohort data includes  
7 36 patients with metal-metal implants and 27 with PMMA metal  
8 implants. There is a significant reduction in pain from  
9 both groups of patients through four years implant duration.

10           [Slide.]

11           This slide represents the reduction in pain from  
12 patients implanted with a patient-specific total joint  
13 replacement. Again, a significant reduction in pain is  
14 demonstrated with both the cross-section data and the cohort  
15 data. The slight rise at three and four years is most  
16 slightly attributable to the low sample size at these time  
17 period.

18           The following is the results of our analysis of  
19 interincisal opening.

20           [Slide.]

21           This first slide represents the cross-section  
22 analysis of the improvement in opening from the registry  
23 through five years implant duration. These data represent  
24 all patients who provided at least preoperative opening  
25 data. A significant improvement in the opening is

1 demonstrated through five years.

2           Although these data are a cross-section  
3 representation, the mere numbers of patients reporting at  
4 six months and two years again, as with the pain data, tells  
5 the same story, that patients do achieve a significant  
6 improvement in opening from the use of these prostheses.

7           [Slide.]

8           This slide represents the cohort analyses of 265  
9 patients, each having pre-op, six month and two year opening  
10 data. A significant pattern in the increase in opening for  
11 two years, as well as a significant increase between pre-op  
12 to six months, and pre-op to two years was demonstrated.

13           There is virtually no difference between the data  
14 from 265 patients and the cross-section data.

15           [Slide.]

16           In this cohort, 55 patient with opening data at  
17 pre-op, one month, six, 12, 18, 24, and 36 months are  
18 presented. Applying the same statistical methods, a  
19 significant pattern in the increase in interincisal opening  
20 was demonstrated with similar patterns demonstrated with the  
21 cross-section data.

22           An improvement, although not statistically  
23 significant, was seen between pre-op and the one month  
24 period. Although pain is significantly reduced immediately  
25 post-op, it appears that significant improvement in

1 mechanical function may take a little longer.

2           This may be the result of a number of variables  
3 including, but not limited to, disease state, age of the  
4 patient, the time it takes the muscles that were manipulated  
5 or cut during surgery to heal. However, this cannot be  
6 confirmed with our existing data.

7           [Slide.]

8           Comparing the preoperative period and the  
9 postoperative period to all other post-op periods, a  
10 significant difference was also demonstrated.

11          [Slide.]

12           This slide represents the improvement in opening  
13 from patients implanted with a partial joint replacement and  
14 those implanted with a total joint replacement. The cross-  
15 section data, as demonstrated by the solid lines,  
16 demonstrates a pattern of improvement for both groups  
17 similar to all patients presented earlier.

18           The cohort data represented by the dotted lines  
19 includes 45 patients with partial implants, 29 patients with  
20 total implants. The cohort data demonstrates a similar  
21 pattern of improvement through three years implant duration.

22          [Slide.]

23           This slide represents the improvement in opening  
24 from the patients implanted with metal-metal total joint and  
25 those implanted with a PMMA metal total joint. As you can

1 see, there is similar improvement from both groups through  
2 four years with virtually no difference among the cohorts.

3           The cohort data includes 30 patients with metal-  
4 metal implants and 26 patients with PMMA metal implants.  
5 The slight drop in opening at three and four years again is  
6 most likely attributable to the low sample size at these  
7 time periods.

8           [Slide.]

9           This slide represents the improvement in opening  
10 from patients implanted with a patient-specific total joint  
11 replacement. Again, a significant improvement is  
12 demonstrated with both the cross-section data and the cohort  
13 data.

14           [Slide.]

15           In the PMA, we also presented data from a number  
16 of other sources which support the effectiveness of  
17 Christensen design TMJ prostheses and confirm the results  
18 demonstrated with the data from the registry.

19           These supportive studies demonstrate a significant  
20 reduction in pain and improvement in intercuspal opening, the  
21 pain and opening data being presented from the University of  
22 Tennessee and Dr. Hensher will be a cross-section analysis  
23 out to three years implant duration.

24           The pain and opening from Drs. Curry and Latta and  
25 the retrospective study will be from a cohort of patients

1 with pre-op data and data from the last post-op visit  
2 recorded in their charts.

3 [Slide.]

4 This slide represents a significant reduction in  
5 pain from both the University of Tennessee study and the  
6 data independently collected from Dr. Hensher.

7 [Slide.]

8 This slide represents two cohorts, 44 patients  
9 from the retrospective study and 79 patients from Drs. Curry  
10 and Latta. Both groups demonstrate a significant reduction  
11 in pain based upon the mean VAS score from the last post-op  
12 visit recorded. The mean follow-up for the retrospective  
13 study was approximately two years and nearly four years for  
14 Drs. Curry and Latta.

15 [Slide.]

16 This slide demonstrates a significant improvement  
17 in opening through one year from the University of Tennessee  
18 and through three years from the data from Dr. Hensher.

19 [Slide.]

20 This slide represents two cohorts, 170 patients  
21 from the retrospective study and 52 from Drs. Curry and  
22 Latta. Each group shows a significant improvement in  
23 opening from about two to nearly four years implant  
24 duration.

25 [Slide.]

1           The retrospective study represents a significant  
2 source of our safety data. That was the primary objective  
3 of the study. The charts of 249 patients from six oral and  
4 maxillofacial surgeons were reviewed. In order to minimize  
5 any bias on the part of the data abstractors, all clinical  
6 events regardless of the nature, severity, or outcome were  
7 recorded.

8           [Slide.]

9           Of the 334 events recorded, 56 were related to the  
10 surgical procedure, 275 were considered as either patient or  
11 disease related, and only 3 events were considered as  
12 related to the prosthesis.

13          [Slide.]

14          The 3 events considered related to the prosthesis.  
15 The 3 events considered related to the prosthesis each  
16 lasted less than one month, each patient required additional  
17 surgery to correct the problem, and all 3 patients recovered  
18 without complication.

19          [Slide.]

20          I would like to briefly touch on the controlled  
21 clinical study currently ongoing. The primary objective of  
22 the study is to assess the reduction in TMJ pain after  
23 implantation of a Christensen prosthesis. Secondary  
24 objectives include the evaluation of adverse events, diet,  
25 and improvement in opening.

1 [Slide.]

2 These data will confirm the data from all other  
3 sources presented here today. There have been 113 patients  
4 from 9 investigators enrolled to date. We are seeing  
5 similar patterns in pain reduction, lessening of diet  
6 restrictions, and improvement in opening as has been  
7 presented here today.

8 As you can see, the data from the pain, diet, and  
9 life VAS scores are virtually identical. Overlaid is the  
10 paid data from the registry which demonstrates a similar  
11 pattern of pain reduction between both sources.

12 [Slide.]

13 This slide represents a comparison of opening data  
14 from the prospective to the registry data. A similar  
15 pattern in the improvement in opening again is demonstrated.

16 [Slide.]

17 Additionally, the adverse events that have been  
18 reported today are similar to what we have seen in the  
19 retrospective study. There has been only one reported event  
20 that was deemed device related, and that was postoperative  
21 pain, and that is 1 out of 27 events.

22 [Slide.]

23 This slide is a chronological representation of  
24 TMJ Implants' MDR history since 1992. The MDR regulation is  
25 a very subjective tool to measure device-related events, and

1 the company has adopted a conservative reporting philosophy.

2 There is no discernible pattern of device-related  
3 events, and the overall MDR incident rate is less than 1  
4 percent.

5 I would like to just touch on a few of these  
6 reports here. As far as condylar fracture, we submitted 8  
7 reports, however, upon further evaluation, we found that 1  
8 was not a Christensen device after we had reported it, and  
9 1, upon surgical entry to retrieve the device, found that it  
10 was not fractured after all. So, therefore, if only 8  
11 reports were submitted, only 6 were true fractures, and the  
12 majority of them were most likely due to screw placement,  
13 where screws were not placed at the top of the condylar  
14 prosthesis, therefore, putting more stress at the top of the  
15 condylar prosthesis.

16 We have since revised our labeling to instruct  
17 physicians to be sure that at least 3 to 4 screws are placed  
18 at the top of the prosthesis, therefore, reducing that  
19 incident. You can see since 1996, 1997 was the one that was  
20 not fractured, so we have not had a fracture since 1996 with  
21 the condylar prosthesis.

22 With regard the fossa fractures, again, it is 0.1  
23 percent incident rate of fossa fractures since 1992. The  
24 majority of them were due to manipulation of the device  
25 prior to implant, either bending the flange or increasing

1 the size of the screw holes, therefore, compromising the  
2 integrity of the device once implanted.

3 Two reports were due to a monotonic stress  
4 overload, one due to a motor vehicle accident, and  
5 therefore, none were truly seen as a wear-through or any  
6 problem with the device at all.

7 [Slide.]

