

UNITED STATES OF AMERICA

\* \* \*

FOOD AND DRUG ADMINISTRATION

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

OFFICE OF DEVICE EVALUATION

\* \* \*

DENTAL PRODUCTS PANEL

\* \* \*

MEETING

\* \* \*

THURSDAY,

AUGUST 22, 2002

\* \* \*

The Panel met at 8:00 a.m. in the Whetstone/Walker Rooms of the Gaithersburg Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, Maryland, Dr. Leslie Heffez, Chairperson, presiding.

PRESENT:

LESLIE HEFFEZ, D.M.D., M.S., Chairperson

KRISTI ANSETH, Ph.D., Member

**NEAL R. GROSS**  
COURT REPORTERS AND TRANSCRIBERS  
1323 RHODE ISLAND AVE., N.W.  
WASHINGTON, D.C. 20005-3701

PRESENT (Continued):

PETER BERTRAND, D.D.D., Consultant

RICHARD BURTON, D.D.S., Consultant

DAVID COCHRAN, D.D.S., Ph.D., Member

JAN E. FAULK-EGGLESTON, D.D.S., Consultant

ELIZABETH R. HELMS, Patient Representative

EDMOND R. HEWLETT, D.D.S., Member

ELIZABETH HOWE, Consumer Representative

JANINE JANOSKY, Ph.D., Consultant

STEPHEN LI, Ph.D., Consultant

MARK PATTERS, D.D.S., Ph.D., Consultant

ELIZABETH DIANE REKOW, D.D.S., Member

DANIEL SCHECHTER, J.D., Industry Representative

JON B. SUZUKI, D.D.S., Ph.D., Member

PAMELA D. SCOTT, Executive Secretary

## C-O-N-T-E-N-T-S

|   | PAGE |
|---|------|
| Introductions .....   | 4    |
| Conflict of Interest Statement .....                                    | 6    |
| Sponsor Presentation:   |      |
| Introduction, Joel Pratt .....  | 10   |
| Device Description and Mechanical Testing<br>Summary, Shawn Roman ..... | 11   |
| Clinical Investigation:   |      |
| Dr. Peter Quinn .....   | 20   |
| Mary Verstynen .....  | 33   |
| FDA Presentation:   |      |
| Introduction, Dr. Susan Runner .....                                    | 114  |
| Engineering Review, Angela Blackwell .....                              | 116  |
| Clinical Review, Dr. Kevin Mulry .....                                  | 119  |
| Questions to the Committee .....  | 128  |
| Presentation of Primary Reviewers:                                      |      |
| Dr. Diane Rekow .....   | 162  |
| Dr. Richard Burton .....  | 165  |
| Dr. Janine Janosky .....  | 175  |
| Open Committee Discussion .....   | 179  |
| Public Comment, Terry Cowley .....                                      | 282  |
| Open Committee Discussion and Voting .....                              | 283  |

1 P-R-O-C-E-E-D-I-N-G-S

2 (8:04 a.m.)

3 MS. SCOTT: Good morning, good morning. I'd like  
4 to welcome everyone to the Dental Products Panel meeting.

5 Before we get into our topic for today I would like  
6 to introduce our panel, and then I have a conflict of interest  
7 statement to read into the record.

8 My name is Pamela Scott. I'm the Executive Secretary  
9 for the Dental Products Panel.

10 Our Chair is Dr. Leslie Heffez. He's Professor and  
11 department head of oral and maxillofacial surgery at the University  
12 of Illinois at Chicago.

13 And as I call out the panel members and panel  
14 consultants' names, if you could just raise your hand so that people  
15 know who you are, we have

16 Dr. Kristi Anseth. She's Patten Associate Professor with the  
17 Department of Chemical Engineering at the University of Colorado.

18 We have Dr. David Cochran, who's Professor and chair  
19 of the Department of Periodontics at the University of Texas, Health  
20 Science Center at San Antonio.

21 We also have Dr. Edmond Hewlett, who is Associate  
22 Professor in the Division of Cardiology and Restorative Dentistry,

1 University of California at Los Angeles School of Dentistry.

2 We have Dr. Diane Rekow, who is Director of  
3 Translational Research and Professor of Orthodontics with the New  
4 York University College of Dentistry.

5 We also have Dr. Jon Suzuki, Professor, School of  
6 Dental Medicine at the University of Pittsburgh.

7 Our consumer representative is Ms. Elizabeth Howe.  
8 She's Outreach Coordinator with the National Foundation for  
9 Ectodermal Dysplasia

10 Our industry representative is Ms. Daniel Schechter.  
11 He's General Counsel with Parkell, Incorporated.

12 We also have Ms. Elizabeth Helms, who is serving  
13 as our patient representative for this panel. She is President  
14 of the TMJ Society of California.

15 We also have Dr. Peter Bertrand, who is the Director  
16 of the Orificial Pain Clinic and specialty advisor for oral facial  
17 pain and TMD with the National Naval Medical Center.

18 We have Dr. Richard Burton, who is Professor of Oral  
19 and Maxillofacial Surgery with the Department of Hospital Dentistry  
20 at the University of Iowa Hospital and Clinics.

21 We also have Dr. Janine Janosky who is Associate  
22 Professor, Division of Biostatistics with the University of

1 Pittsburgh, Department of Family Medicine and Clinical  
2 Epidemiology.

3 We have Dr. Stephen Li, who is President of Medical  
4 Device Testing and Innovations.

5 We also have Dr. Mark Patters, who's Chair of the  
6 Department of Periodontology, College of Dentistry, University  
7 of Tennessee.

8 And we have Dr. Jan Faulk-Eggleston, Chief of the  
9 Oral and Maxillofacial Surgery Service with the Brooke Army Medical  
10 Center.

11 At this time I'll read into the record our conflict  
12 of interest statement for the Dental Products Panel meeting of  
13 August 22nd, 2002.

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

17 The determine if any conflict existed, the agency  
18 reviewed the submitted agenda for this meeting and all financial  
19 interests reported by the committee participants. The conflict  
20 of interest statutes prohibit special government employees from  
21 participating in matters that could affect their or their  
22 employer's financial interest.

1                   The agency has determined, however, that the  
2 participation of certain members and consultants, the need for  
3 whose services outweighs the potential conflict of interest  
4 involved is in the best interest of the government.

5                   We would like to note for the record that the agency  
6 took into consideration a matter regarding Dr. Stephen Li, who  
7 reported a past interest in a firm at issue, but in a matter that  
8 is not related to today's agenda. The agency has determined that  
9 he may participate fully in all deliberations.

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

15                  With respect to all other participants, we ask in  
16 the interest of fairness that all persons making statements or  
17 presentations disclose any current or previous financial  
18 involvement with any firms whose product they may wish to comment  
19 upon.

20                  And before I turn it over to Dr. Heffez, I also would  
21 like to introduce Dr. Susan Runner, who is the Branch Chief of  
22 the Dental Devices Branch within the Division of Anesthesiology,

1 Infection Control, General Hospital, and Dental Devices.

2 I got that right. We just changed our division name.

3 (Laughter.)

4 MS. SCOTT: Dr. Heffez.

5 CHAIRMAN HEFFEZ: I'd like to proceed to the open  
6 public hearing. Those who wish to speak should state their name,  
7 state their affiliation, and any specific financial interest.

8 We've reserved 30 minutes for this period of time,  
9 and I'll ask if there's anybody in the audience who would like  
10 to come to the podium.

11 (No response.)

12 CHAIRMAN HEFFEZ: Nobody had signed up previously,  
13 despite the advertisement of this meeting, and I don't see anyone  
14 coming to the podium. So we'll proceed then to the industry  
15 presentation.

16 The industry presentation will last one hour, and  
17 I will hold you to the time.

18 MR. PRATT: Good morning. My name is Joel --

19 CHAIRMAN HEFFEZ: Excuse me. Excuse me, sir.

20 Prior to your start, I would just want to have Pamela  
21 Scott list the members and who are voting members for this  
22 committee.



1 MS. SCOTT: I apologize. I need to read into the  
2 record those panel consultants who are deputized to vote during  
3 this meeting.

4 Appointment to temporary voting status, pursuant  
5 to the authority granted under the Medical Devices Advisory  
6 Committee charter, dated October 27th, 1990, as amended April 20th,  
7 1995, I appoint the following people as voting members of the Dental  
8 Products Panel for this panel meeting on August 22nd, 2002:

9 Dr. Peter Bertrand

10 Dr. Richard Burton

11 Dr. Janine Janosky

12 Dr. Stephen Li

13 Dr. Mark Patters

14 Dr. Jan Faulk-Eggleston

15 For the record, these people are special government  
16 employees and are consultants to this panel under the Medical  
17 Devices Advisory Committee. They have undergone customary conflict  
18 of interest review. They have reviewed the material to be  
19 considered at this meeting.

20 Signed, David Feigal, M.D., Director, Center for  
21 Devices and Radiological Health, August 19th, 2002.

22 Thank you.

1 CHAIRMAN HEFFEZ: Mr. Pratt, you may begin.

2 MR. PRATT: Thank you.

3 Good morning. I am Joel Pratt with Lorenz Surgical,  
4 and I will briefly show you a couple slides to start our  
5 presentation.

6 This is sponsored by Biomet, Incorporated. Biomet  
7 consists of a number of different subsidiaries that address  
8 different orthopedic and musculoskeletal specialties. So within  
9 that framework, as you can see by the customers and their  
10 specialization, this would be considered a Lorenz product.

11 Attending today from management are those listed  
12 from both Biomet and from Lorenz, several of whom will be speaking.

13 We have two clinicians present: Dr. Peter Quinn from Philadelphia,  
14 Pennsylvania, and Dr. Douglas Sinn from Dallas, Texas.

15 We are asking approval for the Lorenz TMJ, which  
16 is a total joint replacement for the temporomandibular joint, and  
17 the indications we are pursuing are arthritis, malignancy, benign  
18 neoplasms, functional deformity, revision procedures, avascular  
19 necrosis, ankylosis, degenerated or resorbed joints, fracture,  
20 multiply operated joints, and developmental abnormality.

21 MR. ROMAN: Good morning. My name is Shawn Roman,  
22 and I am the development engineer currently working with the TMJ

1 total joint replacement system at Walter Lorenz Surgical.

2 I will be presenting a description of our device,  
3 as well as a summary of all of the mechanical testing that has  
4 been performed.

5 The TMJ total joint replacement system is a two  
6 component system that comprises mandibular fossa components, as  
7 well as a glenoid fossa component. The purpose of the fossa  
8 component is to replace the glenoid fossa of the temporal bone.

9 Our fossa components are machined from ultra high  
10 molecular weight polyethylene and are offered in three sizes,  
11 small, medium, and large, both the right and left side anatomy.

12 We currently offer two different designs in the sizes  
13 mentioned. The original design included a post on the superior  
14 surface of the implant. We added a second design without the post  
15 in February of 2002, and both designs are secured to the zygomatic  
16 arch using self-tapping, two millimeter diameter fossa screws made  
17 from Titanium 64 alloy. We also offer 2.3 millimeter diameter  
18 screws as emergency screws.

19 This slide shows the difference between the two  
20 designs. The design on the left obviously has a small post  
21 protruding from the superior surface of the implant. This post  
22 was included in the original design to act as an additional

1 anchoring method when using bone cement or other approved  
2 cranio-maxillofacial filler materials to fill spaces between the  
3 fossa prosthesis and the glenoid fossa bone.

4 Both designs include an undercut groove on the  
5 superior surface of the implant, which also offers a securing area  
6 for bone filler material.

7 So, therefore, both designs can be used with or  
8 without filler material. It has been found that the design without  
9 the post is easier to place and requires the removal of less bone.

10 The purpose of the mandibular components is to  
11 replace the articulating mandibular condyle located at the proximal  
12 end of the mandibular ramus.

13 We currently offer three different designs or --  
14 I'm sorry -- our mandibular components are machined from  
15 cobalt-chromium-molybdenum alloy. The ramal portion of the  
16 mandibular component has a roughened titanium plasma spray coating  
17 on the medial surface. This plasma spray coating consists of the  
18 Ti-64 alloy.

19 We currently offer three different designs: a  
20 standard, narrow, and offset. I will go into these in a little  
21 bit more detail with the aid of some slides, but all three designs  
22 are offered in five different sizes for both the left and right

1 side anatomy.

2 We started with the narrow design, added the standard  
3 design in January of 2000, and added the offset design in February  
4 of 2002.

5 All three designs are secured to the mandibular bone  
6 using self-tapping 2.7 millimeter diameter mandibular screws made  
7 from Ti-64 alloy. The 3.2 millimeter diameter screws are offered  
8 as emergency screws.

9 Here you can see the difference between the standard  
10 design and the narrow design. As I mentioned, we started with  
11 the narrow design. We added the standard design in January of  
12 2000 to add additional screw hole options to allow for placement  
13 of the mandibular screws in the best bone possible.

14 This slide shows the difference between the standard  
15 design and the offset design, the only difference being that on  
16 the standard design the spherical head is offset to the medial  
17 side of the ramal plate. In the offset design, the spherical head  
18 is offset to the lateral side of the ramal plate.

19 The offset design was added to allow for medial  
20 lateral or to accommodate for medial lateral discrepancies between  
21 the fossa components and the mandibular components.

22 This is a list of a summary of all the testing that

1 was completed, all of the mechanical testing completed on these  
2 joints. I won't cover these in detail here because I discussed  
3 them in detail throughout the rest of the presentation.

4 Basically we performed three different series of  
5 fatigue testing to insure that the mandibular fossa construct could  
6 withstand the loading seen in the TM joint.

7 The same testing protocol was used for all three  
8 series of testing. Basically the protocol consisted of cyclic  
9 compressive testing, compressive loading of the mandibular  
10 component against the fossa component.

11 We incorporated three different conditions into the  
12 testing protocol to simulate worst case situations. First of all,  
13 the mandibular component was secured below the center line of the  
14 first screw hole to simulate a patient with a large portion of  
15 the ramus removed or missing.

16 The mandibular component was also tilted at ten  
17 degrees to induce a large bending moment in the ramal plate, and  
18 we selected a maximum load of 145 pounds because this loading was  
19 documented in the literature to be the loading seen in patients  
20 with normal musculature that had not undergone previous TMJ  
21 surgeries. This load would obviously be excessive for patients  
22 who had undergone TMJ surgery.

1                   This is just a schematic of the test set-up. The  
2 mandibular component was potted to the bottom test fixture, fossa  
3 component potted to the top test fixture. The bottom test fixture  
4 was held stationary while the top test fixture was cycled at ten  
5 to 30 Hertz.

6                   I included this slide just to show that there was  
7 clearance milled into the top test fixture to allow or to  
8 accommodate for the post on the fossa component. The area around  
9 the post was -- there was bone cement placed in the area around  
10 the post to simulate surgical application in all of the fatigue  
11 testing done.

12                   In the first series of fatigue testing, we tested  
13 the original design of the components, tested five different  
14 joints. All of the five joints made it out to ten million cycles  
15 with no failures.

16                   Although in this first series of testing bone cement  
17 was used, the condition of the bond cement after the testing was  
18 not documented. So we ran a second series of fatigue testing that  
19 looks specifically at the effects of fatigue on the bone cement.

20                   Another five samples were tested. All five of the  
21 joints made it through ten million cycles with no failures, and  
22 there was no fragmenting or chipping of the bone cement noted.

1                   The third round of fatigue testing looked at design  
2 enhancements that were made to the mandibular components. These  
3 design enhancements included adding the titanium plasma spray  
4 coating to the medial side of the implant and also increased the  
5 screw holes slightly in diameter.

6                   Another five samples were tested. Again, all five  
7 samples made it to ten million cycles without failure.

8                   We performed static testing on the mandibular  
9 component to determine the amount of force required to fracture  
10 the condylar neck of the design, and in this testing the mandibular  
11 component was fixated to bovine tibial bone using four 2.7  
12 millimeter diameter mandibular screws.

13                   A direct force, direct Allen force was then applied  
14 to spherical head until failure of the component. The failure  
15 mode that was seen was not fracture of the condylar neck, but rather  
16 the neck portion bent with no breakage at 576 pounds.

17                   This loading or these results were deemed acceptable  
18 because this loading is three and a half times larger than the  
19 145 pounds joint loading discussed earlier in the fatigue testing.

20                   We also performed pull through testing on the fossa  
21 screws to determine the amount of force required to pull them  
22 through the fossa flange. In this testing, test specimens



1 representing the fossa screws were pulled through a polyethylene  
2 sheet made of the same material as the fossa component. This  
3 polyethylene sheet was the same thickness as the fossa flange.

4 Basically a downward force was applied to the test  
5 specimens until they were pulled through the polyethylene.

6 This just shows that there was clearance underneath  
7 the fixture to pull those test specimens through.

8 They pulled through at an average load of 80 pounds.

9 This was deemed acceptable because this was well above what would  
10 be seen in vivo.

11 We also performed compressive testing on the fossa  
12 flange to determine the amount of force required to fracture the  
13 flange. In this testing, we attached the fossa component to wooden  
14 blocks using only two of the 2.0 diameter fossa screws.

15 A direct force was then applied to the articular  
16 surface of the fossa component.

17 This is a close-up just showing that we simulated  
18 a worst case by not supporting the side of the fossa component  
19 opposite the articular surface.

20 The failure mode that was noticed during this testing  
21 was, again, not fracture of the fossa or fossa flange, but rather  
22 the fossa flange collapsed or bent at an average load of 83 pounds.

1                   This, again, was deemed acceptable because this was  
2 a worst case test in vivo that you would have the support of the  
3 temporal bone on the side opposite the articular surface.

4                   The final mechanical testing that was performed was  
5 pull-out testing on the 2.7 millimeter mandibular screws. In this  
6 testing, the mandibular screws were inserted through a test fixture  
7 into bovine cortical bone. Then an upward force was applied to  
8 the test fixture until the screws were removed from the bone.

9                   This occurred at an average pull-out strength of  
10 373 pounds. This, again, was deemed acceptable because this loading  
11 was well above what would be seen in vivo.

12                   So in summary, we performed three different series  
13 of fatigue testing with a total number of 15 joints. All 15 joints  
14 made it to ten million cycles without failure. In the static testing  
15 of the mandibular component condylar neck bent at an average loading  
16 of 576 pounds.

17                   The pull through test on the fossa screws showed  
18 an average pull through strength of 80 pounds. The compression  
19 of the fossa flange showed that the fossa flange bends at an average  
20 of 83 pounds, and on the pull-out testing of the 2.7 millimeter  
21 screws, there's an average pull-out of 373 pounds.

22                   DR. QUINN: Good morning. My name is Peter Quinn.

1 I'm the Chairman of Oral Surgery at University of Pennsylvania,  
2 and along with Doug Sinn I'd like to stand for a second.

3 We performed the majority of the surgeries in this  
4 study. Doug is the Chairman at the University of Texas Southwest  
5 in Dallas.

6 While I'm waiting for this to boot, I thought what  
7 we might do is look at some of the surgical aspects of this joint  
8 because I think it will help us to understand the development,  
9 and I know there are three surgeons on the panel, but for the  
10 non-surgeons, I thought it would be helpful to look at the unique  
11 aspects of this joint which actually have implications for how  
12 it was designed.

13 We began the design process in 1991 and enrolled  
14 the first patient in 1995. This is the prosthesis with the  
15 polyethylene fossa and cobalt chrome ramal component.

16 I would just like to point out at the beginning the  
17 reasons for pursuing this is that we feel strongly that a prosthetic  
18 joint does have advantages, and on the left they really are in  
19 terms of a quality improvement standpoint lack of donor site  
20 morbidity, reduced intraoperative time, a potential for decreased  
21 hospitalization, and immediate functional ability as opposed to  
22 grafts, autogenous grafts.

1                   Also, you can maintain the occlusion or actually  
2 change it as you'll see, which is an opportunity you get with a  
3 prosthesis over an autogenous graft, the opportunity to manipulate  
4 the design to discourage heterotopic bone formation, and again,  
5 the opportunity to correct occlusion.

6                   These I think are extremely important because we  
7 still do a large number of autogenous rib grafts in children, and  
8 we believe that that is the procedure of choice in the skeletally  
9 immature patient.

10                   In the skeletally mature patient with an acceptable  
11 indication, we think there should be a safe and efficacious stock  
12 prosthesis. We also believe firmly that in patients who are  
13 anatomically mutilated, who have undergone multiple operations  
14 where this stock prosthesis or any would not be appropriate, we  
15 use a CAD-CAM 3D construction by TMJ Concepts, which we also think  
16 is a very safe and effective prosthesis.

17                   The relative contraindications for the alloplastic  
18 joint is allergy, and we'll see we've had two patients with nickel  
19 allergy where we have FDA approval to use titanium instead of cobalt  
20 chromium; chronic infection; skeletal immaturity, as I've  
21 mentioned; and any systemic disease that would increase the risk  
22 of infection.