8 To summarize, presented today was evidence that  
9 the Christensen design TMJ prosthesis product lines are safe  
10 and effective for their intended use regardless of the  
11 source of the data analyzed, whether used as a partial joint  
12 replacement, total joint replacement, whether a metal or  
13 acrylic headed condyle, or a patient-specific condylar  
14 prosthesis, the use of these devices have been shown to  
15 provide in the majority of patients a significant reduction  
16 in pain and significant improvement in interincisal opening.

17 This allows the patient to eat a more normal diet  
18 and enjoy a relatively normal lifestyle.

19 It has also been demonstrated that these devices  
20 are safe. The frequency and type of events reported were to  
21 be expected considering the disease being treated and the  
22 surgical procedure undertaken to treat the patient.

23 There have been no unanticipated adverse device  
24 effects reported. These devices have been available to  
25 treat patients suffering from severe TMJ disorders for over

1 35 years, and we have presented no evidence that would lead  
2 one to conclude that these devices provide an unreasonable  
3 risk of illness or injury associated with their use.

4           Additionally, the clinical benefits experienced by  
5 the majority of patients implanted with the Christensen  
6 designed TMJ prosthesis far outweigh the risks associated  
7 with their use.

8           I would now like to introduce Dr. James T. Curry.  
9 Dr. Curry is a member of the American Association of Oral  
10 and Maxillofacial Surgeons, the American College of Oral  
11 and Maxillofacial Surgery. He is a diplomate of the  
12 American Board of Oral and Maxillofacial Surgery. Dr. Curry  
13 is also past President of both the Arapaho Chapter of the  
14 Metropolitan Denver Dental Society, and the Colorado Society  
15 of Oral and Maxillofacial Surgeons.

16           Dr. Curry.

17           DR. CURRY: Thank you, Doug.

18           [Slide.]

19           Again, I am Dr. James Curry. I practice oral and  
20 maxillofacial surgery in Highlands Ranch, Colorado, with my  
21 partner, Dr. Jim Latta, and we have been together for over  
22 20 years.

23           I have no financial interest in TMJ Implants, Inc.  
24 I am involved in various educational seminars in which we  
25 educate physicians as to the use of these devices, and for

1 that I am paid an honorarium, and they have provided my  
2 expenses for this trip.

3 I have been involved in treating TMJ disease for  
4 29 years, and my experience with the Christensen devices is  
5 in its eleventh year. In fact, my partner and I early on,  
6 in the mid-1980s, had considered discontinuing treating  
7 temporomandibular joint disease surgically in our practice  
8 because of the many problems we were facing.

9 We have been plagued, as many other oral and  
10 maxillofacial surgeons had been, with problems with Silastic  
11 and Teflon Proplast. We had also been plagued with problems  
12 with autogenous grafting methods that we had used for our  
13 patients.

14 We are very interested, vitally interested in  
15 safety and effectiveness of any device that we recommend for  
16 our patients for treatment of this disease. The outcomes  
17 that we have seen in our practice have been so dramatic that  
18 we continue to use this device for treatment of severe and  
19 disabling temporomandibular joint disease.

20 When I was first introduced to the Christensen  
21 device, I was able to review a patient who had had a  
22 Christensen device implanted some 25 years before, and this  
23 was the primary thing that convinced me to try to device in  
24 patients in my own practice.

25 [Slide.]

1           Our treatment philosophy is based on science at  
 2 this point and some of that science has been presented both  
 3 yesterday and today for your consideration. It is also  
 4 based on significant clinical experience.

5           In my own case, I am in my eleventh year of  
 6 utilizing the Christensen devices for treatment of severe  
 7 and disabling temporomandibular joint disease, but aside  
 8 from that, these devices have been used by many surgeons for  
 9 over 35 years, not to mention the several thousand devices  
 10 that have been implanted in this country by experienced  
 11 surgeons, as well as those who are just beginning their  
 12 surgical experience.

13           Our treatment philosophy is also based on common  
 14 sense. The materials used in the production of these  
 15 devices have had long and successful orthopedic histories.  
 16 The system is a simple design, it is relatively simple to  
 17 place for the surgeon. It cuts down on surgical time, it  
 18 provides me with the only partial joint replacement that is  
 19 available to me for my patients.

20           The anatomical design of the fossa prosthesis  
 21 protects the base of the skull from additional destruction  
 22 in diseased joints following placement.

23           [Slide.]

24           I have developed some practical goals for  
 25 alloplastic reconstruction for my patients, and we have

1 already seen that we really expect moderation of joint pain,  
2 not elimination, improvement in joint function as evidenced  
3 by acceptable vertical opening and the ability for these  
4 patients to chew solid food once again.

5           Restoration and maintenance of facial aesthetics  
6 is critical. Restoration and maintenance of functional  
7 occlusion is essential. We want to limit the period of  
8 disability, limit the progression of the disease, and look  
9 for long-term maintenance of restored function, comfort, and  
10 aesthetics.

11           [Slide.]

12           The indications in my practice for a partial joint  
13 replacement include painful and dysfunctional internal  
14 derangements where nonsurgical efforts have failed. It also  
15 includes previous failed joint surgery failures as you can  
16 see here of various types, and other pathology where the  
17 condyle remains healthy.

18           [Slide.]

19           Indications for a total joint replacement include  
20 destruction and loss of the condyle due to trauma, pathology  
21 of various kinds, and ankylosis.

22           [Slide.]

23           This represents my clinical experience in a group  
24 of consecutive patients, and our experience is consistent  
25 with the registry that you have already seen.

1 [Slide.]

2 We looked at opening in a group of my own  
3 patients, and it also, even when you compare the total joint  
4 with the partial joint, mirrors the information that you  
5 have already been provided.

6 [Slide.]

7 In an effort to assist the panel in understanding  
8 better some of the types of patients that I see in my  
9 practice, I want to present a few clinical case reports, and  
10 I will run through these fairly rapidly.

11 In the first couple of cases, I want you to pay  
12 particular attention to some of the questions that I have  
13 been asked around the country as I have presented my  
14 clinical data.

15 This particular patient is a relatively young  
16 female. She had had some previous surgical experiences that  
17 had failed, and in 1990, she had bilateral partial joint  
18 replacements. The x-ray slides that you see here of the  
19 right and left jaw joints, the CT scan done in 199, and what  
20 I want you to notice, yesterday, I think a really good  
21 description of the way a condyle looks is a drumstick in the  
22 glenoid fossa, and so this condyle looks a little bit like a  
23 drumstick, and this one does, too.

24 The question is how does a condyle, a relatively  
25 normal condyle respond to partial joint reconstruction, and

1 in my patient population, the condyle responds very  
2 favorably. This is a nine-year, postoperative view  
3 following partial joint reconstruction.

4 [Slide.]

5 Another question that I am often asked is how does  
6 the contralateral joint respond to unilateral joint  
7 reconstruction in a partial way. This is a 10-year,  
8 postoperative picture of a CT scan. You can see the partial  
9 joint replacement on the left and no surgery on the right,  
10 and this condyle still remains relatively healthy, and so  
11 does the one on the left.

12 [Slide.]

13 As we move into the total joint arena, this case  
14 will be representative of some of the other data that you  
15 have been presented with, multiple attempts at correcting  
16 pain and dysfunction in a nonsurgical fashion, orthodontics,  
17 orthognathic surgery when the occlusion is off, finally,  
18 open joint procedure that failed, and then in 1991,  
19 bilateral total joints.

20 [Slide.]

21 This is the Panorex view of the right ramus, the  
22 entire condyle is missing. This is the lateral head plate  
23 of this same patient showing the incredible open bite  
24 deformity, a very significant aesthetic problem. You can  
25 see telltale clues of the previous orthognathic surgery in

1 an attempt to correct this patient's worsening bite and  
2 aesthetic considerations.

3 This is the lateral head plate following stock  
4 total joint reconstruction for this patient. We were able  
5 to improve her facial aesthetics, correct her open bite  
6 deformity. She had a significant speech pre-surgery,  
7 significant pain, and dysfunction.

8 [Slide.]

9 This is the same patient clinically for you to  
10 consider. What I want you to see here is the significant  
11 aesthetic dilemma that some of these patients find  
12 themselves in, not to mention the functional dilemma, the  
13 huge open bite. The only teeth that are touching are the  
14 posterior teeth.

15 This patient has a significant speech impediment,  
16 tongue thrusting problems, lip incompetence, and all sorts  
17 of problems associated with her significant pain and joint  
18 dysfunction.

19 Following total joint replacement, we have  
20 increased her facial aesthetics and corrected her dental  
21 problems, as well. This patient is continuing to be  
22 followed in my practice, and she is doing beautifully.

23 [Slide.]

24 Another typical example relates to a young female.  
25 She had had a traumatic incident with a right condylar

1 fracture in 1980. In 1985, she was involved in another  
2 motor vehicle accident, and we did total joint replacement  
3 on the right and a partial joint replacement on the left.

4 [Slide.]