1                   Now, briefly, and I usually talk fast, but I'll talk  
2 faster today, I just wanted to show you the unique aspects because  
3 I do think after 22 years I have been humbled by this joint. It  
4 is a unique joint in its mechanics and also in terms of its approach  
5 because when I watch my orthopedic colleagues, they're able to  
6 make bigger incisions and see the entire construct.

7                   We are always working in a tunnel between the facial  
8 nerve, and the other issue we have to deal with is the vasculature.

9                   So this is a standard procedure with a modified face lift or  
10 rhytidectomy incision to place the fossa in a posterior mandibular  
11 incisions, to place the ramal component.

12                  I'm going to go through these just because I do think  
13 after Shawn's presentation we can understand the design based on  
14 the surgical technique, and once the preauricular and posterior  
15 mandibular incisions are made, I think the first thing you will  
16 note is the thickness of the fossa which is dictated by the minimal  
17 thickness that you can have in polyethylene to have sufficient  
18 wear resistance.

19                  That does push condylion, which is the point of  
20 rotation. The normal condyle is higher, and you'll see in some  
21 radiographs that it just pushed that point out.

22                  It also means that we remove more bone in the superior

1 surface than other joints. This is a standard condylectomy  
2 osteotomy cut. This actually is still performed for ankylosis  
3 where the condyle is just removed and nothing is replaced, which  
4 we don't think is indicated.

5 In this joint we use a two-step osteotomy where we  
6 remove the upper part of the condyle. Then in the space created  
7 by that cut, we push the ramus up, which is a safer way of removing  
8 further bone, to accommodate the fossa, and in multiply operated  
9 patients, we remove the coronoid because it gives them a greater  
10 opening.

11 Special instruments have been designed, and thee  
12 are condylar retractors, and what these are protecting against  
13 is the internal maxillary artery that runs medial to the neck of  
14 the condyle, and these are designed to avoid any damage to that.

15 Here's a standard cut through an ankylose joint,  
16 and you can see we don't like to instrument more inferior here  
17 because of the facial nerve that's coming through the junction  
18 of the auricle. So what we do is remove the upper portion.

19 The lower incision has been made. You can just see  
20 the hint of it here, for two reasons. If there's any bleeding,  
21 we can control it from the lower incision by ligating branches  
22 of the carotid.

1                   And, secondly, once this portion is moved, we  
2                   literally move the ramus up and remove what other additional bone  
3                   may have to be removed to fit the fossa.

4                   As Shawn said, this is an ultra high molecular weight  
5                   polyethylene in the fossa. It was designed to have maximum mating  
6                   between the condyle and the fossa. Remember this is a ginglimal,  
7                   arthrodial joint that both rotates and translates. Prosthetic  
8                   joints only rotate because we are going to remove the lateral  
9                   pterygoid head.

10                  I'm going to talk about the PMMA because it was used  
11                  early in the study. We have not place PMMA cement after 1998.  
12                  What we did in the early cadaver studies when we designed the joint  
13                  was found that over 70 percent of the variability in the human  
14                  temporomandibular joint is in the articular eminence.

15                  So this implant is designed to flatten the articular  
16                  eminence, and there are specially designed burrs to do that, which  
17                  flatten the articular eminence to give you tripod stability of  
18                  the fossa implant.

19                  And here is an articular eminence that has been  
20                  flattened, and as you'll see, the burr was designed not only to  
21                  take the eminence off, but to give you the radial curve of the  
22                  implant itself.

1                   This is a fossa and the condyle in position. In  
2 terms of timing, we actually place the fossa, and then go back  
3 and put the patient in fixation, and this is, again, what's unique  
4 to this joint as opposed to orthopedic joints.

5                   Here's a picture of the fossa with the burr design,  
6 and this was one of the major reasons why we're able to discontinue  
7 the use of the cement because after the fit got better and better  
8 with time, we were using less than one cc of PMMA, and it did not  
9 seem to be appropriate to continue its use.

10                   These are sizers, and this fossa is in three  
11 different sizes. What is uniform is the articulating surface.  
12 This doesn't change.

13                   What does change is the number of preconstructed  
14 holes to give you options in the zygomatic arch.

15                   Again, in the beginning of this study, we were  
16 approved to use PMMA only for void filling. Our original intent  
17 was to ultimately replace it, but we have stopped using it  
18 completely because it was designed in the beginning -- this is  
19 one of the first devices we used in the laboratory. You can see  
20 what the peg was used for in terms of retention. Other than that  
21 it has no role.

22                   So once the fossa is placed in position we then put



1 the patient in fixation. This is work done in the Netherlands  
2 in 1993, which determined that if you move the point of rotation  
3 inferiorally -- and these are cadaver studies that we first did  
4 in 1992 -- there was some pseudo translation. The jaw is being  
5 opened on the right, and you can see there's almost a ramping,  
6 gliding effect of this prosthesis, which is not true translation  
7 which you can only get with a lateral pterygoid muscle.

8 In this slide you can see these are TMJ implants  
9 incorporated. This is a metal to metal joint that had to be removed  
10 because of metallosis and foreign body reaction, but what you  
11 see is when it's replaced with the Lorenz, that you've lowered  
12 the point of rotation. If you compare where a normal condyle and  
13 even this prosthetic condyle seats in an inferior/superior  
14 component.

15 The condylar component, again, is a cobalt chromium.

16 It's secured with 2.7 millimeter screws. This is the narrow  
17 design, and we have both designs because we do see a patient  
18 population who on the average has over five surgeries, and some  
19 as many as 29 surgical procedures.

20 In those cases we did come up with a broader footplate  
21 here to give us more options to put screws because in some of these  
22 rami there are multiple screw holes. There's damage to the cortical

1 bone from previous rib graphs.

2 You can see an ankylose joint here that's been  
3 replaced with the standard design. This is the approach to place  
4 the lower component or the condylar component, and you can see  
5 we get complete visibility of the ramus, and we can place all of  
6 the screws through this lower incision.

7 The other aspect that Shawn mentioned is this Swan  
8 neck design, and this does differ from all of the -- some of the  
9 other prosthetic joints that have a right angle, a 90 degree bend  
10 at the condylar head, and that somewhat assumes that you can predict  
11 where the osteotomy cut will be, which is usually not the case.

12 This allows you to have some medial lateral change  
13 by moving this condylar up and down, and it allows you to change  
14 the medial lateral position somewhat by altering the bone at the  
15 superior edge of the ramus.

16 It's in contrast to some other joint prostheses that  
17 have been used. Briefly, this is the Kent-Vitek. This was Synthes.

18 This is Delrin Timesh. This is Christensen I, with an acrylic  
19 head, and Christensen II, with an acrylic head. And you can see  
20 part of the difference is the angulation, and this mimics the  
21 angulation of the normal condyle at approximately 20 degrees.

22 So the mating is spherical. We made the condylar

1 head as large as possible to give us a greater surface area for  
2 the load distribution. These are the templates we use to determine  
3 what size condylar component we'll use.

4 And you can see here a patient who has had -- this  
5 patient actually had 16 operations. These are two failed rib graphs  
6 that you can see have detached completely from the ramus and are  
7 free floating, and this is the wider design because in these  
8 patients who have had multiple surgery, we sometimes wind up with  
9 poor quality cortical bone on the ramus.

10 The current available lengths of the prosthesis are  
11 45, 50, and 55, and this is the standard design. What this allows  
12 you to do is if there's damage to cortical bone with a preoperative  
13 X-ray that you can determine where the inferior alveolar nerve  
14 is, you are able to place screws anterior and posterior to the  
15 nerve and find better cortical bone where it has been destroyed  
16 by previous surgery.

17 Again, after the fossa is placed, we place the  
18 patient into intermaxillary fixation because there is very little  
19 leeway in the placement of these joints. In my clinical experience,  
20 there's about 25 to 30 percent of the time we literally change  
21 the position of the condyle after checking the occlusion and the  
22 range of motion.

1                   It's originally placed with two screws only, and  
2 if you remember, the other unique thing here is we are in and out  
3 of the mouth. We're in and out of from a sterile to a non-sterile  
4 field.

5                   So we place the condylar prosthesis tentatively,  
6 check the range of motion, and then only secure it when we're happy  
7 with it. We have designed some special sterile mandibular  
8 manipulators that allow the surgeon to move the mandible and check  
9 the actual mechanics of the joint, but it clearly has to be checked  
10 before the final screws are placed in the condylar prosthesis.

11                   This is a patient who is four months out. You can  
12 see these rhytidectomy incisions can be hidden rather well in the  
13 preauricular crease and in the post mandibular crease.

14                   Lastly, just an example of a patient, the type of  
15 patient we see. This is a 28 year old male who had bilateral condylar  
16 fractures as a child, I would guess anywhere between seven and  
17 eight years of age, just given the retrognathia. He is completely  
18 fused. There's no oral opening at all.

19                   He's had four operations. Most of them are gap  
20 arthroplasties, which is the standard way of just going in and  
21 cutting it, all of which refuses. And you can see he's completely  
22 fused to the base of the skull.

1                   This is a case where even though we used a lot of  
2 custom joints, even this one, I think, would be difficult because  
3 it would be difficult to somewhat predict exactly where your surgery  
4 cuts would be because of the massive amount of bone here that is  
5 fusing him to the base of the skull.

6                   The other thing we mentioned earlier is the ability  
7 -- and you only have this ability with bilateral prostheses. You  
8 can't do it with the unilateral prosthesis -- is to change the  
9 occlusion. Once the mandible is freed, if you're going to place  
10 bilateral joints, you can bring the mandible forwards or backwards,  
11 and you can change the preexisting occlusion, which I think is  
12 a major advantage of prosthetic joints.

13                   And you can see here that we do remove large amounts  
14 of bone because we do have concern of heterotopic bone. When I  
15 discuss adverse events, you'll see our reasonable goal for entrance  
16 size of opening is approximately 30 to 33. Remember normal opening  
17 in an adult can be 45 to 53. We don't achieve that because these  
18 joints only rotate. They don't translate.

19                   So that's what we think is a reasonable outcome.  
20 We have complications just briefly. I'll show you the two that  
21 I think are most vexing, but you'll see the numbers are more than  
22 acceptable -- is infection. This is a fistula that has developed.

1 The fossa had to be removed, and after a protracted course of  
2 IV antibiotics, we were able to reinsert one.

3 That's not always the case, as I'll show you later,  
4 and I think one of the most difficult problems we have is heterotopic  
5 bone, as the orthopedic surgeons do as well. This is a young African  
6 American female who has got horrific keloids, and I think that  
7 heterotopic bone and keloids are simply analogous genetic  
8 aberrations in soft tissue and bone.

9 But we placed a prosthesis in her, and you can see  
10 she has completely fused to the base of the skull. This is a very  
11 difficult problem.

12 Actually this patient has had a revision where we  
13 removed the prosthesis, removed the bone, and in this patient we've  
14 radiated her with 1,000 rads of radiation over five days, and she  
15 seems to be doing very well, maintaining an opening of about 26  
16 millimeters at this time.

17 So that's a quick overview of the clinical  
18 application, and do you want me to start the other one?

19 And Mary Verstynen, whom I'd like to introduce, is  
20 the Director of Clinical Affairs of Biomet, who has also been my  
21 monitor and guiding light. We are going to kind of off and on  
22 give you the statistical results of the study.

1 MS. VERSTYNEN: The clinical investigation will be  
2 presented by Dr. Quinn and myself, and please note the handouts  
3 that you have. We have done an abbreviated form of this slide  
4 presentation in order to keep with the time frame required.

5 In 1994, an IDE was submitted to the FDA for a  
6 prospective multi-center clinical trial. It was designed to  
7 document patient improvement from baseline to postoperative  
8 visits. In other words, the patient was serve as their own control.

9 The patient population was purposely defined very  
10 broadly. There were very few exclusions, and the inclusions are  
11 listed on this slide with unilateral and bilateral cases being  
12 used.

13 There were multiple diagnoses that were included  
14 within the study protocol. One of the only exclusions or one of  
15 the few exclusions was the patients had to be skeletally mature,  
16 but most importantly, the patients had to be selected after  
17 nonsurgical treatment failure or previous implant failure.

18 A study design included collection of baseline data,  
19 operative data, and follow-up data. The follow-up data as listed  
20 ran from one month to three months or three years, with the three  
21 years being a study endpoint, and this was based on an FDA draft  
22 guidance document that was available at the time.

1           The primary efficacy assessments as defined in the  
2 protocol were jaw pain intensity, interference with eating, and  
3 MIO. The jaw pain intensity and interference with eating were  
4 collected on ten centimeter VAS scales which went from zero to  
5 ten with zero being either no pain or no interference with eating,  
6 and ten being worst case.

7           The MIO was collected in terms of millimeters.  
8 Additional efficacy assessments included occlusion and anterior  
9 open bite, cross bite, and wound healing.

10           Safety assessments were documented as adverse  
11 events, device related or otherwise, and in addition, radiographic  
12 assessments were collected at each of the follow-up time periods  
13 which are listed as follows.

14           The position of implants were compared to immediate  
15 post-op, and then additional X-ray findings.

16           We also defined patient and study success, which  
17 will follow on the next slide, and in addition, we identified  
18 primary efficacy endpoints and secondary efficacy endpoints.

19           The study was based on improvement from baseline  
20 to three years. So the primary efficacy endpoint was the difference  
21 between baseline and three years for pain, interference with  
22 eating, and MIO.



1                   And then in addition, the secondary endpoints looked  
2 at the same pain interference with eating and MIO at baseline and  
3 then at each of the individual follow-ups.

4                   In addition, we included as a secondary efficacy  
5 endpoint patient satisfaction, which also included a question of  
6 whether or not the patients would be willing to have the surgery  
7 again.

8                   Patient success is defined as follows with patients  
9 having to meet both criteria to be a success. In order to be a  
10 success, they had to have no permanent joint removal in two of  
11 the following three assessments, which were the primary efficacy  
12 endpoints.

13                   There had to be a one centimeter reduction in pain  
14 from baseline to three years and/or a one centimeter reduction  
15 in eating also at the same time frame, and an increase of MIO of  
16 ten percent once again from baseline to three years.

17                   A study success was determined that if 60 percent  
18 of the patients met the success criteria, the study would be a  
19 success.

20                   The statistical plan analyzed three different groups  
21 of which there were two cohort groups and the total study group  
22 which was comprised of 180 cases and 256 joints.

1                   The first cohort group is the cohort unimputed group,  
2                   which included 45 cases which actually had follow-up at the  
3                   three-year time frame. The cohort imputed group included those  
4                   45 cases, plus imputed data from the closest follow-up time point  
5                   to the three years but not past it.

6                   So if a patient was seen at the one-year time point  
7                   and wasn't seen at three years, we would input the values for that.

8                   In addition, the statistical plan outlined that we  
9                   would do T test analysis and repeated measures analysis for the  
10                  primary and secondary endpoints, and we also would do subgroup  
11                  covariate and multivariate analysis.

12                  Dr. Quinn will take over from here now with the  
13                  baseline findings and the following tables will show the cohort  
14                  and the total groups to show how comparative these groups were.

15                  DR. QUINN: And, again, I think it is a unique patient  
16                  population. These are multiply operated patients. There are some  
17                  unique characteristics that tend to be similar to other joint  
18                  studies. So it wasn't that this study was different than other  
19                  TMJ findings, but there is some unique characteristics of that  
20                  patient group.

21                  The mean age -- and, again, I'm going to try to point  
22                  out the similarities in the total group and the cohort group --

1 was 40.2 and 37.8. The gender follows most TMJ studies, and I'm  
2 not sure anyone has a good explanation, but they are usually close  
3 to 90 percent female. There's mechanical reasons for that because  
4 of the differences in Type II collagen between men and women, and  
5 there are some biochemical discussions about estrogen receptors  
6 that may affect some of the issues, but this is clearly consistent  
7 with other studies.

8 The sidedness broke out relatively even between  
9 unilateral and bilateral. It was almost 50-50 in between right  
10 and left side.

11 The majority of the cases, as I've mentioned, they  
12 were done between Dr. Sinn and I, and in the cohort group, it broke  
13 out around the same percentages.

14 The baseline medical history, again, is somewhat  
15 similar for these group of patients, and again, as I mentioned  
16 before, these are humbling patients because the criteria for  
17 success that Mary mentioned, I think one of the reviewers said  
18 we had somewhat lenient criteria for success. I think it was based  
19 pretty much on our experience with these multiply operated  
20 patients. As you'll see, we far exceeded those criteria for  
21 success, as we'll see later on.

22 We used a Wilkes classification, which is named after

1 Clyde Wilkes, which actually just classifies according to pain,  
2 restriction in motion, and radiographic findings, and as you would  
3 suspect, the majority of these patients would fall into the higher  
4 Wilkes stages, which is consistent with these patients should  
5 exhaust all nonsurgical therapy, clearly, before ever proceeding  
6 to a total joint replacement.

7 This, again, I think tempers some of the results  
8 of the study, and they're very similar in the total and the cohort,  
9 the number of prior studies, and you can see they can range anywhere  
10 from zero to 29.

11 Zero would be a traumatic fracture where there's  
12 an irreparable fracture, and you would go right to a prosthesis.

13 The 29 would be an unfortunate patient who underwent a lot of  
14 previous procedures.

15 The three major baseline characteristics we followed  
16 were, again, jaw pain intensity, interference with eating, and  
17 these two were on a visual analogue scale of zero to ten, where  
18 zero was the best and in pain, ten was the worst pain imaginable,  
19 and on the diet scale ten was liquids only. And the maximal  
20 interincisal opening, these are baseline findings between total  
21 and cohort, which are relatively similar, but they started around  
22 19 to 20.

1                   And, again, as we mentioned, we feel it's a  
2 reasonable goal to get probably 30 to 33 millimeter opening in  
3 the multiply operated patient.

4                   The diagnoses are multiple because obviously these  
5 don't add up to 100, but if we look at the two most common, they  
6 are osteoarthritis and ankylosis, and then we had a separate  
7 traumatic arthritis when there was an identifiable event that began  
8 these symptoms.

9                   In cement usage, as we mentioned early on, when we  
10 were using PMMA cement, of the total cases 38 were cemented and  
11 142 are uncemented, and the last cemented case was 1998.

12                  In the mandibular component, as we discussed the  
13 different designs, the narrow design, we've used 197. The standard,  
14 which is the broader that gives you just more options for screw  
15 placement, and in two patients who had documented nickel  
16 sensitivity, and these patients are actually tested with nickel  
17 patch testing by a dermatologist prior, and then in both cases  
18 we got FDA approval to make the mandibular component out of  
19 titanium. As you recall, the screws are the titanium alloy.

20                  This is the follow-up. If you look at the landmarks  
21 of follow-up, and Mary is going to go through the statistics from  
22 this point on, and then I'm going to discuss the adverse events

1 tat the end.

2 MS. VERSTYNEN: Patient accountability. This shows  
3 once again while the study went from one month to three-year  
4 follow-up, I also did include the four and five-year follow-up  
5 because we did make an effort to follow the patients past the  
6 three-year study time point.

7 As you can see, the bottom line and the most important  
8 thing on this slide is the percent follow-up from the one month  
9 to the three years, and at all time points we were at greater than  
10 80 percent.

11 The only loss to follow-ups that were calculated  
12 on this slide were deaths and total joint removals, but obviously  
13 people do not return for visits. People move; people are lost.

14 So that accounts for why we would have some patients theoretically  
15 due at one month of 180 when we actually saw 170 patients.

16 I mean, the patients schedule, and they don't come  
17 back. And Dr. Quinn and Dr. Sinn can probably talk a lot more  
18 in detail why patients don't come back for follow-up.

19 The clinical findings, the primary effort to see  
20 endpoints in both T tests and repeated measures analysis. They  
21 showed a significant change from baseline to three years, and  
22 remember this study was designed to show improvement.

1                   This slide shows perfectly how well the three groups  
2 that were analyzed compare, and if you look to see, they follow  
3 the exact same pattern from baseline to three years throughout  
4 the course of the study, with the baseline mean being at eight  
5 and the error bars are put in for just the standard deviation only  
6 just so it wouldn't complicate the slide.

7                   But you can definitely see even at the one month  
8 time frame there was a tremendous amount of improvement in jaw  
9 pain, continued down at three months, and pretty much plateaued  
10 from the six-month to the three-year time frame.

11                   This was also seen very similar on the interference  
12 with eating. Remember these were all in the ten centimeter VAS  
13 scale where, once again baseline mean for all three groups was  
14 approximately eight centimeters, dropped drastically at one month,  
15 continued going down at three months, a little decrease still at  
16 six months, and then pretty much plateaued out to three years,  
17 which pretty much seemed to be somewhat predictive then.

18                   By the three and the six month mark, the patients  
19 had pretty much plateaued to what they were at the end of the study.

20                   The same thing for the MIO. They started off with  
21 approximately a 19 millimeter opening and went up drastically at  
22 one month and at three months and was continuing up, and this pretty

1 much looked like it plateaued then out to the three-year mark.

2 So you can definitely see that there was a tremendous  
3 amount of improvement seen in the primary efficacy endpoints.