5 This represents a stock prosthesis, total joint  
6 replacement for a significant deformity resulting from  
7 trauma. Here is the glenoid fossa. This is the stump that  
8 is remaining of the condyle. This patient is continuing to  
9 be followed in our practice. I have seen her within the  
10 last month, and she is doing beautifully, as well.

11 [Slide.]

12 This is just the representation of the partial  
13 joint replacement on the opposite side.

14 [Slide.]

15 This is a young female who has been through a  
16 litany of other procedures with the Teflon Proplast  
17 replacement devices that have failed so miserably that we  
18 are all involved with now, and she underwent bilateral  
19 temporomandibular joint patient-specific Christensen type  
20 total joints in 1995.

21 [Slide.]

22 This x-ray picture shows the immense destruction  
23 of almost the entire ramus of the jaw and the glenoid fossa  
24 area. This is a 3D reconstruction for your consideration,  
25 and you see how much bone loss has occurred underneath the

1 previous prostheses.

2 [Slide.]

3 This is an SLA model, and you can see that both  
4 joints, both the right and left joints are completely  
5 mutilated and completely destroyed, and this the patient-  
6 specific device on the right that was designed for this  
7 patient. We designed a similar one for the other side.

8 [Slide.]

9 This is just an x-ray representation of the  
10 patient postoperatively. I have been in touch with this  
11 patient in the last two months. She lives in Houston,  
12 Texas, and is being followed at the University of Texas, and  
13 she is just doing beautifully.

14 [Slide.]

15 This gives you some idea clinically of the amount  
16 of destruction that takes place in multiply operated joint  
17 patients, as well as those who have had previous failed  
18 alloplasts, and the way we have been able to reconstruct  
19 them.

20 [Slide.]

21 This is an example of bony ankylosis. I know we  
22 have talked a little bit about ankylosis, and just for your  
23 consideration.

24 When we see total bony ankylosis, it is an  
25 incredible thing. The mandible fuses to the base of the

1 skull. These patients many times can't move in any  
2 direction. There is no way they can have a general  
3 anesthetic for any kind of normal surgery without severe  
4 risk to life and limb. They can't have any dental work  
5 done. They can't get their mouths open at all.

6 This is a clinical picture of this case, and you  
7 can see there is just a mass of bone there and no anatomy at  
8 all.

9 [Slide.]

10 One of the beauties of the design of this  
11 particular joint prosthesis, and whether you are going to do  
12 a patient-specific design or whether you are going to do a  
13 stock replacement, we have available to us templates for  
14 reconstructing the glenoid fossa, and we use these  
15 templates. They have holes through them in several  
16 different places, so that we can actually reconstruct the  
17 glenoid fossa for these patients.

18 [Slide.]

19 As you see, we are continuing our surgery here,  
20 and then we do a total joint replacement. I would like to  
21 make a comment about the design, as well, from a clinical  
22 perspective. The oval shape of the condylar head makes it  
23 very easy for the surgeon when he is placing the ramus  
24 device, which we have to attach to the ramus of the jaw, and  
25 those jaws come in various configurations. They may be

1 slanted one way or the other, and the real nice thing about  
2 this is that if you have to slide this around a little bit  
3 to get it to fit properly and to get solid contact, you  
4 don't change the dynamics of the joint itself.

5 [Slide.]

6 This is an 11-year explant. I would like for you  
7 to see clinically, this is PMMA head and a fossa liner, and  
8 this is what the bone looked like after we took the  
9 prosthesis out. All of this tissue was biopsied. We found  
10 no giant cell reaction, and the bone is just beautiful  
11 underneath these prostheses.

12 [Slide.]

13 This is the replacement that was done for that  
14 patient.

15 [Slide.]

16 In conclusion, I would like to offer that  
17 alloplastic devices are needed by surgeons and patients  
18 alike to reconstruct a variety of diseases affecting the  
19 temporomandibular joint system. No other device is  
20 currently available for me that will so effectively and  
21 safety partially replace the diseased temporomandibular  
22 joint.

23 These devices are simple to place, reduce surgical  
24 time in my hands, and revision surgery, as you have seen, is  
25 pretty simple to do because the bone is really maintained

1 underneath the devices, and clinically, I have not seen a  
2 single case of giant cell reaction or bony erosion, and I  
3 encourage this panel to recommend the continuing  
4 availability of the Christensen designed prosthesis system  
5 for my patients who are suffering from a disabled joint.

6 Thank you.

7 MR. MORGAN: Dr. Janosky, if I could just  
8 summarize very quickly, your decision today, as Dr. Curry  
9 has said, is whether or not a product first introduced in  
10 the 1960s will remain in commercial distribution.

11 Your decision impacts the surgeons' and the  
12 patients' choice in alloplastic devices and treatments. We  
13 trust that you will agree with our conclusion that the TMJ  
14 Implants, Inc., prostheses are safe and effective when used  
15 in accordance with their labeling and that you will agree to  
16 continue to allow this choice of treatment in  
17 temporomandibular joint disorders.

18 We encourage you to vote to approve this device  
19 for continued commercial distribution for the sake of the  
20 patients suffering from temporomandibular joint disease, for  
21 the sake of the surgeons seeking, as Dr. Curry has stated,  
22 the only viable alternative available to certain patients,  
23 and for the sake of the public health.

24 Thank you.

25 I would like to pass around some samples if that

1 is all right.

2 DR. JANOSKY: At this time, are there any  
3 questions from panel members for the sponsor? If there are,  
4 I ask that you state your name before asking the question,  
5 please.

6 DR. HEFFEZ: Leslie Heffez. I have a question for  
7 Dr. Latta.

8 In your mind, what are the specific indications  
9 for an eminence-fossa replacement only?

10 DR. CURRY: Dr. Curry, Dr. Latta is my partner.

11 DR. HEFFEZ: Sorry.

12 DR. CURRY: And he is much less gray-headed than I  
13 am. Would you repeat the question? I am sorry.

14 DR. HEFFEZ: Dr. Curry, could you please tell me  
15 what are some specific indications for eminence-fossa  
16 replacements only?

17 DR. CURRY: The specific indications are when the  
18 joint is diseased and has not responded to nonsurgical care,  
19 and the patient is debilitated to the point that they have a  
20 functional disorder and/or concomitant pain disorder that  
21 has been shown to be joint related, in the joint itself, and  
22 if we have documented evidence of internal derangement, and  
23 the condylar head remains healthy, at least in the testing  
24 that we are able to do, then, we believe partial joint  
25 reconstruction early on is the treatment of choice.

1 DR. HEFFEZ: So, let me clarify. You are stating  
2 that the condyle is in normal configuration, anatomical  
3 configuration, yet, what is going on in the eminence that  
4 leads you to place the implant at the site of the eminence-  
5 fossa?

6 DR. CURRY: Well, there may be no MRI or  
7 radiographic evidence of significant destruction even of the  
8 eminence, but sometimes there is, and the other joint  
9 elements, the interarticular disc, if there is functional  
10 problems and serious adhesions, we place the fossa-eminence  
11 prosthesis to, number one, protect the base of the skull,  
12 and, number two, to reduce the likelihood of adhesions  
13 postoperatively in ankylosis.

14 DR. HEFFEZ: You are taking out the cases of  
15 ankylosis. I would like specifically to know if the  
16 eminence in your mind, in your experience, can undergo  
17 degeneration and the condyle not undergo degeneration, and  
18 this leads you to the placement of this eminence-fossa  
19 implant.

20 DR. CURRY: Yes, that occurs occasionally, as  
21 well, and that would be a specific indication.

22 DR. HEFFEZ: How frequent do you see the need for  
23 placing an eminence-fossa device without placing a condyle  
24 device?

25 DR. CURRY: In my clinical experience, about 60 to

1 70 percent of the patients that we do open procedures on are  
2 indicated for partial joint replacement rather than total  
3 joint replacement.

4 DR. HEFFEZ: What type of procedures would that  
5 patient have undergone prior to placement of this eminence-  
6 fossa device, or is this a primary surgical procedure?

7 DR. CURRY: It can be a primary surgical  
8 procedure. In my hands, if a patient has not been multiply  
9 operated, I won't hesitate to put the fossa prosthesis in at  
10 the first surgical insult. We are making every effort to  
11 reduce and eliminate eventually the multiply operated  
12 patient from our practices.

13 We have seen over and over again that multiple  
14 procedure after multiple procedure results in nothing but  
15 failure for these patients.

16 DR. JANOSKY: Ms. Cowley.

17 MS. COWLEY: Theresa Cowley, TMJ Association.

18 I notice in your promotional materials that you  
19 are actually encouraging that patients have one surgical  
20 procedure, if that. I would like to know how you ethically  
21 can espouse this when, in your instructions for use, you  
22 say, "Although total temporomandibular joint replacement in  
23 an option in patients," and so forth, "the long term  
24 outcomes with currently available total joint implants have  
25 yet to be determined," and your studies are actually

1 voluntary on the part of the physicians.