4 Also, to show this even in another visual way, once  
5 again, this was the baseline reading. We wanted to see the  
6 difference between baseline and each of the time frames, and this  
7 slide actually incorporates both primary and the secondary efficacy  
8 endpoints.

9 We can drastically see the difference between  
10 baseline and three years, which was the primary endpoint, and then  
11 each of the secondary endpoints then are shown at the one month  
12 and all of the follow-ups.

13 And you can definitely see there was a tremendous  
14 amount of significance in improvement for jaw pain, and you can  
15 also see the exact same thing then for the interference with eating  
16 and the same thing for the MIO.

17 Once again, this was just to visually show you what  
18 the baseline reading was and then to actually show the improvement  
19 over time.

20 Secondary efficacy endpoints also included the  
21 degree of patient satisfaction. Ninety-three percent or more of  
22 the patients were satisfied or better at all time frames, and that



1 includes out to the six years, and for the hindsight question,  
2 whether patient would choose to have a surgery, 91 percent or more  
3 said yes at all of the time frames.

4 This slide is just to show you that with the  
5 additional efficacy data that was collected for collusion, anterior  
6 open bit, and cross bite, there was also an improvement seen from  
7 baseline to three hears in these three assessments.

8 I will hand it over now to Dr. Quinn to complete  
9 the clinical presentation, and he will start off with safety  
10 findings.

11 DR. QUINN: Thanks.

12 As we mentioned, we reported adverse events. You'll  
13 see, I think, we over reported them. We're very conservative with  
14 that.

15 There weren't any mechanical failures. There were  
16 permanent device loss, and we'll go over all of them. And the  
17 permanent device removals occurred in 11 cases and 12 joints.

18 Now, we defined "permanent" that it was removed.  
19 In three of these the fossas have been replaced. One of them is  
20 as long as two and a half years later, but we are still listing  
21 these as permanent device removals because the other definition  
22 we used was same day revision.

1 I don't want it to be confusing, but same day revision  
2 is where we went in, removed a prosthesis, for example, for  
3 heterotopic bone, removed the heterotopic bone and replaced the  
4 prosthesis. And that occurred in five joints, four cases where  
5 we had to remove the heterotopic bone, and in one case where there  
6 was a dislocation of the condyle, and we went in and replaced it  
7 with a 50 millimeter to a 45 millimeter to reseal it.

8 This is the total number of adverse events which  
9 are not requiring device removal, and again, I do think that we  
10 made an effort to over report. I'll give you some examples of  
11 these.

12 Excision of tissue included both removal of  
13 heterotopic bone and also removal of incisional neuroma because  
14 a lot of these patients especially who have had multiple incisions  
15 have incisional pain that can occur in any type of incision, and  
16 some of them postoperatively were taken back to remove the scar  
17 in an attempt to remove an incisional neuroma.

18 We reported any time when there was a motor vehicle  
19 accident even if there was no direct facial trauma because we did  
20 see that it did correlate with an increase in symptoms even if  
21 there was no direct maxillofacial trauma.

22 Coronoidectomy, I think there's some experiential

1 wisdom here. In the beginning of the case, we probably did not  
2 remove coronoids as much. We were recommending in the multiply  
3 operated patient at the time of the original surgery that the  
4 coronoids were removed.

5 We did have to go back and remove coronoids. That's  
6 from an intraoral approach, and it does avoid contaminating the  
7 implant.

8 Again, these are all adverse events that did not  
9 require a device removal, and as I mentioned, we had no mechanical  
10 failures. This does come out to a 30 percent AE incidence, and  
11 55 patients at the 180 cases, but it was six cases or 3.3 percent  
12 that had AEs that were device related. And, again, as I mentioned  
13 before, the number that had the permanent removals.

14 Given the patient population where I think the term  
15 "reasonable expectations" comes in, these patients do have,  
16 especially in the multiply operated patient, preexisting  
17 conditions, nerve pain secondary to multiple surgery which will  
18 not be addressed by a prosthesis, and some of these patients are  
19 chronic pain patients as well.

20 Looking at the surgical site, most of the wounds  
21 healed within the first three months postoperatively. The ones  
22 where we had wound infections I showed an example of where we had

1 device removal.

2 Radiographic assessment was done at all of the  
3 landmarks, and we used the baseline of the day after surgery where  
4 a PA cephalometric X-ray was taken, a lateral cephalometric X-ray,  
5 a Panorex, and they were compared at the other landmarks for change  
6 in position of the fossa or the condyle.

7 Most of the radiographic changes were associated  
8 with the heterotopic bone or in the joints that were removed.

9 There was a subgroup analysis done for a covariate  
10 analysis and multivariate analysis, and all the detail of that  
11 is in your handout.

12 What did occur from that analysis was that there  
13 were some statistically significant differences in the variable  
14 analysis, but none of them were clinically significant.

15 If you looked at groups where one has a three  
16 centimeter improvement in opening, the other subgroup had a four  
17 centimeter. They were, again, statistically significant, but all  
18 of the groups did well enough, and so they weren't clinically  
19 significant.

20 In summary then we had a success rate by the  
21 definition that we went over in the beginning of the presentation  
22 in the cohort on imputed group, the 97.8 percent, and the cohort

1 imputed group of 94.9, and then the total study group of 95.1,  
2 and we had greater than 60 percent of the cases met the patient  
3 success criteria, and as we said, those criteria were a centimeter  
4 improvement in pain scale, a centimeter improvement in diet scale,  
5 and ten percent improvement in the MIO.

6 The study conclusions is that we feel this is a safe  
7 and efficacious implant. There was a significant improvement with  
8 a significant P value seen in the primary and secondary efficacy  
9 endpoints.

10 Patient satisfaction was what we reported,  
11 approximately 91 percent, and the rate of AEs even including device  
12 removal was an acceptable rate considering the patient population,  
13 and we had no unanticipated adverse events.

14 In summary, we think this prospective study has shown  
15 that the Water Lorenz total TMJ replacement system is safe and  
16 effective for the variety of diagnoses that we've shown.

17 Thank you.

18 CHAIRMAN HEFFEZ: Thank you very much.

19 I would like now to proceed to any questions that  
20 the panel may have. Any panel member who wishes to ask a question,  
21 please signal to me and identify you name prior to the question.

22 DR. PATTERS: Mark Patters.

1                   A question for Dr. Quinn. Could you discuss the  
2 patients lost to follow-up? Because there's always a concern that  
3 that represents a population that's dissatisfied rather than that  
4 is consistent with the total population.

5                   DR. QUINN: I'll separate the amount of patients  
6 who are lost to follow-up. There were three deaths in the study,  
7 and the three deaths were one was a patient who had a temporal  
8 lobe tumor who died of a recurrent brain tumor.

9                   The second patient died from a fulminant hepatic  
10 reaction to Toradol three weeks after surgery.

11                   And the third patient died from complications of  
12 back surgery. So there were three loss to follow-up from death.

13                   Of the other patients that were lose to follow-up,  
14 the majority of the problem is distance. We do a zip code analysis  
15 at the University of Pennsylvania, and based on this study I now  
16 have the widest zip code analysis patient referral base. So most  
17 of the patients, it's distance.

18                   And my impression is that if they're doing well they  
19 don't want to get on a plane and fly back from Oregon for a 20  
20 minute appointment in Philadelphia. That is a problem.

21                   So my impression is that the percent follow-up, given  
22 this patient population, is laudable, but you're right. It is

1 a concern, and the problem is coaxing patients back in. We have  
2 no problem getting patients back in who have complaints.

3 DR. BURTON: Richard Burton.

4 This question, Dr. Quinn, deals with your  
5 indications and your patient population. The first one is that  
6 one of your indications and one of your exclusion criteria was  
7 that they would be skeletally mature.

8 But then looking at the demographics, that shows  
9 at least one male that was 12, and then a 13 year old female, and  
10 most of us would obviously not consider those to be skeletally  
11 mature. So I guess my question is why. There was no indication  
12 why they were included.

13 DR. QUINN: The 13 year old female was by hand wrist  
14 filmed, finished skeletal growth.

15 DR. BURTON: Okay.

16 DR. QUINN: And she's the patient I showed, the young  
17 Afro-American female with the keloids and the ankylosis.

18 DR. BURTON: Okay.

19 DR. QUINN: That is her. The 12 year old patient,  
20 the patient of Dr. Sinn's -- and, Doug, if you want to comment  
21 -- that patient was approved by the FDA as an exclusions even given  
22 his age.

1 DR. BURTON: Well, they were an exception to that.

2 Also, what is your intent in the section? You talk  
3 about one of the indications is developmental abnormalities.  
4 That's sort of a broad term, but what you really intend by that  
5 statement.

6 DR. QUINN: Development abnormalities, we may have  
7 a congenital absence of the whole -- rami are kind of like hemifacial  
8 microsomia or Golden-Harr syndrome.

9 Obviously, the procedure of choice in a  
10 developmental abnormality prior to skeletal maturation in our hands  
11 is still a costocondyle graft, but developmental abnormalities  
12 after skeletal maturation could be addressed with the prosthesis.

13 DR. BURTON: And lastly you had some individuals  
14 who were -- at least a couple that were Wilkes Class I and then  
15 a couple of IIs and IIIs. What were the other co-morbidities that  
16 usually would indicate that they would be included? Was that a  
17 fracture patient or something along that line?

18 DR. QUINN: Either fractures or a tumor where the  
19 amount of bone removed in the tumor excision would require either  
20 a prosthesis or an autogenous joint.

21 DR. BURTON: Okay. Thank you.

22 DR. SUZUKI: Jon Suzuki.



1 This is a question for Dr. Quinn.

2 Apparently the condylectomies that are required to  
3 place this device are somewhat radical, and an additional part  
4 of the mandible is taken off. Given the morbidity, what options  
5 does a surgeon have for reconstitution or replacement of it should  
6 this fail?

7 DR. QUINN: That's a good question. You do have  
8 to remove more of the condyle approximately three millimeters below  
9 the sigmoid notch to accommodate the thickness of the glenoid fossa.  
10 That is an irreversible step, as you point out.

11 And I'll phrase it in two questions. You always  
12 have the option in a failed prosthesis to go back to an autogenous  
13 graft. I think there's some complications there because the more  
14 these patients are operated on, the more scarred the bed is and  
15 the more complications you will get with autogenous grafts.

16 The other option, and I should mention this, is that  
17 this is a stock prosthesis, and it comes in three different sizes,  
18 and humans always don't come in three different sizes. You always  
19 have the option at the time of surgery, the stock prosthesis once  
20 the surgeon is in the joint. It doesn't fit, is inappropriate.  
21 you stop the procedure, put the patient in IMF. Do a 3D CT scan  
22 in the hospital, and you can proceed with a well designed custom

1 joint like the TMJ Concepts.

2 And we do encourage surgeons that that is an option  
3 if they run into anatomical problems. Is that addressing your  
4 question?

5 DR. SUZUKI: Yes. Thank you.

6 DR. COCHRAN: David Cochran.

7 I had a question about the timing of your adverse  
8 events. When those occurred, it looked like from some of the  
9 information they occurred around the six month time point. Would  
10 you elaborate on that a little bit?

11 DR. QUINN: The timing of when the adverse events  
12 occurred?

13 DR. COCHRAN: Yes.

14 DR. QUINN: I think they occurred throughout the  
15 entire study. Maybe I'm misinterpreting the question.

16 DR. COCHRAN: Yeah, it looked like just from what  
17 was listed in the material we had, it looked like they were occurring  
18 from four to ten months. The main ones were listed. I think there  
19 was one lost later on, but normally four to ten months seemed to  
20 be when most of the adverse events occurred.

21 DR. QUINN: Well, for the major adverse events,  
22 infection and heterotopic bone, that would be the time frame it

1 would occur in. I'd ask either Mary or Joe Canner if you want  
2 to discuss the statistics. Maybe I can't answer the question as  
3 well.

4 MS. VERSTYNEN: Yeah. Mary Verstynen.

5 I believe that the adverse events occurred  
6 throughout the study, but I guess if you go back and look and  
7 remember the patient accountability, the majority of whole joint  
8 revisions were done between the six month and the one and a half  
9 year time point. It seemed to be at that point is when the patients  
10 went back for the total joint.

11 So I don't know. Does that answer it somewhat?

12 But literally the rest of the adverse events occurred  
13 throughout the study.

14 CHAIRMAN HEFFEZ: Dr. Rekow.

15 DR. REKOW: Diane Rekow.

16 I have a question for Dr. Quinn, and then I have  
17 another question for Shawn, please.

18 Dr. Quinn, can you talk about and have you done any  
19 correlation -- let me start again.

20 My impression as I read the materials was that you  
21 used the bone cement with a post early on, and then you started  
22 removing the post and not using the cement. Then that evolved

1 into a new design. Is there any correlation between the adverse  
2 effects and the use of cement or non-use of cement and the design  
3 of the fossa?

4 DR. QUINN: I believe that was one of the subgroup  
5 analysis, and I don't think there was a statistical significant  
6 difference because as you mentioned, we stopped in 1998.

7 Of the patients who were out -- Mary, can you help  
8 me with the numbers? -- of the patients who were out three years,  
9 of the breakdown, I think it's 38 and six.

10 MS. VERSTYNEN: Well, there were 38 cemented cases,  
11 and they were obviously done early on in the study. So there were  
12 31 of Dr. Quinn's and there were seven of Dr. Sinn's. So these,  
13 this grouping of patients, were their first patients that were  
14 enrolled into the study.

15 Does that answer it or do you want --

16 DR. REKOW: And there's nothing different?

17 MS. VERSTYNEN: And the thing is I guess you could  
18 kind of go back and look at the key numbers. I mean, with the  
19 listing of adverse events, they probably fell within the first  
20 40 key numbers. I don't know that those cases had more adverse  
21 events than the rest of the patients.

22 DR. REKOW: Have you -- have you --

1 MS. VERSTYNEN: But we haven't actually looked at  
2 the 38 and correlated it back to the numbers of adverse events.

3 DR. REKOW: Okay. That was really my question.

4 MS. VERSTYNEN: Actually it was a good point. The  
5 38 cases were all in the cohort group, but once again, we didn't  
6 list adverse events by cohort. We just listed them by the total  
7 of 180 cases.

8 DR. REKOW: Okay, and then, Shawn Roman, you provided  
9 some nice information about averages for your mechanical testing,  
10 but I didn't see any ranges or standard deviations. Can you give  
11 us some sense of how closely the five joints performed relative  
12 to each other?

13 MR. ROMAN: With respect to the?

14 DR. REKOW: Well, the fatigue testing and your screw  
15 pull-out tests and those sorts of things. The averages are  
16 wonderful, but you could have interesting results with nice  
17 averages.

18 MR. ROMAN: Right. I don't have those numbers off  
19 the top of my head, but I can get those from the test reports if  
20 you'd like me to do that.

21 DR. REKOW: I think at some point it would be useful  
22 to see those.

1 MR. ROMAN: Okay.

2 DR. REKOW: Thanks.

3 CHAIRMAN HEFFEZ: We can entertain another question.

4 MR. ROMAN: Just pointing out the fact that on fatigue  
5 testing there is no variability. The fatigue testing just stops  
6 at the --

7 DR. REKOW: Right, right, but for the bending tests  
8 and for the pull-out tests?

9 MR. ROMAN: Sure. How would you like to work this?  
10 I can get the numbers and then come back to the podium and answer  
11 that question for you?

12 CHAIRMAN HEFFEZ: Yes.

13 MR. ROMAN: Okay.

14 CHAIRMAN HEFFEZ: We'll proceed.

15 Ms. Helms.

16 MS. HELMS: Thank you.

17 Elizabeth Helms.

18 I have several questions around the function of the  
19 mandible after implantation with the screws. The screws loosen  
20 up. Do you have to go back in? Has there been a change in the  
21 body of these patients?

22 If you could describe how many patients have had

1 screws that have loosened up. What happens to the body if any  
2 of this is reabsorbed?

3 And for the nickel testing, do you do any type of  
4 testing for nickel allergies prior to implantation?

5 DR. QUINN: Maybe I'll answer them in reverse.

6 MS. HELMS: All right.

7 DR. QUINN: Nickel testing, if a patient tells us  
8 they have nickel sensitivity, and most patients who have nickel  
9 sensitivity, it's a jewelry issue because of the preponderance  
10 of nickel in jewelry, and we have small samples of the materials.

11 The polyethylene and the cobalt chrome from the  
12 company that we send to a dermatologist, have the patient seen  
13 by the dermatologist, and they're patch tested. I'm not sure  
14 there's any other way other than taking a history and doing a patch  
15 test.

16 If there's a reaction to the patch testing, then  
17 we have gotten permission to use titanium in the ramal component  
18 as well as the screws.

19 We haven't had any screws loose in there. I have  
20 had screws loose in implants that we've used in the past.

21 Fortunately we've had no device failures.

22 The question about wear, I think there is wear in

1 all prosthetic implants. The implants that we have gone back into  
2 for infection or for heterotopic mode, we've taken tissue samples.

3 One of the samples came out with a foreign body reaction. When  
4 it was put under polarized light, the official diagnosis that it  
5 was corn starch because it polarizes in a very particular way was  
6 probably from a glove.

7 So we haven't seen any evidence of foreign body  
8 reaction yet.

9 CHAIRMAN HEFFFEZ: Dr. Hewlett, you had a question?

10 DR. HEWLETT: Yes. Edmond Hewlett for Dr. Quinn.

11 I noticed in your statistical analysis or actually  
12 in your demographic data collection that patient ethnicity was  
13 not one of your demographic variables.

14 A two-part question: have you considered at any  
15 point or make a specific decision not to include that?

16 And the second part is that did you nonetheless based  
17 on just your empirical experience in the study notice any propensity  
18 for specific adverse effects, such as heterotopic bone or ankylosis  
19 with respect to any particular ethnic groups?

20 DR. QUINN: Well, the numbers wouldn't be high  
21 enough. Anecdotally, I think in my patient population and only  
22 in the females, there were three African American females. Only



1 one of them have this serious heterotopic bone. I do think there  
2 is a higher propensity in African Americans in general for keloids.  
3 I don't know whether that translates into heterotopic bone.

4 My experience with heterotopic bone is it gets worse  
5 as the number of operations gets. I think the actual surgery in  
6 and of itself is the trigger for further and further scarring in  
7 heterotopic bone, but I'm not sure I'm an expert in it beyond that.

8 As you said, we did not follow up density. We  
9 followed gender alone, and gender is the striking differential  
10 in all of these TMJ studies, as you well know.

11 CHAIRMAN HEFFEZ: Dr. Bertrand.

12 DR. BERTRAND: Peter Bertrand.

13 For Dr. Quinn, I seem to remember reading that ten  
14 sites were okayed to participate in this study. Yet almost all  
15 of the surgeries are done by you and Dr. Sinn. Can you shed some  
16 light on why predominantly just you and not more sites?

17 DR. QUINN: One of it is a temporal issue. Since  
18 we started this process in 1992, I think we were somewhat geared  
19 up for that patient population.

20 The other is this is exclusive what I do. I only  
21 do TMJ surgery. My five partners won't do any of it, and we have  
22 a large center.

1                   We also have, as you know, a TMJ clinic that sees  
2 a huge number, and our surgery rate is about six percent out of  
3 100. So we tend to draw from a larger population.

4                   Dr. Sinn is in a similar position at Southwest Texas.  
5 He came out in 1998. I think the other investigators, I think  
6 there's two sides to that. There are investigators who have given  
7 us the impression that they have lots of patients and they didn't  
8 materialize, and they came in later in the course, as in the last  
9 year or so we have been holding off and not doing more IDEs and  
10 IRBs because they're so labor intensive to do for somebody who  
11 may do two or three surgeries.

12                   DR. BERTRAND: I understand. The second question,  
13 there seems to be an evolutionary process in the design of the  
14 standard mandibular component. Do you anticipate any more design  
15 changes for the product?

16                   DR. QUINN: No. And it is. It's experiential wisdom.  
17 I think as you go on and you run into joints where you don't  
18 have adequate bone, where a bigger footplate would give you more  
19 options, that clearly was one.

20                   The other one was the medial lateral issue because,  
21 again, this is a stock prosthesis, and it does take some experience  
22 on the surgeon's hands to fit this. But if the fossa is fit first

1 and there is some variability between where the condyle sits under  
2 that fossa, you have some leeway in terms of encountering bone,  
3 but we wanted to have the option to have the same offset in a lateral  
4 direction as the medial direction, if you did get one of them where  
5 you could.

6 It's relatively easy if the prosthesis is too lateral  
7 to do bony contouring to get it in. If it starts off to medial,  
8 you would have to do a lot of shimming with bone, which we don't  
9 want to do. So we made the other offset size.

10 I don't anticipate any more at this time, but I'm  
11 not sure I could sign an affidavit to that.

12 DR. BERTRAND: I understand. There seems also to  
13 be an experience level with how quickly and efficaciously you can  
14 do this surgery. Do you anticipate, with all of your experience  
15 and somebody new, anticipating using these devices having some  
16 type of mentorship program?