2 MR. MORGAN: Jim Morgan. I think that Dr. Curry  
3 has responded to the early procedure aspect of it, that  
4 there are certain indications clinically that would be  
5 beneficial for the patient. In addition, there is certain  
6 aspects of our labeling that are required by the FDA, I  
7 think you read just part of that, and our objective is to  
8 assist the temporomandibular joint disease patient to  
9 improve their condition, and we leave it to the clinician to  
10 make final determination as to when to exercise that  
11 discretion.

12 MS. COWLEY: Can I follow up? What instructions  
13 do you give your clinicians when a device fails, who are  
14 they to report it to? Apparently, I saw 60 MDR reports. We  
15 have approximately twice that in our registry, and a lot of  
16 people in this country don't even know we exist.

17 MR. MORGAN: I guess the question deals with  
18 filing MDR reports. We believe that we have taken a rather  
19 conservative regulatory approach towards filing MDRs, that  
20 is, if there is some question as to whether or not we would  
21 be required to file an MDR, generally, we do file.

22 So, when we obtain information, we evaluate that  
23 information relative to the MDR regulation, and we believe  
24 make the appropriate determination to file.

25 MS. COWLEY: Can I follow up? What happens to the

1 devices and who do you deem owns the devices once they are  
2 explanted?

3 MR. MORGAN: When devices are returned to us, we  
4 perform an evaluation on those devices, and we retain them  
5 in our archives. The question of ownership, I don't quite  
6 know how to address.

7 DR. JANOSKY: Dr. Rekow.

8 DR. REKOW: This is Diane Rekow. I have a real  
9 simple question. What is a device? When I start adding  
10 things up, I end up with more devices than patients times 2?

11 MR. MORGAN: What we are really talking about is a  
12 system, and we have a partial joint system that consists of  
13 the fossa-eminence device, along with the screws and  
14 accessories to implant that device, and we have a total  
15 joint system that consists of the fossa-eminence and the  
16 condylar prosthesis.

17 Within that, there is a condylar prosthesis with a  
18 metal head and one with a PMMA head. Finally, we have  
19 perhaps one would consider another subset, and that is that  
20 there are patient-specific devices, which may be either be  
21 either fossa-only or fossa and condyle with metal or PMMA.

22 DR. REKOW: I understand that, but, for instance,  
23 in the literature that we had, you had 3,914 patients with  
24 8,600 devices, but 3,900 patients only have a total of 7,800  
25 joints, so I got confused about what you are counting in the

1 numbers that you report.

2 DR. CHRISTENSEN: I am Dr. Christensen. Per  
3 patient on the average we are seeing about 2.2 devices. It  
4 could be a fossa, it could be a condyle, or it could be a  
5 fossa on one side, a fossa on the other side, so when we  
6 report different numbers, that is sort of how it goes.

7 You could have a partial on one side, you could  
8 have a total on one side, you could have a total on both  
9 sides, and if you had a total on both sides, you would have  
10 basically four devices. I think that is maybe where the  
11 confusion is.

12 DR. REKOW: I was thinking of a total joint being  
13 one joint, but it is two pieces.

14 DR. CHRISTENSEN: That is correct.

15 DR. JANOSKY: Dr. Patters.

16 DR. PATTERS: I would like the sponsor to address  
17 the MDR issue. The panel has been provided with information  
18 from FDA that between 1984 and June of 1998, 434 MDRs were  
19 filed regarding the generic TMJ implant; 75 percent of those  
20 were Silastic or Proplast Teflon, however, 14 percent were  
21 the Christensen implant.

22 Then, after those two were taken off the market,  
23 the Proplast Teflon and the Silastic, from August of '96  
24 until May of '99, there were 63 MDRs filed, and 65 percent  
25 of those were Christensen devices.

1 Do you find that alarming at all, and can you  
2 comment in the significance of it?

3 DR. CHRISTENSEN: I think if you looked at what we  
4 projected up there, the percentage of MDRs or events listed  
5 per the population that doctors have operated on is less  
6 than 1 percent. Most of them are less than half of 1  
7 percent. That generically, or not generically, but  
8 globally, should tell something.

9 Jim?

10 MR. MORGAN: I have nothing to add.

11 DR. PATTERS: One additional question. Based upon  
12 your total clinical data, can you at least give estimations  
13 of the percentage of implants placed that the patient did  
14 not improve? Not necessarily those which failed  
15 mechanically, but that the patient did not report any  
16 improvement in the measured parameters?

17 MR. ALBRECHT: Doug Albrecht. We did look at  
18 that, and we looked at patients whose pain or opening did  
19 not improve at each time period throughout the continuum,  
20 and overall, approximately 5 to 6 percent of patients did  
21 not have a VAS score lower than their baseline or intercisal  
22 opening higher than their baseline at six months, 12 months,  
23 and every six months after to three years implant duration.

24 So, on that, approximately 95 percent of the  
25 patients do show an improvement in their pain and their

1 function post-surgery.

2 MR. MORGAN: Could I just add something to that?  
3 In that time period, we were essentially the only marketer  
4 or certainly the primary marketer of the device at that  
5 time. That might also be a reflection of the percentage of  
6 MDRs filed.

7 DR. JANOSKY: Dr. Heffez.

8 DR. HEFFEZ: I have a follow-up question to Dr.  
9 Patters' question.

10 Have you looked at specific diagnoses of the  
11 patients, for example, the Proplast Teflon patient, as far  
12 as its failure rate as opposed to just if you have already  
13 treated patients for primary, with these devices as primary  
14 surgeries, it muddles the data. So, if you could look at  
15 just the Proplast Teflon patients and advise us on your  
16 data.

17 MR. ALBRECHT: Yes, we have looked at those  
18 patients with history of Proplast or Silastic, and we have  
19 shown--I have slides if you would like me to put them up or  
20 I can just annotate--we have seen the same type of  
21 improvement in pain and the same type of improvement in  
22 opening for those patients.

23 DR. JANOSKY: A question from Dr. Burton.

24 DR. BURTON: This question is for Dr. Christensen.  
25 I am still sort of curious, though. You have a multitude of

1 treatment options that you have developed here, but there  
2 doesn't seem to be any kind of guidance that I could see in  
3 terms of between metal-on-metal, PMMA-on-metal, or the now  
4 your custom, which didn't seem quite as well defined in  
5 terms of indications or differences between these various  
6 systems and your utilization.

7 DR. CHRISTENSEN: The use of this patient-  
8 specific, of course, depends upon the amount of anatomic  
9 structure there as to what we need to anchor that to, to the  
10 bone, and make it one that would hold up.

11 The use of the metal versus--and that the  
12 physician choice really--but the use of the plastic versus  
13 metal, we are attempting to, of course, reduce any wear that  
14 we can and get down to as small amount as possible. I think  
15 in several articles, like the Sulzer article, and so forth,  
16 that talks about the metal versus, say, other things, such  
17 as polyethylene, being anywhere from 20 to 100 times less  
18 wear debris, and we are finding that I think in our studies,  
19 too.

20 DR. BURTON: Thank you.

21 DR. JANOSKY: A follow-up question from Dr.  
22 Heffez.

23 DR. HEFFEZ: Again, a follow-up question. Could  
24 you give us data on the percentage of patients that were  
25 operated as primary surgical procedures and the percentage

1 in which you placed in either of these devices in mutilated  
2 joints?

3 DR. CHRISTENSEN: Anecdotally, it's a little bit  
4 more than anecdotally, but he will have the real answer, but  
5 in my practice, when I saw internal derangement and  
6 perforation of that meniscus, I realized that meniscus will  
7 not repair itself, and I put in the fossa-eminence implant  
8 and partial joint, those patients almost never had to be  
9 reoperated. We are seeing a group of people now that have  
10 been operated in many ways, and that, of course, compounds  
11 the problem.

12 Fortunately, I think our results--and he will show  
13 you--are quite significant in both areas.

14 MR. ALBRECHT: Doug Albrecht. To respond to Dr.  
15 Heffez' question, in our clinical report, which was included  
16 in the PMA, on page 4.9 of the clinical report, we reported  
17 from the University of Tennessee study patients who had been  
18 multiply operated versus patients who had been operated for  
19 the first time, and both of those, we looked at pain and  
20 opening for those groups of patients, and we found similar  
21 results although the patients that had been multiply  
22 operated did have higher pain scores, but both groups of  
23 patients did show improvement postoperatively.

24 DR. HEFFEZ: What wasn't the question. My  
25 question was how many patients were treated as a primary

1 disease and how many were treated in mutilated joints. Do  
2 you have that data for the total amount of patients that you  
3 reported? If not, if you only have it for the University of  
4 Tennessee study, could you say it for the audience?

5 DR. ALBRECHT: Yes, for the University of  
6 Tennessee study we had 211 patients that had been multiply  
7 operated, and 109 patients who were operated for the first  
8 time, and again both groups of patients showed improvement  
9 after surgery, however, the multiply operated patients did  
10 have higher pain scores.

11 DR. JANOSKY: A question from Dr. Skinner.

12 DR. SKINNER: I have two questions. One was  
13 regarding the wear debris studies that you did. That was  
14 polymethylmethacrylate that you put in a rabbit's joint. Do  
15 you have any idea what the wear debris particle size  
16 distribution and size was?

17 MR. ALBRECHT: I think I will direct that question  
18 to Dr. David Gerard who did that study.

19 DR. GERARD: David Gerard. I don't have any  
20 financial interest in this company although I performed two  
21 animal studies for this company.

22 The particles that we looked at were ranging from  
23 50 to 250 microns in size and were irregular in shape, and  
24 they were injected into the joints, the TMJ joints of  
25 rabbits, and on the contralateral side, saline was injected

1 as a control.

2 DR. SKINNER: Do you have some rationale for using  
3 such large particle sizes?

4 DR. GERARD: The particles we used were actually  
5 generated from wear studies, and in analyzing the size of  
6 those particles--this study was done in '94, at that time we  
7 didn't fully appreciate the importance of very small  
8 particles--and we analyzed the size of those particles using  
9 SEM and just a settling technique, and so we may have had  
10 small particles in that sample that we did not see, but I  
11 cannot say that for certain.

12 But if you look at the wear pattern, for example,  
13 on the test condyle versus the retrieved condyle, you will  
14 see that the wear patterns are very similar, and that would  
15 indicate to me that particles generated in a wear test would  
16 have the same range of sizes as particles that you would see  
17 in vivo.

18 DR. SKINNER: And that was a single injection  
19 rather than a continued injection?

20 DR. GERARD: Yes, it was a bolus rather than  
21 continuous generation, yes.

22 DR. SKINNER: A second question was regarding the  
23 clinical data. The cross-section and the cohort data  
24 overlapped, didn't it?

25 MR. ALBRECHT: Yes, they did. They pretty much

1 mirrored each other.

2 DR. SKINNER: No, no, overlapped. There were the  
3 same patients in each group.

4 MR. ALBRECHT: Yes, the subset, the cohort was a  
5 subset of the cross-section data for patients with complete  
6 data at every time point presented.

7 DR. SKINNER: So, the cross-section data included  
8 the cohort group.

9 MR. ALBRECHT: That is correct.

10 DR. JANOSKY: A question from Dr. Gonzales.

11 DR. GONZALES: This is a question for Dr. Doug  
12 Albrecht regarding the way the pain scales were performed.

13 First of all, I understand that you performed 10  
14 cm pain scales on these patients. In the prospective study,  
15 I understand in the handout that was given, that yes/no  
16 scales and also 5 cm or 5 point scales were also performed.

17 The other question is why the dropout or reduction  
18 in the number of patients in the second cohort. You start  
19 off with 1,794 patients. At two years, you are down to 447,  
20 and three years, 234 patients.

21 Was that based on the fact that was a  
22 questionnaire that was sent to patients and you just weren't  
23 getting the return on those questionnaires?

24 Finally, when were the patients required or asked  
25 to fill out the questionnaires in terms of when they were

1 measuring their pain, when were they asked to measure their  
2 pain since pain is not--it is rare that pain is a  
3 consistent, constant painful symptom. Oftentimes these  
4 patients will have pain after eating, during eating, or at  
5 other times. I am interested in finding out what the  
6 questionnaire instructed the patients, how they were  
7 instructed to fill out the questionnaires.

8 MR. ALBRECHT: Just to clarify, you indicated that  
9 we just used yes/no in the prospective study. We collected  
10 yes/no data from the retrospective study.

11 Let me just clarify the types of studies, and then  
12 I can answer your questions. We did the retrospective study  
13 primarily to collect adverse event data. While we were in  
14 the patients' charts, we also collected data on pain and  
15 opening.

16 Yes, we did find that in a number of cases, the  
17 notes in the physician's chart did not always indicate a  
18 pain scale. They said yes, I am still having pain, or no, I  
19 am not having any pain. We probably underestimated the  
20 amount of data like that in the charts, but we had to record  
21 it, and we had to analyze it somehow.

22 That purely is a retrospective evaluation. We  
23 just recorded what was written in the physician's charts at  
24 that time.

25 To answer your question regarding when the

1 questionnaires and when the patients filled them out, for  
2 the prospective study, which is currently ongoing, those  
3 visual analog scales are filled out by the patient when they  
4 are seen in the office by the physician.

5           The forms state to ask the patient to rate their  
6 pain, diet, and life problems averaging over the last month,  
7 how have you felt over the last month, and they are to mark  
8 on the scale what that value is.

9           DR. GONZALES: And the dropout of patients?

10           MR. ALBRECHT: The dropout of patients from the  
11 registry. Again, the registry, the primary function of the  
12 registry is for device tracking. We initiated trying to  
13 track the progress of patients on a voluntary basis since  
14 1993, and again it is not a complete cohort.

15           There is dropout because, number one, it is a  
16 voluntary system, that we sent the questionnaires to the  
17 physicians on a monthly basis. If the physician wishes to  
18 return the questionnaire to us, he does, and we record the  
19 data. So, it is not designed as a clinical study to be  
20 active in that sense. It is to give us a sort of feel of  
21 how patients are doing over time. That is the reason for  
22 the dropout, plus we are continually enrolling, so your pre-  
23 op patients are going to be higher than your patients out to  
24 four or five years.

25           DR. GONZALES: But this study is giving you a feel

1 of how these patients are doing, and unfortunately, when one  
2 fifth remain after a two-year period, the feel that you are  
3 getting is from those patients who are actually filling out  
4 the form, and since it is being stressed that these patients  
5 are continuing to do better over time, and you are not  
6 really capturing the majority of these patients, so an  
7 impression to be made regarding this is very difficult to  
8 make any statements when, again, four-fifths of the patients  
9 are not really being measured.

10 MR. ALBRECHT: And we understood that, and that is  
11 why we conducted the cohort analyses where we looked at  
12 patients who provided data, at every time point, versus  
13 having a cross-section of data where patients do not report  
14 data at every time point.

15 As you can see from the presentation, the cohort  
16 data mirrored the cross-section data almost identically all  
17 the way through, and even with our prospective trial in  
18 which we are measuring those patients on a prospective basis  
19 in a clinical study, when compared to the registry data, we  
20 are still seeing the similar results.

21 DR. GONZALES: Thank you.

22 DR. JANOSKY: A question from Dr. Li.

23 DR. LI: We have a couple of questions on the  
24 nonclinical data that was provided.

25 First, the PMMA that you appear to be using is

1 clearly different from the bone cement used to fix total  
2 joints, and I didn't find all the properties, although they  
3 might have been in there.

4           Could you describe a little bit the difference  
5 between the PMMA you are using now and the PMMA we typically  
6 use as a bone cement?

7           MR. LIPPINCOTT: Thank you for identifying that,  
8 Dr. Li. Yes, it is different. The material characterized  
9 in the Christensen device has a similar chemical composition  
10 except that this does not have a radiopaque identifier, such  
11 as barium sulfate or zirconium oxide, and it is a common  
12 material that is used in the lens industry. It has got a  
13 long history of use.

14           Also, this device is premanufactured compared to  
15 the acrylic that is used in orthopedics from the standpoint  
16 that you have total release of the monomer that is used to  
17 solidify the material. That is also further released  
18 through gamma irradiation of the product to make sure that  
19 it is fully released because it is tissue destructive.

20           DR. LI: In particular, I was interested. There  
21 is one component that is very different from bone cement. I  
22 think it is the dimethacrylate that is in the powder, that  
23 is used as a cross-linking agent. I would guess that the  
24 effect of that cross-linking agent would be it perhaps would  
25 lower wear, but actually would reduce the fracture

1 toughness.

2           So, my question is what is your fracture toughness  
3 of your PMMA versus bone cement either in terms of the K1C  
4 or a J or a materials fracture number? I didn't see that in  
5 the application.

6           MR. LIPPINCOTT: Well, we have done testing such  
7 as tensile testing.

8           DR. LI: I am looking for a fracture toughness.

9           MR. LIPPINCOTT: Like a Charpy-impact test?

10          DR. LI: No, I am looking for a fracture toughness  
11 value, actually, the inherent fracture toughness of the  
12 material. It is typically provided either as a critical J  
13 or a critical K value in the ASTM vernacular.

14          MR. LIPPINCOTT: Unfortunately, we don't have that  
15 information.

16          DR. CHRISTENSEN: We did do a static load test on  
17 that in which we put about 790 pounds or 800 pounds or maybe  
18 900 before the thing ever fractured.

19          DR. LI: I understand. That just isn't the same  
20 as a fracture test, that is more of a total device test. It  
21 was more of a materials question.

22                 In your finite element modeling, did you allow for  
23 the creep of your methacrylate as part of your model or did  
24 you consider it as a rigid body?

25          MR. LIPPINCOTT: We considered it as a rigid body.

1 DR. LI: Because the deformation of your PMMA  
2 also, the other substantial difference appeared to be the  
3 deformation under load, which was substantially higher than  
4 bone cement, so I guess the question would be the  
5 appropriateness of modeling that material as a rigid body.