17 DR. QUINN: Clearly. I think without training and  
18 education this is very experience based. In fact, I think one  
19 of the things that did occur during the course of the surgery is  
20 it's a much faster procedure when you have all of the instruments  
21 that are designed specifically for it, the burs, the retractors.  
22 Our average time per side now is about two hours and 20 minutes.

1 In the beginning it was over four.

2 DR. BERTRAND: Thank you.

3 DR. BURTON: Richard Burton, again, for Dr. Quinn.

4 I'd like to continue with what Dr. Bertrand asked  
5 because I have concerns which you explained regarding the site  
6 and the question of site bias, but my concern looking through your  
7 surgeon materials is the fact that they're very good, but again  
8 don't obviously convey some of the complexity of this.

9 And whether or not you looked at whether your  
10 complication rate -- and when I went through the adverse events,  
11 it appeared that there was not a -- that they spread throughout  
12 the study, but there were certainly, it seemed, a slightly higher  
13 rate. Did you look at that earlier in the early patient groups?

14 And again, whether there was a learning curve,  
15 obviously you said your own surgical time improved, which would  
16 be a normal expectation, but again, how you may address the surgeon  
17 education issue when this was released.

18 Because, again, you know, currently virtually all  
19 of these have been done by yourself and Dr. Sinn, and again, both  
20 of you are, I think, well known and well experienced, but when  
21 his product is released and given out to hands with much less  
22 experience, and again, none with this particular product and how

1 you intend to address that.

2 And then one other question that sort of goes in  
3 with that if you've addressed many times that one of the most common  
4 problems you had was heterotrophic bone formation, again, in  
5 multiply operated joints. You made a comment earlier about the  
6 use of radiation in one of the patients.

7 Are you advocating that, and if so, how many patients  
8 did -- I didn't see anything where it said how many patients had  
9 received radiation in conjunction with their overall treatment.

10 DR. QUINN: Okay. Well, the only one patient received  
11 it, and it was actually three weeks ago after this data was closed.

12 I only have experience with three patients, and our  
13 experience is really drawn from the orthopedic literature because  
14 there isn't a lot in our literature how you deal with heterotopic  
15 bone, except for EDTA chelating agents which don't seem to be very  
16 effective, and indomethacin, which we have also tried.

17 A dose of 100 rads, given 200 rads per day, seems  
18 to be efficacious, but our n is too small for me to make any  
19 statement.

20 To go to your original statement about adverse  
21 events, I do think there are some correlates that, in general,  
22 in the maxillofacial literature, you can look at infection rates,

1 and they do correlate in general in orthognathic surgery, where  
2 it is published more, the longer that site is open, the higher  
3 the infection rate. I think there is some correlation to time  
4 of surgery.

5 It wasn't part of our analysis, but I do think if  
6 you take a two-hour operation and take ten hours to do it, you're  
7 probably going to increase your rate of infection. That's  
8 anecdotal. I have no data to support that.

9 To the training issue, I couldn't agree with you  
10 more. I think if there is any silver lining to the Proplast debacle,  
11 that as you well know, the majority of oral maxillofacial surgeons  
12 in practice have decided TMJ surgery is not something they're wildly  
13 enthusiastic about. I somewhat hope it stays that way.

14 These are done at centers by people who do at least  
15 a modicum of surgery because experience is part of it.

16 In terms of the training, currently the plan is that  
17 Dr. Sinn or I would do a surgery with anyone contemplating doing  
18 this, and they would have to take a formal course that goes over  
19 all of the testing, the designs, the biomechanical and surgical  
20 technique.

21 We've produced a video that is in preparation.  
22 Beyond that I would be open to suggestions because I do think it's

1 an important point.

2 DR. BURTON: Thank you.

3 DR. ANSETH: I had a question for Mr. Roman.

4 CHAIRMAN HEFFEZ: This is Kristi Anseth.

5 DR. ANSETH: My name is Kristi Anseth.

6 And my question relates to some of the wear  
7 properties of the components that you were testing, and I was  
8 wondering if you could comment more specifically on that.

9 And then also, with some of the changes in using  
10 the cement and noncemented, if you could comment on the differences  
11 that might exist both in fatigue and wear.

12 MR. ROMAN: Okay. The materials used for both the  
13 fossa component and the mandibular component are materials that  
14 we've had a wide range of experience with previous to this design  
15 in orthopedic applications.

16 The wear characteristics were looked at on all of  
17 the fatigue testing. The articular surfaces of the fossa components  
18 were looked at, and there was no sign of wear after the ten million  
19 cycles in the fatigue testing.

20 Does that answer your first question?

21 And the second question, could you repeat?

22 DR. ANSETH: So you also presented data on even the

1 cemented version of the fossa.

2 MR. ROMAN: Right.

3 DR. ANSETH: And I was curious what you think of  
4 differences when you have no cement.

5 MR. ROMAN: Okay. We're actually trying to -- well,  
6 the cement that -- first of all, the bone cement was never intended  
7 to be used as a means for fixating the fossa component. It was  
8 just meant to fill voids between the fossa component and the glenoid  
9 fossa component. The sole means of fixation would be the fossa  
10 screws.

11 But we are currently doing some fatigue testing to  
12 look at the difference between the fossa components that had the  
13 post manually removed as compared to fossa components that were  
14 machined without the post, and in both of those cases, we're redoing  
15 that fatigue testing without using bone cement because that is  
16 how they would be implanted.

17 And we're testing five devices. Four of the devices  
18 are complete now, and they have all made it out to ten million  
19 cycles with no failures of the devices.

20 DR. REKOW: Can I ask a follow-up?

21 Diane Rekow. Can I ask a follow-up question?

22 When you're doing that fatigue testing, what do you



1 have as your supporting system under the fossa? Does it have a  
2 modulus that's similar to the bone or is it a steel or you know?

3 MR. ROMAN: Yeah, it's aluminum. So it would be  
4 stiffer than the bone. That would be in vivo.

5 DR. REKOW: Okay.

6 MR. ROMAN: Did you want me to follow up now with  
7 the question I was asked earlier on the standard deviations or  
8 do you want to --

9 CHAIRMAN HEFFEZ: Sure, yes. Go ahead.

10 MR. ROMAN: I was able to find the standard deviations  
11 on two of the four tests that weren't the T testing. On the fossa  
12 screw pull-through testing, there was a standard deviation -- there  
13 was an average of 79.8 pounds with a standard deviation of 2.5  
14 pounds.

15 On the pull-out strength of the 2.7 millimeter  
16 self-tapping screws, it was an average of 373 pounds with a standard  
17 deviation of 68.8 pounds, and it's a slightly larger standard  
18 deviation that was discussed, and it's probably the result of using  
19 bovine cortical bone for the testing.

20 There was a concern over the standard deviation there  
21 because the loading was so high, and the other two tests that were  
22 performed, the static testing of the mandibular component and the

1 static testing of the fossa component, there were no standard  
2 deviations listed in the old test reports.

3 DR. REKOW: Do you have the ranges?

4 MR. ROMAN: Actually there's -- that data is not  
5 listed in the testing report. I think that the reason for that  
6 was because of the mode of failure that was seen. It was anticipated  
7 that the mandibular component would fracture at the flange.  
8 Actually the mode of failure occurred in two different stages with  
9 the mandibular component.

10 The first stage actually involved splitting of the  
11 bone, the tibial bone from the first screw up to the top surface  
12 of the bone, and then once that splitting occurred, then the bending  
13 of the mandibular component occurred.

14 So then on the fossa components, again, the  
15 anticipated mode of failure was fracture of the fossa flange, but  
16 when the fossa flange bent with no breaking, that was deemed  
17 acceptable solely because they would have the support of the  
18 temporal bone in vivo.

19 So were those numbers that were reported then the  
20 minimums for the set that were tested or were they the average?

21 Do you -- I know that this is probably old data, and you may not  
22 have the answers immediately available.

1 MR. ROMAN: I don't, but they are discussed as the  
2 average in the test reports.

3 DR. REKOW: Okay. Thanks.

4 MR. ROMAN: But as long as we're catching up on  
5 questions, we did have some additional information for adverse  
6 effects that can be answered by our contract statistician.

7 MR. CANNER: My name is Joe Canner. I'm a statistical  
8 consultant with Hogan & Hartson in Washington, and I have financial  
9 interest in Biomet or Lorenz.

10 There was a question asked about adverse events after  
11 cement or noncement, and we did do that analysis, but I would  
12 strongly encourage caution with respect to the interpretation of  
13 it, although the results are fine. There was no statistically  
14 differences.

15 But any time those kinds of issues come up, keep  
16 in mind as was mentioned that the cemented cases were the first  
17 38 cases and the noncemented were following that. So any patient  
18 selection issues, any learning curve issues will by nature  
19 complicate that analysis.

20 It does appear that, as was mentioned before, most  
21 of the removals -- and I'm sorry. I meant to say that I'm talking  
22 specifically about removals here because those are the adverse

1 events that probably are most relevant to the device. Most of  
2 them do appear to occur in the first 12 months and even in the  
3 noncemented cases, all of the removals were in the first 12 months,  
4 and even though there were a number of patients who were in that  
5 group who were followed out to two and three years.

6 So to recap, there was no statistically significant  
7 difference between cemented and noncemented cases in the rate of  
8 removal, but again, it would be difficult to make too much of that  
9 one way or the other because of changes over time and patient  
10 population and in surgeon experience.

11 CHAIRMAN HEFFFEZ: Dr. Li.

12 DR. LI: Steve Li, either for Dr. Quinn or Mr. Roman.

13 I'd like to revisit the polyethylene wear issue.  
14 As you've mentioned the TMJ is kind of a corollary to the total  
15 hip and total knee system, and in this case it's a more conforming  
16 joint, so more similar to a total hip than a total knee, and yet  
17 your stresses are about two to three times that of a total hip.

18 So my question is: do you see signs of polyethylene  
19 wear either in radiographs or on your explants or in tissue  
20 analysis? And if you don't, why would that be?

21 DR. QUINN: I'll ask Shawn to answer some of the  
22 general questions about polyethylene wear because I'm not the

1 expert, but I think if you -- first of all, there's on real consensus  
2 as what are the stresses place on not only the prosthetic joint,  
3 but on the human joint.

4           You could start an argument as to what is the pounds  
5 per square inch under normal mastication. We used 145 pounds as  
6 the upper limit, which I think is a good estimate, but in this  
7 patient population in the multiply operated joints, there are  
8 studies that have viewed something as crude as a dynamometer in  
9 multiply operated. Their masticatory forces are much less.

10           So I think although by definition this is a patient  
11 population who has already had multiple procedures, I wouldn't  
12 expect that they could even achieve the normal range of stresses.

13           The other is I'm not sure I correlate directly to  
14 a conforming hip joint where there's confluence because there is  
15 some aberrant motion in this joint that is not directly related  
16 to a hip.

17           DR. LI: But that would tend to increase the wear  
18 though.

19           MR. ROMAN: Right.

20           DR. LI: So my question is: do you see clinical  
21 signs of wear, either radiographically in the analysis of removed  
22 components or in surrounding tissues when you've gone in to do

1 procedures?

2 DR. QUINN: Excuse me. Radiographically we haven't.

3 Of the joints I opened for other reasons, heterotopic bone and  
4 infection, when we did tissue samples, the only foreign body, as  
5 I mentioned, was what they came back and said was more likely to  
6 be corn starch and not polymeric debris. So --

7 DR. LI: Were those just -- I'm sorry -- were those  
8 just optical micrographs, with your eyes? It wasn't electron  
9 microscopes?

10 DR. QUINN: These were histologic EMN and then they  
11 were under polarized, but looking for foreign bodies.

12 DR. LI: Right. So typically in the larger joints  
13 the particles that form osteolysis are below the levels of visible  
14 observation. So if you can actually see it with your eyes, they're  
15 too big to cause osteolysis. So unless you do some tissue analysis  
16 to look for these submicron particles, there could be millions  
17 in there, and you'll never see them just by looking with a  
18 histological sample.

19 So have you looked at anything other than  
20 histological samples?

21 DR. QUINN: No, we haven't, and I'll ask Shawn if  
22 we have data on the wear of this particular high molecular

1 polyethylene, ArCom, which I think there is statistics on or Ken  
2 Beres might be able to answer that for us.

3 DR. BERES: I'm Ken Beres from Biomet.

4 I have a little bit more experience in the orthopedic  
5 realm. This joint is a cross between a total hip and a total knee.

6 There is rotation of the joint similar to a total hip.

7 However, as Dr. Quinn said, there's also some  
8 translation, which would, again, move more towards a knee when  
9 you do have some sliding motion as well.

10 We thought about wear testing. We don't have a good  
11 wear simulator for a TMJ. So we couldn't do actual wear testing.

12 There was no wear noted in a fatigue test and no clinical signs  
13 of wear noted.

14 I don't have the data here. We could do the stress  
15 analysis, the surface stress analysis on the polyethylene. We  
16 could do that easily. I don't think we have that data today.

17 DR. LI: Well, the stress really isn't that important  
18 because a total hip is about a quarter, 15 percent to 25 percent  
19 of the yield strength of the polyethylene, well below what you  
20 reported for your Fugii film, but even at ten percent of the yield  
21 stress, the rate of wear on total hip is more than enough to cause  
22 the osteolysis over a five to seven-year period.

1                   So even if the stresses were half of what you said,  
2                   that would still put you with a high enough stress to cause  
3                   significant polyethylene wear.

4                   So I think a more accurate contact stress would be  
5                   useful, but it doesn't get you away from the wear question.

6                   DR. BERES: Well, you know, wear is a very good  
7                   question. We're trying to avoid the question. I don't know.  
8                   Besides the clinical data, I don't know we could do simulator  
9                   testing. I'm not sure how we do that right now because the fixtures  
10                  and the machines are just not available.

11                  DR. LI: In your laboratory test, I would not guess  
12                  looking at the schematic of the fatigue test that that actually  
13                  would be a very good wear test, but you said you looked at the  
14                  components and saw no wear. So is that just a visual "I see now  
15                  wear" or did you actually weigh samples before and after or do  
16                  something quantitative?

17                  DR. BERES: No. No, there was no quantitative or  
18                  no -- it was just simply visual.

19                  DR. LI: Okay. Thank you.

20                  DR. BERES: Now, on the other side, you mentioned  
21                  the polyethylene is the ArCom polyethylene, which I believe in  
22                  orthopedics is one of the more well known and gold standard, if



1 you will. So we're using the same processing and all as with all  
2 the others.

3 DR. LI: Actually as you raise the issue, my  
4 understanding is ArCom actually can refer to several different  
5 products. For instance, I believe you have a product that you  
6 take the powder and you compression mold it into a bar, and then  
7 you machine the bar, and then you sterilize that in argon and call  
8 that ArCom.

9 There's also another product that you make where  
10 you take the powder and directly mold it into the final form with  
11 no machining and also call that ArCom, and they also may or may  
12 not use the same base polyethylene.

13 So when you say ArCom in this case, exactly what  
14 do you mean? And would it make a difference if you used one of  
15 the other versions of ArCom?

16 DR. BERES: ArCom, Ar stands for argon packaged.  
17 It's packaged in an argon package. Air is removed to reduce the  
18 amount of oxidation of the polyethylene while it's on the shelf.

19 So we remove all of the oxygen from the package, replace it with  
20 argon, and it's vacuum sealed.

21 Com refers to compression molded. So the  
22 polyethylene we use is compression molded. We either compression

1 mold our bar stock, which is a unique method where we mold a bar.

2 It's molded. Most of the other processes for making bar stock  
3 is an extrusion process, where it's an extrusion process to make  
4 a bar.

5 We compression mold the bar. So we compression mold  
6 the part. The part just happens to look like a bar, and then if  
7 the component is complicated enough, it has to be machined, but  
8 the starting material is powder. It's compression molded into a  
9 particular generic shape, and then machined further to get the  
10 intricacies.

11 The other method of producing a part if the part  
12 is processable in a mold, you can directly mold the powder, put  
13 it into a mold, and mold the part as a finished component, but  
14 that requires that the part be somewhat generic enough that you  
15 don't have all of these intricacies that you just cannot mold.

16 DR. LI: Okay. Just one last, quick, detailed  
17 question. On your laboratory testing were the parts sterilized  
18 or not sterilized?

19 DR. BERES: I don't believe that's mentioned in the  
20 test reports.

21 DR. LI: So were they sterilized or not?

22 DR. BERES: I don't know the answer to that.

1 DR. LI: Because that could make a difference,  
2 particularly in your fatigue testing.

3 DR. BERES: We could go back to the original test  
4 reports.

5 DR. LI: Thank you.

6 CHAIRMAN HEFFEZ: I have a related question that  
7 perhaps Mr. Roman or Dr. Quinn could jointly answer. It's regarding  
8 the mating of the surfaces.

9 At the time of surgery you do your best effort to  
10 mate the surfaces, but clearly due to the access, sometimes it's  
11 difficult from a three dimensional point of view to mate them the  
12 way you'd really like.

13 So Part A of the question is have you had significant  
14 problems or not and how you have addressed them, and Part B of  
15 the question is was all of the fatigue stressing was done with  
16 them mated perfectly. Was any fatigue testing done with them mated  
17 incorrectly?

18 DR. QUINN: Okay. I'll answer the first part and  
19 Shawn will answer the second.

20 I think you're right. One of the most difficult  
21 parts of the procedure is mating the condyle to the fossa because  
22 we have to deal with the occlusion as well, and as I mentioned

1 before, in approximately 20 to 25 percent of the cases I usually  
2 move it after that first mating, after I'm able to take the  
3 patient's mandible and move it.

4 Under anesthesia there is some issue as to is that  
5 the same muscle tone that the patient will have when they emerge  
6 from anesthesia. What we normally do is put the patient in fixation,  
7 go back and place the prosthesis, and there is a point where we  
8 want to place the prosthesis posteriorally in the fossa so that  
9 if there is any pseudo translation, you're starting in a more  
10 posterior position, which is why we angulated the head.

11 We've had the experience where under anesthesia a  
12 patient with light in the mating appeared to be adequate. This  
13 is the dislocation patient that we dealt with.

14 When the patient recovered from anesthesia, there  
15 was a relaxation of the muscle, and the condyle came forward, and  
16 we had to actually replace it. So we recommend actually at the  
17 time of surgery to check it with muscle tone and with full paralysis.

18 So at the time we actually check it to make sure that visible  
19 when you use the sterile mandibular manipulator, you're looking  
20 at the mating of the condyle and the fossa, which you have to do  
21 in any system, whether it's custom or stock.

22 And there's where I think it's up to the surgeon

1 to make sure that before they leave that operating room, it's  
2 optimal mating. But it is surgeon experience that can determine  
3 how well that's mated, and it should start in the more posterior  
4 aspect of the fossa.

5 CHAIRMAN HEFFEZ: How do you judge the spacing?  
6 Because it's very difficult to judge it completely across the  
7 condyle, what the adequate spacing would be between the two  
8 surfaces.

9 Actually it's a good question. Some of the older  
10 systems, in the Vitek System there was the recommendation that  
11 you put actually a small pad between the condyle and the fossa  
12 because it would seat with time, and that was true because it was  
13 compressible Proplast in that fossa.

14 We are recommending that it's just a manual seating  
15 without any directional forces from the screws, which is an  
16 important question. If the screws are placed in the ramus offset,  
17 you can literally drive the prosthesis up against the fossa. So  
18 we use drill guides so that we make sure that the screws are placed  
19 passively.

20 The other way you can tell whether there's excessive  
21 compression between the condyle and the fossa is literally move  
22 it, is to go back to the mandibular manipulator and move it under

1 direct vision.

2 CHAIRMAN HEFFFEZ: But what is the spacing that you're  
3 asking the two surfaces or there is no spacing?

4 DR. QUINN: There is no spacing. It's direct contact,  
5 and then using the drill guide so that the screws don't present  
6 any driving forces superiorally.

7 CHAIRMAN HEFFFEZ: Okay.

8 DR. QUINN: It's a good question. We've had that  
9 problem with all of the other systems we've used.

10 CHAIRMAN HEFFFEZ: Because you also have the problem  
11 really with the glenoid fossa. You initially had the cement to  
12 take out the void, but you really don't know how to judge the void  
13 without actually putting the cement in.

14 DR. QUINN: That's true.

15 CHAIRMAN HEFFFEZ: So any thought given to, for  
16 example, using a template to know whether truly the void is  
17 significant enough in that particular case?

18 DR. QUINN: Well, I think the whole issue of void  
19 was whether there was significant dead space that would lend to  
20 an increased rate of infection from hematoma formation in the dead  
21 space under the prosthesis.

22 CHAIRMAN HEFFFEZ: Was it dead space from infection

1 or stability of the prosthesis?

2 DR. QUINN: No, because the stability has to be tripod  
3 stability that's fit regardless whether there's additional void.

4 If you have tripod stability, and remember the majority of  
5 stability comes from the zygomatic arch where the screws are placed,  
6 but you're right. There's no way once you fit it to estimate what  
7 the amount of void is under the presses.

8 CHAIRMAN HEFFEZ: Could Mr. Roman address the Part  
9 B?

10 MR. ROMAN: In Part B there was no -- in the fatigue  
11 testing there was no set protocol for specifically testing them  
12 out of alignment, but just the general nature of potting the  
13 components into the test fixtures. There was a little bit of  
14 variability there. They weren't exactly set up with each other.

15 And just a follow-up. It was listed in the testing  
16 reports that all of the components were manufactured and were gamma  
17 sterilized.

18 CHAIRMAN HEFFEZ: Do you see any advantage to testing  
19 it with offset? Because even though what position you have them  
20 in, even if you have them properly mated, the patient doesn't  
21 function with them properly mated. The patient really functions  
22 with them not mated.

1 MR. ROMAN: Right. There may be some justification  
2 for testing at not exact alignment.

3 CHAIRMAN HEFFEZ: Thank you.

4 Janine.

5 DR. JANOSKY: Janine Janosky.

6 The question was primarily -- I don't know who would  
7 prefer to answer them; probably Dr. Quinn and Dr. Sinn or Ms.  
8 Verstynen.

9 Two issues right now that I'm grappling with. The  
10 first is the follow-up, and the second is the use of two primary  
11 sites. So since we addressed both of those issues separately,  
12 why don't we look at the interaction of those two?

13 So my primary question is: at what point do you  
14 have at least 80 percent of your data available for follow-up?  
15 And then from which sites are those coming in terms of proportions?

16 MS. VERSTYNNEN: Mary Verstynen.

17 Going back to that patient accountability, at every  
18 time point we had better than 80 percent follow-up. So that answers  
19 the first question.

20 And obviously the study is pretty much Dr. Quinn  
21 and Dr. Sinn. There were only eight patients that were not part  
22 of that. I believe that probably one patient wasn't returned to



1 follow-up from the eight. So the rest of them that were missing  
2 follow-up were either at Dr. Sinn's or Dr. Quinn's sites. It's  
3 just that the other sites only did one or two.

4 We had the one site that did five, and they have  
5 one patient that is truly lost. We can't locate her. So at all  
6 time periods we did have better than 80 percent.

7 And even to kind of add to my patient accountability  
8 slide, I don't know if you noticed, but at the four years we had  
9 the best follow-up. There were only, I think, 23 patients out  
10 to four years, but the investigators made an extreme effort to  
11 try to get all of the patients back in the three-year follow-up.

12 In some cases it took almost a whole year to get  
13 them in. So actually we got a higher follow-up at four years,  
14 and actually three of the patients that missed the three-year  
15 follow-up were actually seen at the four-year. I think I did that  
16 calculation.

17 If I combined and made a three-year plus and added  
18 those four years, the follow-up, I think, was bumped up to 87 or  
19 88 percent, even at three years, which was the lowest follow-up.

20 So we did have greater than 80 percent then.

21 DR. JANOSKY: Let me get more specific with my  
22 question. If we think that you started with 180 patients in the

1 study, at what point did you have 80 percent follow-up of those  
2 180 patients? Complete data, 80 percent of them. At what point  
3 was that?

4 MS. VERSTYNEN: The thing is that only at the one  
5 month time point were there 180 patients.

6 DR. JANOSKY: Okay.

7 MS. VERSTYNEN: Well, no. Actually only at the  
8 baseline were there 180 patients because enrollment is occurring  
9 as we speak. I'm guessing Dr. Quinn did cases this week. So if  
10 you even looked at the one month, there were already ten patients  
11 who had missed follow-up because one of the requirements in my  
12 data cutoff was that each patient should have at least been for  
13 their one month follow-up.

14 So even at the one month, we had ten of the 180 that  
15 missed.

16 DR. JANOSKY: Okay. So you're down to 95 percent  
17 at that point.

18 MS. VERSTYNEN: Right, exactly.

19 DR. JANOSKY: So I understand that you have rolling  
20 enrollment. That's typically how we do clinical trials in also  
21 this type of forward looking study.

22 But my question is at what point do you have 80

1 percent complete data of those 180, irrespective of when they were  
2 due. So at what point do you have 80 percent of 180 patients?

3 MS. VERSTYNEN: I calculate the six month point.

4 MR. CANNER: Maybe we're on the same wave length  
5 since I'm a statistician, too, but that's a joke.

6 DR. JANOSKY: I didn't hear your name earlier.

7 CHAIRMAN HEFFEZ: Yeah, identify yourself.

8 MR. CANNER: Sorry. Joe Canner, a statistician with  
9 Hogan & Hartson.

10 I think what you're getting at is take 80 percent  
11 of 180, which is -- I can't do the math in my head -- maybe 140  
12 or 150 or whatever, and when those patients would all have  
13 three-year follow-up.

14 I don't know the answer to that, and I think Mary,  
15 now that she understands what the question is, can answer that.

16 But I think probably the more relevant answer is that the original  
17 sample size calculation for the study was only 86 patients, and  
18 FDA has granted Biomet permission to enroll 300 patients  
19 altogether, but 86 was the original sample size.

20 So I think probably a more relevant question would  
21 be when 80 percent of the patients will have reached three years  
22 among the first 86, and as you can see, we're already up to close

1 to 50, and so that time frame is probably not very far off, although  
2 Mary could probably answer that a little bit better.

3 DR. JANOSKY: I understood the primary endpoint to  
4 be three years.

5 MR. CANNER: That's right.

6 DR. JANOSKY: So my question then is at what point  
7 do you have 80 percent, which is a liberal follow-up level?

8 MR. CANNER: Of the 86 that were originally  
9 anticipated?

10 DR. JANOSKY: Of the 180 that were enrolled, and  
11 that period of time is at the six month follow-up. If you're going  
12 to go with 86, what are you choosing? The first 86 that were  
13 enrolled?

14 Then we get into the issue of what were cemented  
15 and what were not cemented, and some of the other issues, but we  
16 can leave this point because I'm sure it's going to go throughout  
17 the day.

18 MR. CANNER: Yeah. It's just that --

19 DR. JANOSKY: But what if we return to the second  
20 point. The second point that I had mentioned is that at that point  
21 that you have 80 percent follow-up, which is the six month point,  
22 what percentage of the patients at six months are Dr. Quinn's and

1 what are Dr. Sinn's?

2 It's essentially zero. So we can leave that out.

3 So what percentage are Dr. Quinn's? What percentage are Dr. Sinn's  
4 at the six month point?

5 MR. CANNER: Okay. I'll have to look that up for  
6 you now that I understand what you want.

7 DR. JANOSKY: Okay. I'll return to the issue later  
8 so that we can.

9 CHAIRMAN HEFFEZ: Dr. Patters.

10 DR. PATTERS: Mark Patters.

11 A question for Ms. Verstynen and perhaps Dr. Quinn.

12 One of the issues that FDA charges the panel is to make a  
13 determination as to whether the data in the PMAs support the safety  
14 and effectiveness of the device for its indicated uses.

15 You have in your labeling ten indicated uses, but  
16 my review of the data says that some of the indications have no  
17 data or minimal data, such as use in malignancies or the  
18 nonneoplasms. How is the panel to look then at whether there's  
19 safety and efficacy and effectiveness are supported for that  
20 specific use?

21 DR. QUINN: That's an excellent question. I think  
22 what we have to do is put the numbers in perspective, first, in

1 terms of the total potential market for a safe and effective  
2 prosthesis. I think there are 450,000 hips done a year. Nobody  
3 has a very precise way of predicting what is the total population,  
4 but I've heard anywhere between 1,500 and 2,500 a year. It defines  
5 a very small population to begin with, which I think is  
6 appropriate. I don't think this should be widely used unless there  
7 were indications.

8           The more common indications that you saw are  
9 osteoarthritis, traumatic arthritis, ankylosis. I think it is  
10 reasonable to assume that if a prosthesis is safe and efficacious  
11 because the surgical technique would be very similar in a multiply  
12 operated joint who has had seven operations, in a joint that has  
13 an osteochondroma where there's been no surgery, I would be  
14 comfortable making that assumption that it's safe and effective  
15 and that indication.

16           The problem is the numbers. I've probably seen two  
17 osteochondromas in 15 years. So I'm not sure whether we'll ever  
18 be able to answer that question with the appropriate numbers.

19           DR. PATTERS: I guess my concern then: should that  
20 be included in the labeling as an indication or should the labeling  
21 state that there's no data available for treatment of bases with  
22 malignancies?

1 DR. QUINN: I think I'd leave that to somebody more  
2 expert in labeling. Does that allow a reasonable surge in the  
3 off label indication to use the prosthesis in that rare instance?

4 Because I do think that should be the ultimate outcome for a safe  
5 and effective prosthesis.

6 DR. PATTERS: I'm not an expert in the off label  
7 use, but my understanding is that off label use by the practitioner  
8 is always available. You know, they accept the liabilities when,  
9 of course, there is no specified use in the labeling.

10 DR. QUINN: Yeah, I'm not sure I'm expert enough  
11 to answer it other than what I've said.

12 MS. VERSTYNEN: Mary Verstynen.

13 It would be reasonable to add that language to the  
14 labeling, and if FDA would agree with that, I mean, it would be  
15 reasonable because we don't have malignancies. We probably don't  
16 have any benign neoplasms or very few, and maybe we need to qualify  
17 that directly in the labeling with either little or no clinical  
18 data.

19 It's a reasonable request.

20 DR. PATTERS: Thank you.

21 CHAIRMAN HEFFEZ: Dr. Cochran.

22 DR. COCHRAN: David Cochran.

1 I had a question on the radiographic analysis. It  
2 said that the heterotopic bone formation was evaluated osseous  
3 erosion and fossa resorption. So certainly when you deal with  
4 bone and screw into bone, and I think the question was a little  
5 bit earlier about screw loosening was never answered.

6 Was the radiographic analysis standardized or was  
7 it done under blinded condition? And how as each of those aspects  
8 addressed?

9 DR. QUINN: Yeah, the radiographic analysis was a  
10 Panorex lateral ceph. and a PA ceph. They're standardizing such  
11 that sites with the same machines are used. I'm not sure you can  
12 standardize them any more than that.

13 As you know, it's difficult because they are -- at  
14 best Panorex is an elliptical tomogram. You are looking for gross  
15 osteolysis or gross radiolucencies around them. It is difficult  
16 because there's metallic objects. So it would be probably a gross  
17 malposition that you would pick up.

18 The heterotopic bone was probably the easiest  
19 finding, but the X-rays were standardized to those three views.  
20 Does that answer the question?

21 DR. COCHRAN: Well, from a standardization, but did  
22 Dr. Sinn do the same radiographs at each of the same time points?



1           That's what I mean by standardization. In the protocol were set  
2 radiographs taken at set time points?

3                     DR. QUINN: Yes.

4                     DR. COCHRAN: And then from a screw loosening point  
5 of view, the fossa component is the plastic. So that isn't going  
6 to get in the way of looking at screws and positioning of screws.

7           I just wondered if there was like a third person or a radiographic  
8 investigator who would evaluate the position to see if they had  
9 changed.

10                    I think in some of your cases there was some movement  
11 in some of the components. I just wondered if there was an  
12 independent evaluator to evaluate the X-rays.

13                    DR. QUINN: Well, as I said, we had no device  
14 failures. We had no screws, and we had change in the position,  
15 but that was gross dislocation. That wasn't movement of the  
16 prosthesis itself.

17                    The only finding of note was the heterotopic bone  
18 formation. I could let Dr. Sinn address if he followed it the  
19 same way, but they were the standard three radiographs based on  
20 the baseline films taken postoperatively in the hospital at each  
21 landmark.

22                    Now, at the times when we had patients refused, like

1 for example pregnant patients, we documented that there was a visit  
2 without radiographs.

3 MS. VERSTYNEN: I think to answer that question more  
4 directly, with some of our newer IDEs it has become a major issue,  
5 and included into our protocols that we have independent  
6 radiographic assessments.

7 This IDE was filed in 1994, and we weren't quite  
8 that sophisticated to add that to the protocol. Therefore, each  
9 of the investigators did their own radiographic assessments.

10 DR. BURTON: Richard Burton.

11 A question for Dr. Quinn. On your technique portion  
12 which you published, and Step 4 talks about performing an osteotomy,  
13 and they have a traditional condylectomy, and then once you're  
14 able to retract the stump down, it talks about removal of a larger  
15 segment of the condyle, and it wasn't clear in reading some of  
16 the other surgical materials whether or not a coronoidectomy was  
17 included with that.

18 Then in your adverse events there were 15 joints  
19 that required an additional coronoidectomy to improve I would  
20 assume range of motion associated with that.

21 Is that a long enough time frame out that there was  
22 regrowth, reformation of the coronoid? And is that actually a

1 standard portion of the procedure is a coronoidectomy?

2 DR. QUINN: It's not a standard. I think in the  
3 multiply operated joints where they start with large restriction  
4 of motions, I'd recommend that the way to do the two-step osteotomy  
5 is the second osteotomy is to include the coronoid in it in a one  
6 piece step, and we've designed instruments to do that.

7 I do think that the 15 cases show that early on there  
8 are probably cases where we should have removed it because you  
9 have the option of making almost a C cut. The way you determine  
10 how much bone you take off is once the fossa implant is in place  
11 and you put the patient in fixation, if you haven't removed enough  
12 bone, you will actually hit the lip of the implant with the superior  
13 edge of the ramus. That determines how much bone is removed.

14 I think it's surgeon dependent whether they  
15 determine whether to take the coronoids off at the time. I think  
16 in multiply operated patients who start with a ten millimeter size,  
17 I would remove it.

18 If they were largely being operated on more for pain  
19 than mechanical obstruction, it's not necessary that all of the  
20 coronoids have to be removed.

21 DR. BURTON: Okay. Thank you.

22 CHAIRMAN HEFFEZ: Dr. Li.

1 DR. LI: Steve Li.

2 I have a question for the designers of the device,  
3 perhaps Mr. Roman.

4 The one thing that I'm a little uncomfortable with  
5 in your prosthesis design and the fossa design is -- let me make  
6 sure I understand it. The fossa component is fixed with what,  
7 five screws through the polyethylene to the bone?

8 MR. ROMAN: That's correct.

9 DR. LI: So typically we don't -- I would say  
10 generally designers typically don't fix polyethylene directly with  
11 screws. When the polyethylene would be under load because of the  
12 creep that's going to occur, and so on the fossa I would never  
13 expect the bone screws to pull out because if there's any load  
14 on the polyethylene, the polyethylene is going to creep and  
15 essentially make the screw holes bigger and the fossa component  
16 would become loose.

17 So in general, you never see or hardly ever -- this  
18 is the only device I've ever seen where the polyethylene is actually  
19 screwed to the bone to accomplish the load.

20 So my question is: have you ever looked at the change  
21 in the fixation of the polyethylene to the bone before and after  
22 loading?

1                   And perhaps, Dr. Quinn, if you've ever noticed on  
2 retrievals if the polyethylene component is actually looser than  
3 it was, because we see this on total hips and total knees. Even  
4 after a six month period if you do a measurement of the fixation  
5 of the polyethylene to a metal backing, that fixation loosens  
6 relatively rapidly even when the whole component is fixed, and  
7 now you've got five individual screws that are much higher stress  
8 concentrators.

9                   So I would predict that eventually that polyethylene  
10 would become loose from the screws, and that's a long way to ask:  
11 have you ever looked at that? And is there a way to measure  
12 that off of your fatigue tests?

13                   DR. QUINN: No. That has not been looked at  
14 specifically, but the design of the fossa screws does have a flat  
15 portion on the under side of the head that serves as basically  
16 a washer. So we are basically sandwiching the polyethylene between  
17 the under side of the head and zygomatic arch.

18                   As far as if that's been looked at from explants,  
19 I don't know.

20                   DR. QUINN: No. The four that were removed were  
21 for infection, and we didn't find any loose screws or mobility  
22 in the fossa implant itself. Just correction. It's a minimum

1 of four screws. They had 2.0 millimeter, and they were designed,  
2 especially designed 2.0 millimeter with a broader head to give  
3 that washer effect.

4 DR. LI: But that won't affect creep in the  
5 superior/inferior direction, will it, unless I've got my  
6 orientation wrong?

7 In other words, you know, it's a three dimensional  
8 piece and that washer effect protects you in one direction but  
9 not the others, and if the polyethylene is loaded against the screw,  
10 it's going to creep.

11 And so the chance, I think, of it remaining tight  
12 forever is near zero. So it may be tight enough to be clinically  
13 successful, but I can't imagine that it's after a million or 500,000  
14 loading cycles that it, in fact, is fixed with the same tightness  
15 it was at the moment you fixed it.

16 DR. QUINN: I'll let Shawn answer it. I didn't see  
17 any clinical, but I obviously am not examining for creep in the  
18 screw holes when we have removed them. I don't know whether the  
19 test was specifically done because it was done at an offset to  
20 see if we would fracture it at the junction between the horizontal  
21 and perpendicular aspect of it, and I latched on to see if there  
22 was any other test done other than seeing whether it fractured.

1 DR. LI: Well, for instance, on that test you  
2 mentioned, had you measured the amount of micro motion before and  
3 after that test, you might have gotten some indication for if it's  
4 going to loosen, but that you have to measure because remember  
5 100 microns is more than enough to cause sufficient motion to change  
6 the biomechanics and the wear properties.

7 So this might not be something you could casually  
8 feel. You would actually have to go in and measure it and actually  
9 see, but the effects could be cumulative, very large.

10 DR. QUINN: Measure it in vivo or?

11 DR. LI: In vivo is tough, but even in the laboratory  
12 test you could make some attempt to measure that, but certainly  
13 clinically as these patients get out longer, when you get out to  
14 five, six, seven years, I think that would be something I recommend  
15 you look at very carefully, is the fixation of the plastic  
16 component.

17 The screws are going to be intact. It's the plastic,  
18 I think, that's going to move independently of the screws.

19 CHAIRMAN HEFFFEZ: I'd like to move on with Ms. Helms  
20 and followed by Ms. Howe.

21 MS. HELMS: Thank you.

22 Elizabeth Helms, and I'm going to follow up with

1 the loading issue because I think it's so vitally important,  
2 especially since I'm a patient that had two open joint surgical  
3 procedures, condylectomy and no implantation and have done really  
4 well.

5 But you know, malocclusion of a Class II or Class  
6 III, where there is a deviation or an asymmetrical mandible, was  
7 the testing done other than just rotating? Was there testing done  
8 where the job deviates, where that would increase the load on that  
9 joint and allow the joint to move at that deviation point?

10 That's my first question and you can respond to that.

11 MR. ROMAN: I did want to clarify from the earlier  
12 discussion of the fatigue testing. As I discussed, in the testing  
13 the mandibular components were angled at a ten degree angle to  
14 place them in a worst case scenario, both subjected the ramal plate  
15 to a large bending moment, and also minimized the surface contact  
16 between the spherical head of the mandibular component and the  
17 spherical seat of the fossa component.

18 MS. HELMS: Okay. Then were there any studies done  
19 in the follow-ups where there was a unilateral joint? Was there  
20 any degeneration or increased stabilization to the opposite joint?

21 MR. ROMAN: Let me go back because I think Dr. Heffez  
22 raised the same issue. I think it's a very important issue. When



1 we placed the condyle in the fossa, I don't know of any methodology  
2 to know exactly what happens to that seating. The relationship  
3 to the condyle and the fossa, which I think is what Dr. Heffez  
4 was getting at, when this patient now wakes up, has muscle tone  
5 and functions.

6 I doubt it's in the exact place we place it  
7 surgically. That would be counterintuitive. The reason we designed  
8 the condylar head as such a large, spherical head is to allow for  
9 some of that because I think it's impossible for us to know at  
10 the time of surgery that this is exactly where this patient will  
11 function.

12 Your second question is a very interesting one, and  
13 that is when you place a prosthesis unilaterally and you have a  
14 normal functioning joint that has a lateral pterygoid, you've got  
15 two different tires on a car.

16 I mean, I've heard surgeons who are much more  
17 aggressive than I am say if you put one in, you should put both  
18 in. I think that's overly aggressive.

19 Theoretically they would function better because  
20 you would have two systems that have no rotation and -- I'm sorry  
21 -- translation and just rotate. I think there's a point at which  
22 when you send patients for physical therapy after joints especially

1 unilateral, I'm less concerned with achieving 30 millimeters.  
2 I'm worried about people going further. These aren't designed  
3 to do that.

4 And I think it's more problematic when you have one  
5 prosthetic joint and one natural joint because at about two thirds  
6 of the opening, you start to get the lateral pterygoid muscle on  
7 the contralateral side take over. The prosthetic joint stops  
8 moving, and you see deviation.

9 So our bigger problem is we've been surprised how  
10 good the results are in increasing the intercisor opening. I'm  
11 worried by people who say, "I think I can go to 40 millimeters,"  
12 because I don't think these joints are designed to do that, and  
13 it's more of a problem in the case you describe where there's a  
14 prosthesis and an otogenous joint.