6 MR. LIPPINCOTT: I really couldn't answer that for  
7 you.

8 DR. LI: What did you use as a failure criteria in  
9 your modeling? In other words, you appeared to calculate  
10 stresses, and you made some little--I forget the phrase--but  
11 that you didn't get near the yield point and thus considered  
12 that an appropriate safety test, but without knowing the  
13 fracture toughness value or the fatigue values, how could  
14 you actually assess from the finite element model that it  
15 was safe using that method?

16 MR. LIPPINCOTT: Well, we modeled simulating loads  
17 in the FEA, and what we did is we looked also in comparison  
18 to the wear testing as far as how the material yield with  
19 certain loads that we used on it, and as well we did a  
20 tensile test on the material, which typically there is very  
21 little yield, if anything, in the material. You usually  
22 have a tensile and elongation factor.

23 DR. LI: So no other failure criteria other than  
24 tensile and yield were used in your FEA.

25 MR. LIPPINCOTT: That is typical, yes.

1 DR. LI: Speaking of the wear test, I had a couple  
2 of questions. You have got two different wear tests. One  
3 is a pin-on-disk, and one that was supposed to be a little  
4 closer to the anatomical case.

5 Did you get the same particle size in both of  
6 those tests?

7 MR. LIPPINCOTT: We did not evaluate the particle  
8 size as a comparison between the two tests. Now, the  
9 particles that were used in the rabbit study were for the  
10 pin-on-disk test.

11 DR. LI: As Dr. Skinner pointed out, those were  
12 rather large compared to the particles we are now currently  
13 worried about.

14 And the fluoroscopy data, working with the same  
15 group and total knee replacements, we find a very large  
16 mismatch between where the fluoroscopy says the components  
17 are relative to each other versus what we find in the  
18 retrieved components.

19 In other words, in the fluoroscopy of total knee  
20 replacement using the same group, the fluoroscopy data will  
21 tell you through a range of motion where the femoral  
22 component was relative to the tibial component.

23 Then, you compare that information to where the  
24 components had to be because you see the damage in your hand  
25 of the retrieved component. There is actually poor match

1 between the fluoroscopy kinematic locations and the  
2 retrieved device locations.

3           So, my question is seeing as how you seem to have  
4 gotten some retrievals, what is the comparison of the  
5 location, the fluoroscopic locations versus your retrieval  
6 damage locations?

7           MR. LIPPINCOTT: I would say that because of the  
8 configuration of the fossa component, that there is a  
9 sulcus, a cavity, that the head would fit into, we are  
10 seeing comparable locations from the study, because it is  
11 almost self-centering as far as its finding its center in  
12 this location.

13           DR. CHRISTENSEN: You won't be able to evaluate  
14 accurately, I don't believe, Dr. Li, the fluoroscopic  
15 picture of that in the patient versus that in the explant.  
16 It is complicated because of the whole skull, because of the  
17 metal, and so forth.

18           DR. LI: Understood. Actually, that was my point.

19           I think it was Volume 4, page 847, let me read  
20 this because I was kind of surprised that it was here. It  
21 says, "The wearing of the PMMA head may progress to the  
22 cobalt-chrome retaining post embedded with the PMMA head.  
23 After that time, the working mechanism would be a single  
24 point, metal-on-metal contact with the resultant lower wear  
25 of the metal-on-metal devices."

1 My question is do you actually believe that, and,  
2 if so, how could that possibly be, and did you actually  
3 verify that independently somehow?

4 DR. CHRISTENSEN: I would like to add that, and I  
5 think Mr. Lippincott will, too, clinically, from the  
6 explants, and so forth, we have seen occasion where the  
7 plastic head comes down almost never to the metal, maybe one  
8 or two cases at most, but if it ever does, that was put in  
9 there for a reason, to be of a highly polished mandril or  
10 point that this implant could fit on. We have never seen  
11 damage to the fossa or that metal strip, and it would slow  
12 down at that point.

13 MR. LIPPINCOTT: I would like to comment also,  
14 that by the time you get down to the post, the acrylic is  
15 conformed to the shape of the fossa, okay, from wear, and so  
16 your contact stresses are distributed quite more out on a  
17 larger area, so you wouldn't expect to see the higher  
18 contact on the metal post.

19 Granted, there may be some load transmitted to the  
20 post, but I think it would be very minimal.

21 DR. LI: Have you verified that?

22 MR. LIPPINCOTT: I don't know how you would verify  
23 that.

24 DR. LI: Well, that was my question actually.

25 DR. CHRISTENSEN: In our wear testing, have never

1 taken it, in the time of 10,000 cycles we have run, has not  
2 gotten it down to the post. That is only a millimeter and a  
3 half in thickness.

4 MR. LIPPINCOTT: In our wear test, the worst wear  
5 test, which showed the greatest wear, typically, we have a  
6 millimeter or 40,000ths to 60,000ths difference in height  
7 between the post and the top of the acrylic, and in that  
8 wear test, we had wear of about half a millimeter as a worst  
9 case with the five test components that were tested.

10 DR. LI: Back to the wear test, the anatomical  
11 wear test, you have a statement in there that you thought  
12 the surface profiling was more accurate than a weight  
13 measurement. Yet, if I read my details right, the weight  
14 measurements were done with a balance that actually couldn't  
15 possibly weigh the wear that you were getting.

16 So, my question is although it may be true the  
17 surface profiling may be more accurate, how did you actually  
18 determine that given that you had no weight measurements to  
19 compare it with?

20 MR. LIPPINCOTT: Well, we did have weight  
21 measurements to compare it with. This was done by an  
22 independent lab. This was Rose, who you are familiar with.  
23 I think they are relatively new in doing this type of work,  
24 and unfortunately, we had some discrepancies in the weight  
25 measurements that were taken.

1 We did take measurements every quarter of a  
2 million cycles, and unfortunately, we got weight gain at the  
3 beginning of the test, and then in many cases, especially on  
4 the condyle units, they did level out and we did have loss.

5 Now, we did have the fossa component on the metal-  
6 on-metal, and we compared that to the surface profile  
7 analysis that we also used as a fail/safe method to check  
8 before and after the test, and we did get very identical or  
9 comparable mass loss measurements with weight versus profile  
10 as a comparison, so that validated us using the surface  
11 profile method.

12 DR. LI: Just a couple more, if you will indulge  
13 me. How does the physician choose whether or not to use a  
14 metal-on-metal or a metal-on-methacrylate component, and why  
15 do you have the choice?

16 DR. CURRY: I am Dr. Curry. In the early stages  
17 of my experience with this prosthesis, I was using all PMMA-  
18 on-metal joints, and I think part of my reasoning is from  
19 unfounded fears that had been generated through discussions  
20 that I have had with my colleagues, problems with previous  
21 alloplasts like Teflon and Proplast, and I was fearful of  
22 particles generated from PMMA wear, and so I have switched  
23 to the metal-on-metal joint just from that fear although I  
24 will say that as it stands now, probably 70 percent of the  
25 patients that I have operated have PMMA-headed condyles.

1 My partner and I made an anecdotal decision early  
2 on that patients that had had pre-existing alloplastic  
3 failures involving Teflon and Proplast and/or Silastic, we  
4 went to the all-metal condyle for those patients early on  
5 and have been very happy with that.

6 So, it is patient and doctor choice. Sometimes we  
7 have patients that say I don't want any plastic, so for that  
8 reason we will use an all-metal condyle.

9 We also consider--and I think you brought this  
10 point up yesterday, Dr. Li--we are dealing with overall a  
11 fairly young patient population when we compare the  
12 population of total joint replacement in the  
13 temporomandibular joint to total hip replacements and total  
14 knees. Although you have made the comment that your patient  
15 age population or the age of your patient population is  
16 being reduced over the last few years, our average age of  
17 our patients is in their forties, if you look at the  
18 demographics over the entire world, and my sense tells me  
19 that metal-on-metal is potentially stronger and potentially  
20 will last longer than a metal-on-plastic, but that has yet  
21 to be proven.

22 MR. LIPPINCOTT: I would like to make a comment on  
23 that also. With my background in orthopedics, I am very  
24 familiar with the complications with lysis. That has been  
25 one of the ongoing things in the last 10 years that has

1 confronted the orthopedic surgeon and is a very big concern.

2           So, there is, you know, now in orthopedics a need  
3 to examine materials and what particular wear debris does,  
4 and they are examining sizes, accumulation of debris, how  
5 the material reacts in the tissue, et cetera, et cetera, and  
6 so this company has taken the measure to go along the  
7 orthopedic route and consider that also, and so has  
8 incorporated various testing parameters to look at that.

9           In this cyclic wear testing we did do using the  
10 same identical physiological conditions, we did see a lower  
11 amount of wear and particulate generated compared to the  
12 acrylic, but understand that also from histology sections  
13 that have been retrieved, from those retrievals we have not  
14 seen a foreign body reaction to the acrylic, and although  
15 acrylic was abandoned in orthopedics 30 years ago from the  
16 Judet prosthesis, that was abandoned I think more due to  
17 mechanical failure rather than wear, although wear was  
18 identified. They did not have the means at that time to  
19 characterize the wear and what it was doing to the joint.

20           But they did not see the lysis back then like they  
21 see today with those acrylic Judet prosthesis.

22           DR. LI: Although those failed by loosening before  
23 osteolysis could catch up with them, but there was wear.

24           MR. LIPPINCOTT: There was wear, there was most  
25 definitely wear.

1 DR. LI: In the last 35 years, have you ever  
2 monitored metal serum levels from urine samples, from metal-  
3 on-metal devices, because when you do that from patients,  
4 even with metal polyethylene components, there is increased  
5 level of metal, for instance, in their urine and even  
6 elevated more in metal-on-metal total hips.

7 MR. LIPPINCOTT: I think I will direct that  
8 question to Dr. David Gerard.

9 DR. GERARD: I don't know of any clinical trial or  
10 any clinical testing that has specifically been done on  
11 these patients to monitor either acrylic or metal in either  
12 blood serum or in urine, although in the animal studies we  
13 did monitor normal blood chemistry, as well as blood  
14 hematology looking for these particles, as well as looking  
15 in organs, the major organs and in the lymph nodes.

16 DR. LI: Although with the size of the particles  
17 you used, they are unlikely to migrate.

18 DR. GERARD: But I would go back again to say that  
19 the size of the particles--the particles were generated from  
20 a wear test, and so there may have been smaller particles in  
21 there that we did not see.

22 The other thing I would point out is if you look  
23 at the histology especially with PMMA--and Dr. Mercuri  
24 showed his slide yesterday of PMMA in tissue--you saw large  
25 particles, and you saw no foreign body reaction.

1 I have looked at over 400 joint tissue samples  
2 from temporomandibular joint patients, not all of those  
3 obviously with PMMA, but with other disease processes, and  
4 giant cell reaction is a very obvious thing to see. It is  
5 not something that you have to hunt for, and we do not see  
6 that either in the animals or in the retrievals that we  
7 looked at.

8 DR. LI: Thank you. One final question, the same  
9 question I asked the folks yesterday. Have you done any  
10 measurement of the relative micromotion or stability of your  
11 implant against the bone, because I think that these  
12 implants are fixed with numerous screws, and often  
13 micromotion of an implant against the bone is what leads to  
14 pain, and so the question is, have you ever checked the  
15 relative stability of your implant in cadaver studies or in  
16 any other way?

17 MR. LIPPINCOTT: No, we have not, and I would  
18 assume if we see--of course, it is hard to judge that in  
19 these type of patients because of the pain complications  
20 that they have, and whether that is one of the factors from  
21 micromotion--now, in many cases, the reason for retrieval is  
22 not from loosening of the screws or loosening of the device.  
23 It is typically due to pain form heterotopic bone or fibrous  
24 adhesions. So, we don't see that.

25 DR. JANOSKY: A final question from Dr. Skinner.

1 DR. SKINNER: Just one more question.

2 Were any of these human studies, were any of that  
3 data collected with an OPRR-approved, IRB approval?  
4 Especially, the fluoroscopy I am particularly concerned  
5 about.

6 MR. ALBRECHT: The ongoing prospective study right  
7 now is being conducted with IRB approval at every center.  
8 With regard to the fluoroscopy, I don't understand or could  
9 you be more clear with that question?

10 DR. SKINNER: There is obviously some inherent  
11 risk in doing fluoroscopy on normal patients and patients  
12 with TMJ problems with implants in, and that sort of thing  
13 should be done with an IRB approval, preferably with an  
14 OPRR/IRB approval.

15 DR. CHRISTENSEN: I don't think other than the  
16 kinematic study, that we have been involved much, Dr.  
17 Skinner, in fluoroscopy of this joint other than maybe Dr.  
18 Curry might want to add to that, to examine those patients.

19 DR. CURRY: I don't have IRB approval, and I don't  
20 do fluoroscopy on all of my patients. I will say that  
21 following patients with total joint prostheses, particularly  
22 when you have metal-on-metal, is sometimes difficult with  
23 standard radiographic techniques, and occasionally I will  
24 take my patient to my hospital and do a short fluoroscopy  
25 and take a still picture because I get a better view of the

1 components, where I can angulate the patient where I feel  
2 that I get the best view rather than just sending them over  
3 a standard x-ray.

4 DR. SKINNER: But weren't there studies done with  
5 Doug Dennis' group looking at these patients under  
6 fluoroscopy, actually cinefluoro? Maybe I misread  
7 something.

8 MR. ALBRECHT: I am sorry, I was speaking to Dr.  
9 Gerard. Could you repeat the question, please?

10 DR. SKINNER: Weren't there studies done with Doug  
11 Dennis' group doing cinefluoroscopy on some of these  
12 patients?

13 MR. ALBRECHT: Not that I am aware of, no.

14 DR. JANOSKY: At this time, we will take a 15-  
15 minute break, returning at 10:25.

16 [Recess.]

17 DR. JANOSKY: We are continuing with the FDA  
18 presentations. There will be presentations by Dr. Susan  
19 Runner, Ms. Angela Blackwell, who is a biomedical engineer,  
20 and Dr. Murty Ponnappalli, who is a mathematical  
21 statistician.

22 **FDA Presentations**

23 DR. RUNNER: Good morning. I am not going to  
24 repeat my comments from yesterday on the history of TMJ  
25 Implants, but those should be taken into consideration, as

1 well, today.

2 [Slide.]

3 TMJ Implants, Inc., or the Christensen device has  
4 submitted a variety of data in support of the Premarket  
5 Approval Application for the various configurations of their  
6 temporomandibular joint prosthesis.

7 These include the total joint with a metal-on-  
8 metal articulation, a total joint with a PMMA-on-metal  
9 articulation, and glenoid-fossa prosthesis, and the patient-  
10 specific total joint with either a metal-on-metal or a PMMA-  
11 on-metal articulation.

12 The data, as you have heard, comes from a variety  
13 of sources including case studies, retrospective data,  
14 significant human experience, partially controlled studies,  
15 and a controlled clinical study that is now in progress.  
16 Endpoints in their studies included pain, function,  
17 intercisal opening.

18 Review of the data reveals that many of the data  
19 points on patients are missing at various time points.  
20 There also does not seem to be a sufficient number of data  
21 points to analyze data consistently beyond the 18-month  
22 point in a consistent fashion. The sponsor has thus  
23 analyzed some of the data into different cohorts to reveal  
24 patterns of success.

25 It is difficult, however, in our clinical review

1 of this data to separate out the various endpoints on  
 2 patients into pain, diet, and intercisal opening and get a  
 3 clear picture of the relative success or failure of any one  
 4 implant in the sponsor's armamentarium.

5 In our opinion, the sponsor has not adequately  
 6 separated the various implant types, i.e., partial versus  
 7 total, all-metal versus PMMA versus patient-specific, in  
 8 terms of the types of results that were achieved in the  
 9 clinical studies.

10 The prospective study does have plan for  
 11 collection of data that could delineate effectiveness of the  
 12 individual implant types, however, data from this study is  
 13 incomplete.

14 The engineering reviews, which you will hear more  
 15 about in a few minutes, have indicated deficiencies in the  
 16 way the sponsor has developed data on dynamic fatigue and  
 17 wear. These deficiencies relate to the absence of  
 18 information on failure of the device and inappropriate loads  
 19 during wear testing.

20 [Slide.]

21 The MDR reports on this device include reports of  
 22 failure including breakage of the condylar element and  
 23 reports of wear-through and fracture of the fossa element in  
 24 the metal-on-metal version of the appliance.

25 [Slide.]

1           Given the inappropriate nature of the engineering  
2 data and the equivocal nature of the clinical data, the data  
3 on failures and the concerns about safety related to these  
4 failures, I feel that the following items need to be  
5 addressed by the company.

6           TMJ Implants, Inc., has four major configurations  
7 of its TMJ prosthesis: the fossa-eminence prosthesis alone  
8 or partial; the total joint with PMMA condylar head; the  
9 total joint with all-metal configurations; and the patient-  
10 specific total joint.

11           The sponsor has not provided adequate separation  
12 of the data regarding safety and efficacy of these different  
13 configurations for the intended use as presented. The  
14 sponsor should provide data that addresses these implant  
15 types separately.

16           In summary, the sponsor should provide data on  
17 sufficient number of patients to demonstrate safety and  
18 effectiveness over at least a three-year time period.

19           Ms. Angela Blackwell will now proceed with the  
20 more detailed engineering review.

21           [Slide.]

22           MS. BLACKWELL: I am going to present the  
23 engineering review of TMJ Implants, Inc., PMA.

24           There were two engineering reviewers for this PMA,  
25 myself and Dr. Gary Fischman from the Office of Science and

1 Technology.

2 [Slide.]