15 Does that answer your question or is that --

16 MS. HELMS: Half way.

17 CHAIRMAN HEFFEZ: Ms. Howe.

18 MS. HOWE: Elizabeth Howe.

19 My question is kind of a blend of both the need to  
20 do professional training as well as this lost follow-up, the  
21 question being: was there any thought given to using sites three  
22 and four to do follow-up data collection enabling people who might

1 be on the other side of the country to actually have that data  
2 collection done?

3 DR. QUINN: No. It's a good suggestion. We did  
4 not do that.

5 CHAIRMAN HEFFEZ: Dr. Hewlett.

6 DR. HEWLETT: Edmond Hewlett for Dr. Quinn again.  
7 Your presentation as well as the proposed labeling  
8 indicate that occlusal relationship changes may, in fact, occur  
9 as a result of the placement of the prosthesis. In your protocol  
10 was there any provision made for assessing occlusion  
11 postoperatively and then treating any potential interference, say,  
12 with a splint in order to eliminate occlusion as a possible etiology  
13 in the adverse events?

14 DR. QUINN: Part of the follow-up form is the  
15 occlusion checklist. What's the intercisal opening? Is there  
16 an open bite? Is there a cross bite? That's part of all the  
17 landmarks.

18 The question is: was the preexisting occlusion  
19 secondary to the temporomandibular joint or vice versa? And that's  
20 a chicken and egg question I don't think anybody can answer.

21 The point we made with the prosthesis is you have  
22 the ability to change the occlusion. So if you started with what

1 we've seen, some of the idiopathic female condylar resorption,  
2 where we see females, late 20s, early 30s, who have marked  
3 resorption of condyles that become Class II, there you know that  
4 the malocclusion was secondary to the temporomandibular joint  
5 disease, and there's a case where I think if we were going to place  
6 the prosthesis, we would try to improve the occlusion.

7 I don't think we would just try to improve everyone's  
8 occlusion who had a prosthesis, but when the malocclusion is  
9 secondary to the temporomandibular joint disease, it is something  
10 that you can address with the prosthesis.

11 CHAIRMAN HEFFEZ: Is your question answered, Dr.  
12 Hewlett?

13 DR. HEWLETT: Well, I guess. Yeah, maybe just to  
14 clarify, I think I'm referring specifically to any assessment in  
15 addition to the assessment they outlined. Any functional  
16 assessment?

17 DR. QUINN: Oh, I'm sorry. Yeah, it is common, and  
18 it wasn't something we reported because I do think it's part of  
19 normal post surgical that we do occlusive adjustments. If somebody  
20 came in two months later and had a very high contact on a canine,  
21 we will adjust it.

22 Most of these patients, we try to get them off

1 splints.

2 DR. HEWLETT: I see.

3 DR. QUINN: If at all possible.

4 CHAIRMAN HEFFFEZ: A couple of quick things, and then  
5 I'd like to move on to the FDA presentation.

6 One is at one point in time you were removing the  
7 peg. How were you doing that?

8 DR. QUINN: Dr. Sinn and I both agreed that we would  
9 use a rongeur and simply clip it at the surface of the inner surface  
10 of the fossa.

11 CHAIRMAN HEFFFEZ: And how many cases were done with  
12 them clipped?

13 I understood -- and I may have not gotten the date  
14 right -- was it February 3rd, 2000 that you stated to use the  
15 manufactured glenoid fossa without the peg?

16 DR. QUINN: Actually the fossa was manufactured  
17 without the peg, and I believe Dr. Sinn used three of them that  
18 were manufactured without the peg, and then the FDA was notified.  
19 So the majority of them were clipped, were actually separated  
20 with a rongeur. Only three were pre-manufactured without the post.

21 CHAIRMAN HEFFFEZ: So in this whole study we only  
22 have three cases where the peg -- manufactured without the peg;

1 is that correct?

2 DR. QUINN: That's correct.

3 Do we have the numbers up?

4 CHAIRMAN HEFFEZ: Fine.

5 DR. QUINN: Okay.

6 CHAIRMAN HEFFEZ: Okay. Dr. Runner.

7 DR. RUNNER: This is Susan Runner.

8 I just want to ask the company if you could clarify.

9 We've gone around and around about the numbers here, and we keep  
10 bringing up the number 180 patients. It's not 180 patients. It's  
11 168 patients and 180 cases.

12 Could you clarify that? Because I think we keep  
13 rounding these numbers around, and I want to be sure we're talking  
14 about the right numbers.

15 MS. VERSTYNEN: Mary Verstynen.

16 Since we had both unilateral and bilateral patients  
17 enrolled into this study, we found out early on that there were  
18 actually patients who were enrolled for one side and later on the  
19 other side was enrolled, meaning they would have different surgery  
20 dates for the two sides.

21 So the cases are defined by the surgery date so that  
22 we could follow the patients because literally we have patients

1 that had maybe the left put in at one point and one year later  
2 have the right.

3 And in order to manage the clinical data and to keep  
4 the follow-ups on track, then that other side later on became a  
5 second case. As it turns out, there were 12 patients that had  
6 -- it turned out in the end to be bilateral cases, but they had  
7 different surgery dates for the side. So as it turns out, there  
8 were 168 patients in the study defined as 180 patients or 80 cases.

9 Does that make sense?

10 There were 12 patients that had different surgery  
11 dates for the two sides. If one bilateral patient who had surgeries  
12 of the sides on the same surgery data it was considered a case.

13 So it all came back to the definition -- the surgery date.

14 CHAIRMAN HEFFFEZ: Okay. Just for the panel, I would  
15 like to also for clarification understand if you can repeat to  
16 us the cement versus the noncemented cases, when the cement cases  
17 were no longer performed, numbers, so that it's a little clear  
18 because we are throwing around different numbers of two  
19 populations.

20 MS. VERSTYNNEN: Right. There were 38 cemented cases,  
21 and I believe in the clinical report it was in August of 1998,  
22 was when the last cemented case was done.

1                   Therefore, all of the cemented cases are actually  
2 incorporated into the cohort, which are three years or longer out.

3                   CHAIRMAN HEFFFEZ: So how many cases, noncement, have  
4 been followed through for three years plus?

5                   MS. VERSTYNEN: Eleven.

6                   CHAIRMAN HEFFFEZ: So the 11 cases, noncement,  
7 followed for three years plus?

8                   MS. VERSTYNEN: That was in the cohort, yes.

9                   CHAIRMAN HEFFFEZ: Okay. Then the other thing I want  
10 to do for the panel is I want to make sure, Dr. Janosky, you feel  
11 comfortable with all of your questions answered.

12                  DR. JANOSKY: I was going to return again to it after  
13 FDA's presentation or this afternoon.

14                  CHAIRMAN HEFFFEZ: Okay. So if we've exhausted the  
15 questions, at this point in time I'd like to suggest perhaps a  
16 15 minute break. So that you understand, it's 10:15. Precisely  
17 at 10:30 we will start.

18                   (Laughter.)

19                   (Whereupon, the foregoing matter went off the record  
20 at 10:15 a.m. and went back on the record at 10:30  
21 a.m.)

22                  CHAIRMAN HEFFFEZ: I'll ask everybody to take a seat.



1                   Okay. I would like to get started. Before I do  
2 get started with the FDA presentation, I want to announce a change  
3 in the schedule. Following the FDA presentation, we'll go right  
4 to open committee discussion, which our primary reviewers will  
5 present, and discussion.

6                   We will break for lunch from 12:30 to 2:00 p.m.  
7 So that's a change. Lunch will be from 12:30 to 2:00 p.m. We  
8 will start precisely at two o'clock. So I ask everybody to be  
9 back in the room at two o'clock and then the rest of the schedule  
10 will follow.

11                   So without further ado, Dr. Susan Runner.

12                   DR. RUNNER: Good morning. I want to thank you all  
13 for coming and deliberating on this important issue this morning,  
14 and I would like to start out by introducing the FDA primary review  
15 team.

16                   We have Ms. Angela Blackwell, who's the lead reviewer  
17 and the engineering reviewer.

18                   We have Dr. Kevin Mulry, who's the clinical reviewer.

19                   And we have Ms. Phyllis Silverman, who's the  
20 statistical reviewer.

21                   Before we hear the FDA review team, I'd like to sort  
22 of step back and set the stage by reminding you of the importance

1 of the history of the patients in whom this device has been  
2 implanted.

3 As you all know, the term "temporomandibular joint  
4 disorder" is a complicated term and a collective term. It has  
5 a lot of different definitions by a lot of different people, and  
6 the treatment strategies range from reversible therapeutic  
7 approaches to highly invasive procedures.

8 There is, however, a patient population for whom  
9 nonsurgical treatment is not an option, and these patients have  
10 often undergone numerous surgical procedures which leave them  
11 debilitated, in chronic pain and with limited options.

12 Presentation of the FDA review will begin with Ms.  
13 Angela Blackwell's presentation of the engineering review. Then  
14 Dr. Mulry will present the clinical review and the statistical  
15 review. Ms. Silverman will be available for questions on the  
16 statistical section.

17 At the conclusion of our presentation you will be  
18 able to ask FDA any questions.

19 MS. BLACKWELL: During the course of my engineering  
20 review I will discuss the materials, the component testing, system  
21 fatigue testing, and the outstanding engineering issues.

22 The materials of the fossa component is ArCom ultra

1 high molecular weight polyethylene. The materials of the  
2 mandibular component are cobalt-chromium--molybdenum alloy and  
3 titanium alloy plasma spray. All of these materials are commonly  
4 used in orthopedics, and they all meet standards that are recognized  
5 by FDA.

6 Component testing. There were several types of  
7 component testing, including static testing, pull-out testing,  
8 and push-through testing. These were all done to demonstrate that  
9 the device was adequately -- had an adequate strength for insertion  
10 and use.

11 Static testing of the mandibular components. At  
12 576 pounds, the net portion bent with no breakage. This is well  
13 above the 20 to 200 pounds reported for bite force in the dental  
14 literature.

15 Static test of the fossa flange. It bent at 83 pounds  
16 without fracture. This was a test just to make sure that the flange  
17 would take some force. There's not an in vivo situation where  
18 this would occur.

19 Fossa screw push-through. Eighty pounds was  
20 required to push the screws through the fossa. Three hundred and  
21 seventy-three pounds was required to pull the screws out of bovine  
22 cortical bone.

1           The component testing indicated that the device  
2 strength exceeded the insertion forces, but fatigue testing is  
3 needed to more completely evaluate device strength during use.

4           Fatigue testing demonstrated that all of the  
5 components working together will last for the expected lifetime  
6 of the device.

7           Device failure is very common in this patient  
8 population. Fatigue testing is used to estimate useful life span  
9 of the device.

10           Fatigue testing of the fossa and mandibular  
11 components. Cyclic compressive loading for the maximum load of  
12 145 pounds for ten million cycles results with no failures in the  
13 five samples. Literature estimates a non-bruxing patient would  
14 load the joint with a force of between 20 and 100 pounds.

15           This testing was adequate to show the devices will  
16 survive five to ten years under a load of 145 pounds.

17           We still have one concern remaining. This deals  
18 with the post removal. I think the company mentioned it earlier  
19 in their presentation. The original design had a post, and after  
20 I think 30-something patients the surgeons started removing the  
21 post.

22           And then in February 2002, when the company realized

1 that all of the posts were being removed, they came in with a new  
2 design that didn't have the post. So we asked them for additional  
3 fatigue testing to address these concerns.

4 They're using the same type of testing that they  
5 used before. So hopefully we'll be able to compare the previous  
6 results with the fossa design without a post and the fossa design  
7 with a post, but with the post removed by rongeur.

8 This test is currently being conducted. I believe  
9 they have four samples of each of these done at this time, and  
10 they've run out with no failures. So we expect the final report  
11 early next month.

12 DR. MULRY: I'm going to present the FDA scientific  
13 review of the clinical data submitted in the PMA.

14 CHAIRMAN HEFFEZ: This is Dr. Kevin --

15 DR. MULRY: Oh, I'm sorry. I'm Dr. Kevin Mulry,  
16 and this is the clinical review.

17 Thank you.

18 FDA is requesting the panel's input today on this  
19 pre-market approval application, and the topics I'm going to  
20 discuss are the previous TMJ treatment, the device descriptions,  
21 indication for use, the clinical study results, the investigational  
22 sites and the investigators, adverse events, fossa and bone cement,

1 and questions for the panel.

2 In advance, many of these topics have already been  
3 discussed previously by the other sponsor's presentations. So  
4 what I'll do is I'm going to run through just the points that I  
5 think will emphasize the issues that relate to the questions for  
6 the panel that we would like you to address today.

7 The clinical review of the PMA involves a careful  
8 consideration of all of the data presented in the application.  
9 You, the panel, recommend based upon the data presented whether  
10 you believe the device is safe and effective for its intended uses.

11 Since there are risks associated with any device,  
12 your recommendation must consider whether the demonstrated  
13 benefits outweigh any known or possible risks.

14 Next slide.

15 Before I begin presenting the clinical data, I think  
16 it's important just to reemphasize again the previous treatments  
17 that these patients that are enrolled in the clinical trial have  
18 had, and we look and we see approximately 70 percent of them have  
19 had nonsurgical treatment. Over 60 percent have had disrepair.

20 Almost 40 percent have had silastic disc. We've had Proplast  
21 grafts, total joint prostheses, partial joint prostheses.

22 So they've had quite a bit of treatment in advance

1 of enrolling in the study. So success for these patients may be  
2 limited based upon the sequelae of the multiple surgeries of the  
3 previous treatments.

4 And we've already kind of gone over this, and I don't  
5 think there's any need to emphasize this too much, but the one  
6 point we want to focus on here today is the fossa with the post  
7 and just the fact that that post is the original design, and that  
8 it has been used in the vast majority of cases either as the post,  
9 the design picture here, or with the post removed with the rongeur.

10 The other thing I'd like to emphasize of it is that  
11 this is a stop device, and it's only intended for total joint  
12 reconstruction and not partial reconstruction.

13 You can move on. Next slide.

14 And also we have had an adequate description of the  
15 mandibular condyles, the standard size on the left and the narrow  
16 on the right. There is, as they described, a third design, the  
17 offset design, but that has not been used in the clinical study  
18 to date, and I do have samples of these devices which I will pass  
19 around after the presentation.

20 The indications for use I think have been adequately  
21 vetted. The important thing we want to emphasize here is that  
22 FDA is seeking your input on the applicant's proposed indications

1 for use and the data presented to support these indications, and  
2 I think you've already started that discussion.

3 We can move on.

4 I think we've had adequate discussion of the primary  
5 efficacy endpoints that's on the ten centimeter scale, and we're  
6 looking for the changes on that VAS scale.

7 Success criteria. I'd just like to go over this  
8 real quickly, although this has already been discussed, that the  
9 success has two phases to it. One, a patient is determined to  
10 be a success if the patient has not had a permanent joint removal.

11 The second aspect is the patient has to meet two  
12 of the following criteria, either a reduction in pain of one  
13 centimeter on the VAS scale; a reduction in interference with eating  
14 by one centimeter on the VAS scale; or an increase in maximal incisal  
15 opening of ten percent, and that's all from baseline to the  
16 three-year follow-up point.

17 And the clinical study's success was defined in the  
18 protocol as 60 percent or more of the patients who at implantation  
19 of the device, having met the above patient success criteria at  
20 three years' follow-up, 60 percent.

21 We do have, as we just discussed, as Dr. Runner  
22 did question the sponsor regarding the issue of cases and the



1 numbers of patients, I just want to reemphasize there were 180  
2 total cases in this study, but there were only 168 total patients.

3 The clinical study had the 180 cases. To date we  
4 have 143 cases at the six month follow-up, 89 at the one and a  
5 half years' follow-up, and then we have 45 at the three-year  
6 follow-up, and the sponsor is terming the three-year follow-up  
7 or the 45 cases as the unimputed cohort, and these are the sponsor's  
8 terms, not FDA.

9 FDA views the 45 cases, which represent 25 percent  
10 of the total cases, as the final three-year data.

11 In looking at the clinical study results, we have  
12 the primary efficacy endpoints of jaw pain intensity, interference  
13 with eating, and maximal incisal opening. I'd like to shift to  
14 the right-hand side of the slide where we have the cohort of 45  
15 that were evaluated at the three-year follow-up visit, and what  
16 we're looking at here is the difference between visit one  
17 pre-operative, and visit eight three-year follow-up visit.

18 The difference in the change in the jaw pain  
19 intensity was approximately 5.7 centimeters on the VAS scale.  
20 The interference with eating was approximately 5.8 centimeters,  
21 and the maximal incisal opening, we see an increase of about 10.27  
22 millimeters.

1                   We're not going to discuss the imputed cohort at  
2 this time because we feel that the 45 patients that were actually  
3 evaluated at the three-year follow-up are the data that we think  
4 is the more relevant data.

5                   The T test analysis that was done on this data shows  
6 that in the total group there was a statistical difference in all  
7 three primary endpoints between baseline and assessments at all  
8 time points from one month follow-up to three years' follow-up.

9                   And for jaw pain intensity and interference with  
10 eating, over 80 percent of the improvement was experienced by six  
11 months with the maximum incisal opening approximately 97 percent  
12 of their overall effect of improvement occurred by six months.

13                   So generally, the results plateaued around six  
14 months, and from there on we didn't see much change in the results  
15 or the outcomes. So the question for the panel is whether the  
16 results for jaw pain intensity, interference with eating, and  
17 maximal incisal opening for the cases with three-year data which  
18 represent 25 percent of the implanted population adequately  
19 represent the expected outcomes for the total study group of three  
20 years.

21                   One clinical study, as Dr. Quinn has presented  
22 already, was conducted to support this pre-market approval

1 application, and the thing I want to emphasize here again is that  
2 we look at the fact that 132 of the 180 cases were treated at site  
3 one and 40 at site two, and the remaining eight were at the other  
4 three remaining site.

5 A multivariate analysis noted a significant  
6 interaction between time and investigational site with jaw pain  
7 intensity at site one. The cases began with a much higher VAS  
8 score of about nine centimeters versus approximately 5.63 at the  
9 other sites combined and also experienced a relatively larger  
10 amount or improvement over time compared to the other sites.

11 So the question for the panel is whether the fact  
12 that 96 percent or 172 of the 180 cases were treated at only two  
13 sites. Does this present a potential for bias in the clinical  
14 outcomes?

15 Next slide.

16 As far as adverse events go, actually it should be  
17 51 of the 168 or approximately 30 percent of the patients have  
18 reports of adverse events, and I think Dr. Quinn has adequately  
19 described that most of these adverse events related to excision  
20 of tissue, either the neuroma or heterotopic bone, facial trauma,  
21 motor vehicle accidents, coronoidectomy or ear problems, ear  
22 infections.

1           Eight patients required permanent device removal,  
2           and two of those were fossa components due to necrosis, infection,  
3           and swelling; five total joints due to pain, swelling, infection,  
4           and ankylosis; and one mandibular component due to dislocation.

5           I think it's most important to note, however, that  
6           117 of the 168 or approximately 70 percent had no adverse events  
7           at all.

8           Now, the 30 percent adverse event rate may appear  
9           to be high. However, I think it's important to emphasize that  
10          most of these adverse events resolved themselves, did not required  
11          device removal, and met the success criteria.

12          The issue for the panel is to discuss the rate of  
13          adverse events in this patient population.

14          I just wanted to emphasize here that the purpose  
15          of the post on the fossa was to facilitate retention of bone cement,  
16          and as I think we just discussed prior to the break, the use of  
17          bone cement was discontinued in August of 1998, and of the 180  
18          cases, 38 or 21 percent had bone cement used and 142 or 79 percent  
19          did not.

20          And the issue for the panel here is that the company  
21          plans to market the device as a noncemented fossa or as a cemented  
22          fossa. In the clinical data set, some of the cases are with cement

1 and some cases are without cement, and the panel needs to discuss  
2 the data in light of these two different methods.

3 In summary, the results of the analysis of the  
4 primary efficacy endpoints demonstrate that approximately 98  
5 percent or 44 out of the 45 cases were successes well beyond the  
6 60 percent which was the definition of success in the protocol.

7 The success criteria for jaw pain intensity and interference with  
8 eating was one centimeter. However, the improvement of  
9 approximately five centimeters was well beyond the success  
10 criteria, and for the maximal incisal opening the improvement was  
11 beyond the ten percent needed for success.

12 Patient satisfaction was over 90 percent of all  
13 visits up to three years. As previously noted the patients enrolled  
14 in this clinical trial were selected only after nonsurgical  
15 treatment had failed or after a previous implant failure and also  
16 after a history of an average of 5.2 previous surgeries of the  
17 TMJ area.

18 Success of the surgical results from this  
19 reconstruction must often be tempered by the realization that  
20 reduction in painful symptoms and increase in function may be  
21 limited at best. To date the clinical study results had exceeded  
22 the criteria for success.

1                   As I noted at the beginning of this presentation,  
2 we are seeking your input today on the applicant's proposed  
3 indications for use and the data presented to support these  
4 indications, and what I'd like to do is just run through the  
5 questions that we would like the panel to address today.