3 The sponsor has deficient fatigue and wear testing  
4 based on our engineering review. In my presentation I will  
5 outline a summary of the data that was presented.

6 [Slide.]

7 The dynamic fatigue testing presented tested only  
8 two of the four configurations. It was tested at 2 Hz for 5  
9 million cycles, in bovine serum, with a sinusoidal load of 2  
10 to 35 pounds

11 [Slide.]

12 There were no failures and no S-N curve was  
13 generated.

14 [Slide.]

15 Literature references show a maximum bite force in  
16 the range of 300 pounds and an average bite force of 35  
17 pounds.

18 The TMJ surgical patient would have a decreased  
19 bite force secondary to loss of muscle attachment.

20 [Slide.]

21 But a load of 35 pounds gives no safety factor  
22 above the reported average bite force.

23 The partial prosthesis (the fossa used alone)  
24 needs to be tested in fatigue. Due to the fact that it is  
25 opposed by a natural condyle, the fatigue data on the

1 partial model cannot be extrapolated from one of the total  
2 joint prosthesis.

3 Justification for not testing the patient-specific  
4 model is also needed.

5 [Slide.]

6 Wear testing was conducted on the same two models  
7 as the fatigue testing, for 2 Hz, 2 million cycles, in  
8 bovine serum, with the same load, sinusoidal 2 to 35 pounds.

9 There was a comment earlier about that the load  
10 was sufficient. The problem with the load in this case was  
11 not the weight per pounds, it was the fact that it was a  
12 sinusoidal load, and for worst case for wear you want a  
13 constant load.

14 [Slide.]

15 The surface profile analysis showed a change of  
16  $0.197 \text{ mm}^3/\text{million cycles}$  for the metal-headed condylar  
17 prosthesis and a change of  $1.64 \text{ mm}^3/\text{million cycles}$  for the  
18 PMMA-headed condylar prosthesis.

19 [Slide.]

20 The testing needs to be redone with a higher  
21 average load, constant as opposed to sinusoidal.

22 Justification for not testing the patient-specific  
23 model is needed, and wear testing is needed for the partial  
24 joint prosthesis (fossa used alone). The same problem as  
25 before, because it has a natural condyle opposed to it, it

1 is a different situation.

2 [Slide.]

3 Pin-on-disk testing was also presented although  
4 this was a little unclear. I had previously looked at a  
5 report in a 510(k) that was pin-on-disk testing, but that  
6 report didn't appear in the PMA. There appeared to be one  
7 that was similar that went for a longer period of time, but  
8 when the reports were compared, the data points didn't match  
9 up. So, it must two different tests run by the same lab.

10 But both of the tests used a 50-pound load.

11 [Slide.]

12 Both reports showed that the volume and weight  
13 they reported would remove a large portion of the PMMA head  
14 in 2 million cycles. If the test was run out to 10, it is  
15 possible that the metal posts would be exposed.

16 I know there was a discussion about that earlier,  
17 about the metal posts being exposed, and from our point of  
18 view, if the head was worn off and the metal post was  
19 exposed, that is a failure.

20 [Slide.]

21 The fossa and condyle are not matched components -  
22 they usually demonstrate point contact.

23 [Slide.]

24 Orthopedic literature suggests that close  
25 tolerances and a tight fit are necessary for a good total

1 joint, particularly on metal-on-metal systems.

2 [Slide.]

3 The company needs to address this concern and  
4 justify why the design has not changed to address this  
5 issue.

6 Thank you.

7 DR. PONNAPALLI: Murty Ponnappalli.

8 [Slide.]

9 I am going to look at the statistical aspects of  
10 this submission.

11 [Slide.]

12 As you know by now, there are several different  
13 sources of data given in this submission. Those are given  
14 in this slide.

15 The primary efficacy parameters in this study are  
16 reduction in pain, measured in 10 cm VAS, and interincisal  
17 opening, measured in mm.

18 The secondary efficacy parameter is reduction in  
19 diet restriction, measured in 10 cm VAS.

20 [Slide.]

21 In my opinion, not all of these throw much light  
22 on the effectiveness of the device. My concentration is  
23 going to be on the effectiveness because the safety data are  
24 not amenable to statistical analysis.

25 In my opinion, the data from registry given here,

1 are given in this slide, the most important to determine the  
2 effectiveness. The first one is Cohort 1 of 284 patients.  
3 These 284 patients, there is data on pre-op levels, 6-month  
4 level, and 24-month levels of pain.

5 The study is done on this cohort by means of the  
6 so-called repeated measure ANOVA F-test. These are repeated  
7 measures because the same patients are observed for all  
8 different time points, and that gives significant  
9 difference. Because there is a significant difference in  
10 the sample averages given in the first row.

11 They are decreased over 24 months. It is a  
12 reasonable conclusion to make that the pain level decreases.  
13 Also, another important point here is the comparison between  
14 pre-op levels and cross-section mean.

15 For example, for this cohort it is 7.7 as the pre-  
16 op, and the cross-section mean is 7.9. They are fairly  
17 close, very close, in fact, and the same thing is true of 6-  
18 month and 24-month.

19 But there is a limitation to this because the  
20 cross-section mean 7.9 is not based on all the 4,000  
21 patients, approximately 4,000 patients. It is based on  
22 approximately 2,000 patients, only about half of them,  
23 because the remaining ones, we don't have data on the  
24 remaining ones.

25 This could introduce some bias, but because of

1 lack of data if you regard these 284 patients as the whole  
2 sample, then, the result is favorable. The conclusion is  
3 that the pain level is decreasing.

4 [Slide.]

5 Then, we go to Cohort 2-pain. Here, we have many  
6 more time points. There are only 60 patients. You can see  
7 from the row here. But it is because there are many more  
8 time points, and this is a subset of the Cohort 1, this  
9 cohort of 60 patient is a subset of Cohort 1.

10 Again, we again perform repeated measures ANOVA F-  
11 test, which gave a highly significant p-value which  
12 indicates the pain level is decreasing. Again, you can see  
13 from the row of means and the cross-section of the means  
14 that these two in every case, at every time point, almost  
15 every time point, these two are pretty close to each other.

16 [Slide.]

17 So, these were about pain. Now we go to the  
18 opening. It turns out that the data are at pre-op, 6  
19 months, and 24 months are available on 265 patients. Again,  
20 we use repeated measures and ANOVA F-test. It showed highly  
21 significant value and a reasonable conclusion is that the  
22 opening is increased this time, because we can see that it  
23 is increasing.

24 Again, compared the pre-op level of the sample  
25 with the cross-section mean, a sample mean with the cross-

1 section mean. It is fairly close to each other. Again,  
2 that limitation to the cross-section mean applies. It is  
3 not the whole set of patients, but approximately only half  
4 the patients.

5 [Slide.]

6 It still is the same with Cohort 2. The number of  
7 time points is much larger. We go up to three years, and  
8 the repeated measures and ANOVA F-test shows highly  
9 significant difference, and the limitation again is that for  
10 the cross-section mean we don't have the data on all the  
11 patients.

12 [Slide.]

13 Our review team thought that the data should be  
14 subdivided into metallic condyle, PMMA condyle, and patient-  
15 specific prosthesis. So, we asked the sponsor to analyze  
16 these subsets, so this gives the data on metallic condyle.

17 Note that this is not a cohort. If you look at  
18 the numbers you see that they go on decreasing. It is not  
19 the same cohort of patients. The patients there at one  
20 month, some of them are there at six months, and some of  
21 them are not there. The patients at six months, some of  
22 them at one month, but some others were not there.

23 Statistical analysis of data of this type is  
24 rather difficult. We cannot use the ANOVA F-test, for  
25 example, because there is difference. We cannot use

1 repeated measures in ANOVA F-test because it is not the same  
2 cohort.

3 But if you look at the first row, for example, the  
4 pain level is decreasing, but there are statistical  
5 limitations to this conclusion, as I just pointed out. The  
6 same thing about diet, the same thing is about opening. To  
7 test it statistically is difficult.

8 [Slide.]

9 Now, I go to patients with PMMA condyle. The  
10 situation is the same here. It is not the same cohort as  
11 you can see from these numbers here. But in the sample, you  
12 can see that the pain level is decreasing up to 12 months.  
13 At 12 months it is somewhat stable.

14 Diet, when I say diet I mean diet restriction,  
15 diet restriction is decreasing up to approximately 12  
16 months, and from there it is stable. Opening is increasing  
17 up to I would say approximately 12 months, and then it is  
18 stable. Again, statistical tests for statistical  
19 significance are difficult.

20 [Slide.]

21 Now, I go to patients with patient-specific  
22 prosthesis. Also, you can see from the numbers again that  
23 it is not the same cohort, and also that pain is decreasing  
24 in the sample. We don't know whether it is statistically  
25 significant or not up to approximately 12 months, and stable