6                   Question one, can the results for jaw pain intensity,  
7 interference with eating, and maximal incisal opening for the cases  
8 presented with three-year data which represent 25 percent of the  
9 implanted population adequately represent the expected outcomes  
10 for the total study group at three years?

11                   Question two, 132 of the 180 cases were treated at  
12 site one, Dr. Quinn. Forty of the 180 cases were treated at site  
13 two, Dr. Sinn. Eight of the 180 cases were treated at sites three,  
14 four, and five combined. Does the fact that 96 percent or 172  
15 of the 180 cases -- the fact that they were treated at only two  
16 sites present a potential for bias in the clinical outcomes?

17                   Question three, 51 of the 168 implanted patients  
18 have reports of adverse events. Of these 51 patients, eight  
19 required permanent device removal. Please discuss the rate of  
20 adverse events in this patient population.

21                   Number four, the company plans to market the device  
22 as a noncemented fossa or as a cemented fossa. In the clinical

1 data set, some of the cases are with cement and some cases are  
2 without cement. Please discuss the data in light of these two  
3 different methods.

4 Question five, the sponsor has provided engineering  
5 test data and a protocol for testing on both the new fossa design  
6 without a post and the fossa with a post removed using the rongeur.

7 Do the engineering test data and protocol as presented give  
8 adequate safety and effectiveness information on this device?

9 And the last question, (a) FDA has reviewed proposed  
10 labeling. Please discuss the draft labeling as presented.

11 (b) Please discuss the need for training and the  
12 type of training protocol that may be necessary for safe and  
13 effective use of this device.

14 (c) The sponsor intends to complete the pivotal  
15 PMA study following all patients for three years. Please discuss  
16 the need for any additional post market studies and issues that  
17 should be addressed were those studies to be required.

18 Thank you for the opportunity to present, and Ms.  
19 Blackwell and I will be happy to answer any questions you might  
20 have.

21 CHAIRMAN HEFFEZ: Dr. Patters.

22 DR. PATTERS: Mark Patters.

1 I have a question actually for Ms. Silverman if that  
2 would be all right.

3 CHAIRMAN HEFFEZ: Sure.

4 DR. PATTERS: Does FDA have an opinion on the  
5 definition of a case and how that definition was applied to these  
6 studies as a case being a surgical procedure, whether it be  
7 replacement of one joint or both joints, and that replacement of  
8 both joints at two different times would be two cases? Do you  
9 have an opinion on that?

10 MS. SILVERMAN: That is not a statistical question.  
11 Phyllis Silverman.

12 That is a clinical question. That really isn't a  
13 statistical question.

14 DR. PATTERS: Well, how does one handle the  
15 statistics when some individuals have a single surgical procedure  
16 as defined as a case and some individuals have two surgical  
17 procedures defined as a case such that there is twice the likelihood  
18 of failure in someone who's had two procedures even if done at  
19 the same time than someone who has done one procedure?

20 MS. SILVERMAN: Right. In this data set the people  
21 that were considered two cases, the 12 patients that were considered  
22 two individual cases, I believe they were treated as if they were



1 independent cases, and because it was such a small percent of the  
2 total population, I didn't make an issue out of it.

3 Generally if you would have bilateral cases, then  
4 you would have to account for within patient correlation. You'd  
5 have to do slightly different statistics, but in this data analysis  
6 I let them treat it as individual cases.

7 DR. PATTERS: Thank you.

8 DR. JANOSKY: Ms. Silverman, I was hoping to catch  
9 you before you walked away. So would you mind? I want to follow  
10 in that vein, but I want to take a little bit further.

11 CHAIRMAN HEFFEZ: Dr. Janosky.

12 DR. JANOSKY: Janine Janosky. Sorry.

13 If I take a look at the plots that the sponsors have  
14 provided and I look at the three baseline data points and they're  
15 graphed, I can tell by looking at those graphs at baseline that  
16 those are not symmetrical distributions.

17 Given that point of information, the second point  
18 of information is there's a controversy in statistics as to whether  
19 Likert type VAS scales should be analyzed as parametric or  
20 nonparametric techniques.

21 Taking those two points together and also adding  
22 the third point that was just discussed about data being dependent

1 and treating as independent, were there other types of analyses  
2 that were done that would have taken into account all three of  
3 these issues?

4 MS. SILVERMAN: Well, they could have done a  
5 nonparametric analysis to show how it compared to the parametric,  
6 but I did not request that. They did a repeated measures analysis,  
7 and I thought that that would account for like some within patient  
8 variability and stuff, but I did not request any other analyses.

9 DR. JANOSKY: That was your decision? That was the  
10 sponsor's decision? How was that decision made?

11 MS. SILVERMAN: Well, the sponsor chooses what kind  
12 of analyses they wanted to do, and we can request additional  
13 analysis if we thought that they were necessary, but when I looked  
14 at the overall picture I thought it was pretty dramatic, that the  
15 effect was pretty dramatic, and I did not ask them to do a different  
16 kind of analyses.

17 DR. JANOSKY: So given the analyses that were done,  
18 did the sponsor provide any information to show that the statistical  
19 assumptions were meant for those particular techniques?

20 MS. SILVERMAN: I don't believe they did.

21 DR. JANOSKY: Thank you.

22 CHAIRMAN HEFFEZ: Any other questions? Dr. Li.

1 DR. LI: Steve Li.

2 A question for I think it's probably Angela on the  
3 mechanical testing.

4 There was a fatigue test where the fossa and  
5 mandibular component was placed in fatigue.

6 MS. BLACKWELL: Yes, there were several.

7 DR. LI: Right, and the conclusion, I think, on those  
8 was that there was no failure of the components.

9 MS. BLACKWELL: Yes.

10 DR LI: So my question is: what was the failure  
11 criteria for the fossa component?

12 MS. BLACKWELL: What was the failure criteria?

13 DR. LI: In other words, how would you know? What  
14 would have counted as a failure for the fossa? Did it have to  
15 break?

16 MS. BLACKWELL: Breakage, fracture.

17 DR. LI: So if there was severe wear or deformation,  
18 would that have counted as a failure criteria?

19 MS. BLACKWELL: I believe so.

20 DR. LI: So at these loads, there was no deformation  
21 and no wear in the fatigue tests?

22 MS. BLACKWELL: They didn't do microscopic level

1 analysis. So you couldn't get a definite answer on that from the  
2 test protocol.

3 DR. RUNNER: I think maybe the specifics of the test  
4 protocol might be better answered by the sponsor in terms of --

5 DR. LI: Okay. That would be a whole -- I'm sorry.  
6 I didn't mean to --

7 MS. BLACKWELL: Yes. Well, also bear in mind that  
8 the gentleman who's here today, he didn't do the tests that we're  
9 talking about. It was done like eight years ago or something.

10 DR. LI: Well, my general question is you're doing  
11 a test and then saying the components pass, but I don't know what  
12 the pass-failure criteria is other than frank breakage.

13 DR. RUNNER: Angela, I think you should have the  
14 company answer that question.

15 MS. BLACKWELL: Yeah.

16 MR. ROMAN: Shawn Roman.

17 The acceptance criteria, there are two things looked  
18 at for the fossa compliance. As Angela mentioned, they are looking  
19 for a fracture or breakage of the fossa component, and also on  
20 a macroscopic level looked at where on the fossa component, you  
21 know, and on the articular surface.

22 DR. LI: That was just a visual surface is there

1 wear or is there not wear.

2 MR. ROMAN: That's correct.

3 DR. LI: How about deformation?

4 MR. ROMAN: Yeah. During the visual inspection of  
5 the fossa component?

6 DR. LI: So there was no indentation of the metal  
7 into the plastic after this test?

8 MR. ROMAN: No, sir.

9 DR. LI: Do you find that a little unusual, given  
10 that you have a high load, small area, millions of cycles, that  
11 there is no indentation?

12 MR. ROMAN: Given the large surface contact between  
13 the mandibular component and the fossa component, I would say no.

14 DR. LI: Because even in a total HEP, we just got  
15 a much larger surface area. There's definite deformation under  
16 these similar conditions. So if there is no wear and no deformation,  
17 one I think is the follow-up question to somebody else. The load  
18 may be going somewhere else, right? Because certainly there's  
19 enough load in there that should cause wear or deformation on the  
20 polyethylene was exactly mechanically appropriate.

21 So one question would be a closer examination of  
22 the materials of construction and how the implants are fixed and

1 just exactly where is the load going.

2 MR. ROMAN: The point was brought up that that is  
3 something that we can take a look at now because we are currently  
4 running fatigue testing to address the issues between removed fossa  
5 posts and posts that are -- or I'm sorry -- fossa components that  
6 were manufactured without the posts.

7 DR. LI: Okay. Obviously my concern is you're  
8 undergoing another set of tests to test a component without the  
9 post, but I can't see how it would help but pass under the current  
10 conditions of the test.

11 MR. ROMAN: Okay.

12 DR. LI: So under those conditions, I'm not even  
13 sure why you would particularly run that test if there's really  
14 no way for the polyethylene to fail, if you see what I mean.

15 DR. ANSETH: Kristi Anseth.

16 And just one quick follow-up. So in the studies  
17 that you're undergoing right now with the non-post fossa, there  
18 will be no other further analysis, the wear or anything other than  
19 macroscopic.

20 MR. ROMAN: That's something that we can. We can  
21 include a more microscopic analysis of the fossa bone that's deemed  
22 necessary.

1 CHAIRMAN HEFFEZ: Dr. Li?

2 R. LI: I'm sorry. I'm back to one one last -- I'm  
3 on the fixation issue. I think the test you did was, if I remember  
4 right, was a screw pull-through. You tried to basically measure  
5 the amount of force it took to pull the screw through the hole,  
6 which obviously was described as not really an in vivo number,  
7 would not have been a much more useful number to essentially apply  
8 a small load. So you cycle the plastic in and out of the screw  
9 and see how long it takes actually to pull the screw that way,  
10 that way through because that's the way it's going to fail. It's  
11 not going to rip out in one giant pull, but it probably will loosen  
12 if you apply kind of an in and out motion along the axis of the  
13 screw.

14 MR. ROMAN: It's my understanding though the fossa  
15 component does not see a cyclical load in the sheer direction.  
16 So --

17 DR. LI: Well, I'm sorry. Pick it in the other  
18 direction. I mean it doesn't really matter in what direction.  
19 I think it's going to move.

20 MR. ROMAN: In the other direction, you would have  
21 this over the temporal bone, keeping that micro motion from  
22 occurring.

1 DR. LI: So it's fully supported on the superior?

2 MR. ROMAN: Yes.

3 DR. LI: Okay. I didn't catch that on the drawing.

4 CHAIRMAN HEFFEZ: Ms. Helms.

5 MS. HELMS: Thank you.

6 Liz Helms.

7 My follow-up. On the 12 patients that went from  
8 unilateral surgery to bilateral surgery, of those 12 patients was  
9 there cause from the load going somewhere else, or was that a  
10 condition that was present and needed to have treatment and you  
11 decided to wait on that? What were the circumstances of those  
12 12? Either, either?

13 DR. QUINN: Yeah. Patients who had initially one  
14 --

15 CHAIRMAN HEFFEZ: Dr. Quinn.

16 DR. QUINN: I'm sorry. Dr. Quinn.

17 You asked the patients who initially had one side  
18 place and then had a sepsis contralateral side?

19 MS. HELMS: Right.

20 DR. QUINN: Okay, and what was the question about?

21 MS. HELMS: Okay. The question was what was the  
22 cause of those other 12 to come back and have the other side done.



1 DR. QUINN: I'm not sure what was the cause. Usually  
2 the two reasons patients get prosthetic plates are usually  
3 mechanical difficulties. It's relatively easy to make the decision  
4 when they are fused, but when it's pain, since it's so subjective,  
5 normally patients are largely the decision maker as to what side  
6 might be.

7 We ask them in terms of their pain if the pain level  
8 is a nine out of ten, but it's 90 percent left sided and they're  
9 functioning on the contralateral side, we will replace the one  
10 joint.

11 I think the issue that Dr. Janosky raised about how  
12 do they play into the statistics, and I'm not a statistician, but  
13 it's difficult for us to follow them when they're bilateral joints  
14 unless we separate them clearly because they'll come in and say  
15 they have pain, and we have to side that pain. So that is one  
16 of the reasons we did separate it out.

17 The major reason for coming back hopefully in this  
18 study was that was that they were pleased enough with the results  
19 in the reduction of pain and the increase in function on the first  
20 set that they requested the second.

21 The only other reason it would be is -- and I can't  
22 speak to this with all of these patients in mind -- at the time

1 of surgery because this is not a knee; it is one bone with both  
2 joints in there. It is sometimes difficult for us to determine  
3 which side is actually causing the ankylosis. We could have  
4 radiographic evidence of fibrous or bony ankylosis, but it's  
5 sometimes difficult.

6 There are times that we get permission to replace  
7 both joints. We will go into the worst joint radiographically  
8 and pain-wise and sometimes stop because if we do achieve 30 to  
9 33 millimeters with replacing one joint, it will stop. Because  
10 if we do achieve 30 to 33 millimeters with replacing one joint,  
11 we will stop.

12 It is the pain issue that I think largely drives  
13 the second side being done and patients will say, "Now this one  
14 is bothering me, and I want the same result that we got from the  
15 first side."

16 CHAIRMAN HEFFFEZ: I think her specific question was  
17 she wants to know whether the surgery on one side caused  
18 deterioration on the contralateral side; is that correct?

19 MS. HELMS: Right. Do you know if any of those 12  
20 was there a shift in the load to the opposite side where the patient  
21 originally had not presented with a problem to the opposite side.  
22 So there was just a decision to go ahead and do a unilateral implant

1 rather than a bilateral implant.

2 Was a load shifted to the other side after the implant  
3 was done that created degeneration in that other joint?

4 DR. QUINN: That's a good question. I don't know  
5 of any way of measuring that. The attempts to measure  
6 intra-articular loads have been less than optimal. I'm not sure  
7 how you can measure that.

8 But if patients have a progressive degenerative  
9 disease as osteoarthritis, it is potential that they could continue  
10 that degeneration of the non-implanted side, and I think that's  
11 the most common we implant the second side.

12 CHAIRMAN HEFFFEZ: Thank you.

13 Dr. Janosky.

14 DR. JANOSKY: The question is for Dr. Mulry and Ms.  
15 Silverman.

16 I want to return to the question that I raised to  
17 the sponsor this morning, if we could address it together a little.

18 On your slide you have clinical study cases, and let's just use  
19 case to be whatever they're defining case to be irrespective of  
20 whether that side or not, just to deal with the issue for a second  
21 more simplistically.

22 Their primary endpoint was three years.

1 DR. MULRY: Yes.

2 DR. JANOSKY: For the study, and based on what you  
3 had presented in the slide and based on what I have gathered from  
4 the information, they had presented is that out of 180 cases at  
5 year three, you had 45 cases.

6 DR. MULRY: That's correct.

7 DR. JANOSKY: To which you had complete data.

8 DR. MULRY: That's correct.

9 DR. JANOSKY: Which given the issue that I was talking  
10 about this morning in calculating follow-up, you calculated that  
11 there would be a 25 percent follow-up.

12 DR. MULRY: That's correct.

13 DR. JANOSKY: Now, one of the questions I asked the  
14 sponsor this morning was: out of those 45 cases, what number came  
15 from Dr. Sinn and what number came from Dr. Quinn. Do you have  
16 that piece of information for us?

17 DR. MULRY: No, I don't believe we do.

18 MS. SILVERMAN: I do know that all 45 were at those  
19 two sites, but I don't recall what -- you know, I might have that.

20 DR. JANOSKY: Because it would be reasonable for  
21 me to think it was a 70-30 split like there was in the patient  
22 recruitment, but that might be unfair to just come to that

1 conclusion.

2 DR. MULRY: Mary, would you have that?

3 DR. JANOSKY: Was the sponsor able to get that piece  
4 of information?

5 It is exactly 70-30. Okay.

6 While they're just confirming that, let me raise  
7 one other issue with you. Maybe you can enlighten me a little  
8 bit. I see the two instruments are paper and pencil, and one  
9 instrument of the outcomes is face to face. The patient needs  
10 to be there.

11 The sponsor gave the discussion that perhaps they  
12 didn't have complete data for all of those follow-up because either  
13 the patients were doing well so that it didn't come back or  
14 geographically they were at such a distance they didn't want to  
15 make the trip, et cetera, et cetera, et cetera.

16 If I go with that second hypothesis that they had  
17 postulated, which was the patients are at such a distance they  
18 didn't want to come back, confirming that hypothesis for me would  
19 be that they would at least have two of those assessments done  
20 per patient. In that they would have said, "Okay. You're not  
21 willing to come back, but will you please complete these VAS for  
22 us because those are patient self-report?"

1 Do you have any indication that that was done, that  
2 they have missing data depending on type of outcome?

3 DR. MULRY: I don't think there was enough  
4 information in the application to tell us one way or the other  
5 whether they did that.

6 DR. JANOSKY: Okay. So it's not fair for me to  
7 necessarily conclude that that second hypothesis, which was  
8 geography, was one of the issues that patients didn't return?  
9 Because that's a very simple thing to do, ask a patient to complete  
10 paper and pencil.

11 DR. MULRY: I don't think there's enough information  
12 in there for us to make that determination. We really have to  
13 depend on the sponsor to let you know what they actually did in  
14 a collection of data.

15 DR. JANOSKY: Based on your experience with these  
16 types of studies, would you expect to see those types of data?

17 DR. RUNNER: I think with our experience we ask  
18 sponsors to get data in any way they can to follow patients.

19 DR. JANOSKY: Based on my experience I have the same  
20 experience, whether that means partial records or not partial  
21 records.

22 Does the sponsor have -- is it a 70-30 split for

1 that n equals 45 at three years?

2 We're still searching. Okay. I'll wait a while  
3 longer then. Thank you.

4 DR. JANOSKY: I'd like to follow up with that question  
5 and ask the 11 patients that were treated with noncemented. What  
6 was the distribution as well?

7 Are there any other questions from the panel? Ms.  
8 Howe.

9 MS. HOWE: Elizabeth Howe.

10 Dr. Mulry, my question has to do with your question  
11 to us, 6(b), about training. Was there any material given to you  
12 to review regarding proposed training that would go along with  
13 this product?

14 DR. MULRY: Not in the clinical section, no.

15 MS. HOWE: Is there anything available from the  
16 sponsor that would show an intent to do a training component?

17 MS. BLACKWELL: We were told that they were planning  
18 to have training for everyone before they were allowed to place  
19 the device, and I believe a video was made, but we haven't seen  
20 it yet. We usually do labeling and real detailed work after the  
21 panel meeting simply because of the time issue.

22 MS. HOWE: Thank you.

1                   CHAIRMAN HEFFFEZ: Mr. Mulry, I have a question for  
2 you. In reviewing the indications, many times the patients had  
3 multiple diagnoses. Was any attempt made to your knowledge to  
4 find a primary diagnosis so that it could be a little bit clearer  
5 what the indications were for this surgery?

6                   DR. MULRY: Not that I'm aware of.

7                   CHAIRMAN HEFFFEZ: I'll ask the sponsor if they made  
8 an attempt to find a primary diagnosis. I'll address it to Dr.  
9 Quinn.

10                   For example, some of them have traumatic arthritis,  
11 deformity, and several diagnoses, and they're all tallied as that.

12                   Is there one table that can tell us what a primary diagnosis is  
13 because clearly many of those have secondary diagnoses.

14                   DR. QUINN: Well, we didn't make an attempt to  
15 identify one as primary. I'm not sure of the multivariate analysis,  
16 whether they were broken. My knowledge is that they weren't.  
17 We didn't list one as the primary.

18                   Mary, do we have the data that Dr. Janosky is  
19 requesting?

20                   MS. VERSTYNEN: Mary Verstynen.

21                   I have the data for the cohort imputed group of 59  
22 where 41 of the 59, which is 70 percent, were Dr. Quinn's and 18,



1 which is 31 or 30 percent, for Dr. Sinn. So it was a 70-30 split,  
2 and there's no reason to believe that it wasn't the same for the  
3 45 number.

4 CHAIRMAN HEFFEZ: How about the 11, the cemented  
5 11? Do you know what the distribution is?

6 MS. VERSTYNEN: It would obviously be more of Dr.  
7 Quinn's because Dr. Quinn had 31 of the 38 and Dr. Sinn only cemented  
8 seven cases, but I don't know exactly of the 11 how many were Dr.  
9 Quinn's and how many were Dr. Sinn's.

10 CHAIRMAN HEFFEZ: And as far as -- while you're up  
11 there, as far as the diagnosis distribution, is that data available  
12 to be able to break it down into primary diagnosis?

13 MS. VERSTYNEN: No. I remember discussing this early  
14 on in the protocol, and it seemed to be very difficult to put a  
15 primary diagnosis on these patients because of the multiple  
16 diagnosis that most of them had. So there's no way to go back  
17 and collect it unless we ask for it retrospectively.

18 CHAIRMAN HEFFEZ: And for the panel, can you define  
19 traumatic arthritis, and could you define aseptic necrosis?

20 MS. VERSTYNEN: I think I'll defer to a clinician  
21 on that one.

22 CHAIRMAN HEFFEZ: Okay.

1 DR. QUINN: I think the difficulty of the diagnosis  
2 question in general is that the patient presents with signs of  
3 late stage degeneration and ankylosis. Which one is primary and  
4 which one is secondary?

5 We defined traumatic arthritis as when there was  
6 in the preoperative form an identifiable event, when the patient  
7 said, "On February 11th, 2000, I was in a motor vehicle accident  
8 with direct facial trauma. Prior to that I had no symptoms."

9 Then we labeled the degenerative changes as  
10 traumatic osteoarthritis as opposed. So it's purely labeling by  
11 history.

12 CHAIRMAN HEFFFEZ: And aseptic necrosis, how did you  
13 define that?

14 DR. QUINN: Well, aseptic necrosis and avascular  
15 necrosis, as you know, is a hot topic in the temporomandibular  
16 joint literature. If there was imaging evidence where avascular  
17 necrosis was mentioned as part of the imaging, I'm not a believer  
18 that the avascular necrosis is as prevalent in the  
19 temporomandibular joint as in other joints, but if the imaging  
20 prior to surgery mentioned avascular necrosis or aseptic necrosis,  
21 we use the term based on the radiologic evidence.

22 CHAIRMAN HEFFFEZ: So it was based on the

1 radiologist's diagnosis?

2 DR. QUINN: Yes.

3 CHAIRMAN HEFFEZ: Okay. Excuse me. Dr. Bertrand.

4 DR. BERTRAND: Peter Bertrand, a question for Dr.  
5 Mulry.

6 You've charged us with understanding whether or not  
7 the three-year data is reflective of the rest of the patient group.

8 DR. MULRY: Yes, sir.

9 DR. BERTRAND: That may very well be true at three  
10 years with the others for pain, chewing ability, and incisal  
11 opening. My concern though is how is the three-year implant arrived  
12 at. Why not six years? And why that three years may not be  
13 sufficient time to see any type of immune reactions manifested  
14 in the patient group.

15 DR. RUNNER: I think -- this is Susan Runner -- I'm  
16 going to answer that question. We developed a guidance document  
17 with input from clinicians some years ago that stated that for  
18 temporomandibular joint implants there would be a three-year cutoff  
19 for data. That was arrived at with input from the various people.

20 Obviously you could continue out patients for a long  
21 period of time to get additional data, but that has been the  
22 standard.

1                   It has also been a primary standard in orthopedic  
2 studies as well.

3                   DR. BERTRAND: I'm going to expose my immunologic  
4 ignorance here, but for my own edification maybe anybody can help  
5 me understand it. Is three years sufficient time to explore the  
6 possibility of immune functions, especially if there's some  
7 material failure at four, five, six, and seven years?

8                   I don't know if anybody can shed any light on that.

9                   CHAIRMAN HEFFEZ: Dr. Li.

10                  DR. LI: Well, I can give an answer from a total  
11 knee side that three years would be an extraordinarily short time  
12 to see any immune response to polyethylene or metal debris. The  
13 wear rate would have to be horrendous for it to show up in three  
14 years.

15                  But a bad or high wear rate would probably take a  
16 minimum of five to seven years before you saw the immunological  
17 response. So if you had -- so unless the wear rate was horrendous,  
18 which does not appear to be in this case, the wear rate still could  
19 be high enough to cause a response at five, which would be invisible  
20 at three if it was a total hip or a knee.

21                  DR. BERTRAND: So a question for Susan Runner then.  
22 Was there consultation with people concerning reactions where

1 a three-year time frame was developed?

2 DR. RUNNER: I don't believe that's the case.

3 DR. BERTRAND: Thank you.

4 CHAIRMAN HEFFEZ: Dr. Suzuki.

5 DR. SUZUKI: Jon Suzuki.

6 A question for Dr. Mulry really. With respect to  
7 the determining what the learning curve is on implanting these  
8 devices, is there a way that the panel can look at either the rate  
9 at which the devices had to be removed or the morbidity that occurred  
10 as the surgeon gave experience?

11 The reason I'm asking this question about the  
12 learning curve is that it may impact on answering like training  
13 issues and whether or not these two sites are acceptable.

14 DR. MULRY: I think all of those could be factored  
15 in. I think it would be helpful if we heard maybe from Dr. Quinn  
16 who has been training the other surgeons for this technique as  
17 to what value it's had and what they've had to do in the process  
18 of training, along with the other information.

19 DR. QUINN: I think it's an excellent point. I don't  
20 think we saw any glaring differences based on the curve, but I  
21 think Dr. Sinn and I would be considered relatively experienced  
22 surgeons.

1 I think it is an issue, and I think it's not only  
2 an issue in this device, but if you look at the leap frog initiatives  
3 in this country that they're looking at a minimum number of  
4 procedures in a lot of things like open heart surgery and  
5 angioplasties, and so I would apply the same logic to this device,  
6 that hopefully it will be done by surgeons and centers where there's  
7 a minimum amount that would determine that expertise.

8 I don't know what that is. Remember we're starting  
9 with a small number, to begin with, and I think we have to keep  
10 that in consideration. Our plan is to have any surgeon who is  
11 going to implant this device train by either Dr. Sinn or myself  
12 and then move to a train the trainer mode.

13 They would also have to take a course, and that's  
14 part of the videotape that's being developed. I feel very strongly  
15 that someone who has no background in this surgery shouldn't make  
16 the hyper leap into placing a total joint prosthesis, but I think  
17 you can use the same logic in any advanced reconstructive procedure  
18 in the orthopedic world as well.

19 CHAIRMAN HEFFEZ: Okay, and we'll just have two  
20 additional questions. Ms. Helms and then Dr. Burton, and then  
21 we'll move on to the reviewers.

22 MS. HELMS: Thank you.

1 Elizabeth Helms.

2 I have a question for Dr. Quinn on number three and  
3 a question for Dr. Mulry on number six.

4 Of the 52 patients that had the adverse effects,  
5 do you know what their quality of life is to date? And were any  
6 of those 52 incorporated into the end of the three-year trial in  
7 that information of the outcomes?

8 DR. QUINN: I think the pat. key that identifies  
9 every patient and also identifies the adverse events, I could link  
10 them to them. I'm not sure I could give you a comprehensive listing.

11 When you say quality of life in terms of the  
12 parameters we followed or something beyond that?

13 MS. HELMS: Right. The pain, for one.

14 DR. QUINN: Well, actually we could link the adverse  
15 events to specific patients and look at the data. I'm not sure  
16 I could recite it for you.

17 DR. RUNNER: Well, excuse me, but didn't all 52,  
18 except for the eight removed, didn't they go on to resolve their  
19 adverse events and become successes?

20 DR. QUINN: Except for the eight, yes.

21 MS. HELMS: Except for the eight. Right, okay.

22 DR. QUINN: And what was the second part of the

1 question?

2 MS. HELMS: The second part of the question is number  
3 six. On the labeling, the disclosure information, is there  
4 significant disclosure information in the labeling for consumers  
5 to understand what is being implanted?

6 DR. RUNNER: Susan Runner.

7 The company has provided the patient labeling, and  
8 that has been reviewed by our Office of Health Industry Programs,  
9 and it's inconsistent with other TMJ implant patient labeling  
10 materials.

11 CHAIRMAN HEFFEZ: Okay. Dr. Burton.

12 DR. BURTON: Richard Burton, and this could either  
13 go to Dr. Mulry or to Dr. Quinn.

14 One thing, we've talked about some wear issues, and  
15 they've talked about whether fatigue testing and how long it would  
16 last and things, but has anyone at least even -- I always say this,  
17 "venture to guess" -- but what is the expected life expectancy  
18 that you informed the patient of?

19 I looked at the patient literature, and it doesn't  
20 really address that, and obviously you're dealing if you're looking  
21 at the demographics with a reasonably young population. You know,  
22 if you have a device that can last whether it's five years or ten



1 years or 15 years and you have a 30 year old patient, and these  
2 are multiply operated patients, what then is the future that they're  
3 looking at as well?

4 And I mean, I think that the patient needs to at  
5 least I don't know whether it's publish or not, but it needs to  
6 at least have some concept of: fine, I'm 30 years old. I'm getting  
7 this joint implant. Hopefully this will improve my pain and  
8 function, but what is my long-term expectancy with this?

9 I know what we tell patients and knowing some  
10 orthopedic colleagues what they tell them. You know, if you're  
11 X years old and you get a knee done, you know, this is what you  
12 can reasonably expect. This is what you can expect from your hip.  
13 What can I expect from this implant in terms of a life expectancy?

14 And obviously there is a range, and at this juncture  
15 obviously given the time frame out, somewhat obviously speculative.

16 DR. MULRY: Yeah, I'm not sure I can answer that  
17 from looking at the clinical data because the data is only out  
18 to six years, and I think that was five patients. So we really  
19 don't have anything beyond that to draw upon in terms of data.

20 So maybe Dr. Quinn or one of the engineers may be  
21 able to answer that.

22 DR. QUINN: It's an excellent question because every

1 patient who has this asks me that question, and in honesty you  
2 have to say, "I can only tell you the longest one out is six years  
3 and one month."

4 I'm not sure there is a method, and if the  
5 statistician could help me to say if 59 of them are out four years,  
6 I can impute that they would last a range. I don't know whether  
7 you can do that, but my experience with the most recent stock implant  
8 that we used in over a period of 12 years, implanted a good number  
9 of them, the average life span was about six and a half years where  
10 we started to see -- but we saw significant, to get to Dr. Li's  
11 point, polymeric debris where the current episodic swelling,  
12 loosening much earlier in the use of that device.

13 And I may have to defer to Dr. Runner, but my  
14 understanding was in 1994 during this initial submission, there  
15 was a definition that five years was a reasonable expectation from  
16 the temporomandibular joint device. I think that was the arbitrary  
17 definition at the beginning of this process, and if anyone can  
18 comment beyond that, I would appreciate it.

19 DR. RUNNER: I believe that was the --

20 CHAIRMAN HEFFEZ: Dr. Runner.

21 DR. RUNNER: I'm sorry.

22 I believe that was the idea behind the ten million

1 cycles with an estimate of two million cycles per year as an  
2 estimate. I believe that's what went into that number for the  
3 fatigue testing.

4 DR. QUINN: I think the variability here is, as you  
5 know, that I thought the latest wear testing I saw was in the normal  
6 adult joint you would have 13 million functioning rotations in  
7 a ten-year period.

8 The problem is that variability in this case because  
9 in the normal patient, your teeth are in contact 18 to 24 hours  
10 a day, and a bruxer can be up to four hours. So I think there's  
11 a huge variability in there.

12 CHAIRMAN HEFFEZ: One of the problems, you say in  
13 six years the other type of prosthesis demonstrated metallosis  
14 and problems, and yet we didn't study very well the microscopic  
15 debris here, and we're not at six years with this device. So I  
16 think you have to just fill in and paint the picture a little bit  
17 better.

18 DR. QUINN: Well, I'm comparing a device that largely  
19 had a methyl methacrylate head, and wear testing is grossly  
20 different than a cobalt chrome head against polyethylene. So I  
21 think that -- is that the point?

22 CHAIRMAN HEFFEZ: Well, it goes back to Dr. Li's

1 point where how much of the testing has been done from a microscopic  
2 point of view to demonstrate the wear.

3 DR. QUINN: I should mention that we did do testing  
4 against what we referred to as the predicate device as part of  
5 the submission, and we did use five of the devices that I was  
6 referring to and compared them, and we do have that data if it  
7 would be helpful.

8 CHAIRMAN HEFFEZ: This data would be representing  
9 five in vitro testing?

10 DR. QUINN: I may ask Shawn to help me.

11 We did test the Lorenz TMJ device against what we  
12 referred to as the predicate device.

13 CHAIRMAN HEFFEZ: We can't --

14 DR. RUNNER: I think for PMAs, PMAs have to stand  
15 on their own.

16 CHAIRMAN HEFFEZ: Right.

17 DR. RUNNER: We don't really compare to previous  
18 devices.

19 CHAIRMAN HEFFEZ: Okay. Thank you.

20 I would like to move forward with the primary  
21 reviewers. There will be three primary reviewers: Dr. Rekow,  
22 Dr. Burton and Dr. Janosky, and we'll go in that order. I'll allot

1 15 minutes maximum for each one, to be followed with five questions.

2 Dr. Rekow.

3 DR. REKOW: Well, I won't use up my 15 minutes.

4 I think that there are a couple of important points  
5 to make. I think that the corporate issues have made it a point  
6 to address the ASTM and ISO standards, and I think that most of  
7 the testing that was done and proposed follows issues that were  
8 completed before the IDE submission, and I think that -- is that  
9 a proper statement, Susan?

10 CHAIRMAN HEFFEZ: Dr. Runner.

11 DR. RUNNER: The testing was approved with the IDE,  
12 but before the PMA submission.

13 DR. REKOW: Right, and so much of this has been  
14 reviewed before. And so I think that we need to keep that history  
15 in perspective.

16 Well, we still need to address the issues of the  
17 safety and efficacy, but we do need to identify that much of this  
18 testing was done some time ago.

19 In my opinion, as I looked at the different designs  
20 as I understood them from the drawings and the information that  
21 was presented to us, there has certainly been an evolution in the  
22 designs, but from my assessment those typically have not changed

1 minimum thicknesses, nor have they made radical changes in areas  
2 that would be the most likely high stress concentration areas.

3 So I think that the tests that have been done, while  
4 there have been changes in the design, don't remarkably change  
5 the anticipated results, with perhaps the small exception of the  
6 pre- and post peg question, and that is being addressed now.

7 I have a small concern about whether or not the test  
8 that was originally designed, where you don't have a compliance  
9 substructure to adequately give you the failure mechanisms under  
10 fatigue loading, but indeed, they are providing information that  
11 will be able to be correlated with the historical testing, and  
12 so it's an interesting question about which of those is the most  
13 appropriate approach to take.

14 A couple of other concerns that I think may need  
15 to be addressed as part of our concern is some of the testing was  
16 done with bovine bone thicknesses. I believe that was the pull-up  
17 test. No. Was that the pull-up test that was done?

18 And there the cortical plate was argued to be twice  
19 as thick as the cortical plate in the mandible, but you would put  
20 your screws through both sides of the mandible.

21 And if that's true that you really go through the  
22 whole cortical plate on both sides of the mandible, it's a good

1 argument. The question is how much of the second side of the  
2 cortical plate the mandible gets engaged in the screws. I think  
3 that that's not a critical issue. I think it's one that just needs  
4 to be addressed, needs to be thought about a little bit.

5 I am slightly concerned with some of the issues that  
6 Dr. Li has brought up about the creep in the fossa component, and  
7 more particularly about the wear debris and the scenario of the  
8 wear debris because that historically has been such a remarkable  
9 issue.

10 I would encourage you to look at the wear debris  
11 with your new testing and to do it rather aggressively, and if  
12 you find things perhaps you might want to propose some other testing  
13 be done to either allay fears or to change your design.

14 I think though that it's also important to note that  
15 these are the materials that are being used in other applications,  
16 and they have succeeded in other clinical applications. So I don't  
17 think that the concerns that I'm raising should be alarmist  
18 concerns, but I do think that we need to know a little bit more  
19 about the wear debris and its outcomes because that to me is a  
20 singular issue that could potentially create some very difficult  
21 in vivo problems.

22 CHAIRMAN HEFFEZ: Any questions to Dr. Rekow from

1 the panel?

2 (No response.)

3 CHAIRMAN HEFFEZ: Then we'll move to Dr. Burton.

4 DR. BURTON: Richard Burton.

5 I'll try to deal just strictly with the clinical  
6 issues. Many of these, as of the issues that I found in my review,  
7 have already been answered, and I'll just try to sort of maybe  
8 perhaps raise them and close some of the questions at the same  
9 time.

10 In reviewing obviously from a clinical standpoint,  
11 I looked at the complication rate, which I would agree is certainly  
12 within the norms for this type of patient population in my  
13 experience. The type of complications which we saw, again, is  
14 that we saw there were only eight explanted joints. Most of those  
15 result, sometimes not spontaneously but within normal conservative  
16 management techniques, and the most common ones being neuromas  
17 and various scar tissue adhesion type of issues, which, again,  
18 are very common in this type of population.

19 And as Dr. Quinn pointed out, the issue of  
20 heterotopic bone with both TMJ surgery and with any type of implant.

21 Over the years we have seen that to be a constant source of problem,  
22 one which at least at this juncture has not had a good answer for



1 that.

2 The concern I had in looking at the complication  
3 rate is that just sort of anecdotally as I reviewed the entire  
4 patient population and the patient key for that, my sort of gut  
5 feeling was the fact that there certainly had been somewhat of  
6 a decrease in rate as you went further on in the study, which again  
7 would play into the fact of experience, time issues, and time of  
8 surgery issues, which Dr. Quinn explained as well, and I would  
9 certainly make the comment that in having treated patients for  
10 a number of years where you had unilateral TMJ problems, that once  
11 you improve their primary complaint site, suddenly the site which  
12 had not been their primary complaint, oftentimes they would return  
13 regardless of the type of procedure that was done in saying, "Gee,  
14 this site is really a lot better. Now my other site."

15 And you know, you raised the question whether or  
16 not that was a shift in load. Many of us have asked ourselves  
17 that question over the years, and this is certainly within the  
18 realm of the possible. Many times, I think, most of us have felt  
19 that that was a fact, is that the patient becomes aware of those  
20 symptoms. Like most of us, you know, if you have one primary  
21 complaint, once that's addressed sometimes you move on to more  
22 secondary issues.

1           Review of the surgical indications I thought were  
2 adequately explained because I had some concern regarding the ages  
3 with that. I would concur with Dr. Quinn in the fact that I think  
4 that avascular necrosis is a vastly overplayed term, which has  
5 become sort of a popular catch-all for some unexplained situations,  
6 and I think that we've sort of allowed some time to our radiographic  
7 colleagues to sort of push us towards that diagnosis where many  
8 of us clinically are not quite sure that that exists to that level.

9           I did have some concerns regarding the issue of site  
10 bias and the fact that, again, if you looked at the original protocol  
11 and you were talking 300 patients, which I thought was quite  
12 laudable, but again, a reasonably large group, in ten sites would  
13 have been good.

14           But again, the point where we have eight surgeries  
15 done by three additional sites, I have concerns whether the  
16 complication rate that we're currently seeing, which is both  
17 reasonable in both the type and the numbers, may be a reflection  
18 of the fact of the experience level of those surgeons placing the  
19 devices and whether as we expand the number of sites, were this  
20 product approved, whether we're going to seek a concomitant  
21 increase in the rate of complications.

22           The change from a clinical standpoint, from a

1 cemented to a noncemented fossa I think Dr. Quinn addressed, and  
2 again, in looking through their surgical guide, they had developed  
3 -- did you develop the burr, the burr that you're using, that diamond  
4 burr, for fossa contouring? It was specifically designed for that.

5 Most of us who had used other systems found that  
6 that was very problematic, and I think that that's where the need  
7 for cement came from. I think that most of us feel, again, any  
8 factor you don't have to introduce into that area reduces that,  
9 and I guess that's not something that personally I have that change  
10 to be much of an issue. I think that that, candidly, an improvement.

11 My last concerns work primarily around the labeling  
12 issues, that we have an adequate review of the labeling and  
13 indications for that, and then again, this has been addressed  
14 several times as a clinician, the fact that I think this is going  
15 to be quite dependent upon having an adequate training program  
16 such that it will release into broader use of hands, we'll continue  
17 to see what are reasonable clinical outcomes with that.

18 And then lastly, like I said, just the life span  
19 issue, that's very difficult to explain, but every patient's idea  
20 with various devices always has to say, "Well, gee, how long is  
21 this going to last me?"

22 Certainly we can't give them that answer, but looking

1 historically at other issues we need to be able to provide some  
2 type of answer to that.

3 And then from a nonclinical standpoint, I think Dr.  
4 Li's question of wear debris because it has been my experience  
5 that everything has some wear debris, and again, usually if you're  
6 not seeing it, you're just not looking at the right level to find  
7 that.

8 I'll take any questions.

9 CHAIRMAN HEFFEZ: Any questions? Dr. Bertrand.

10 DR. BERTRAND: Peter Bertrand.

11 Concerning the longevity of the device being  
12 implanted and the statement that you made, Dr. Quinn, concerning  
13 that most of these patients probably have 18 to 24 hours of tooth  
14 contact a day, either pre-surgically or post surgically is any  
15 attention given to the ability to control tooth contact?

16 It's been pretty well established through neural  
17 science that one of the strongest brain responses to incoming  
18 stimuli is either tongue bracing or tooth touching. Has there  
19 been any work done towards addressing that?

20 Which if you reduce that 18 to 24 hours of tooth  
21 contact, it might in the long run improve the longevity of the  
22 appliances implanted.

1 DR. BURTON: I would say that, you know, that's  
2 something that possibly could and probably should be addressed.

3 Again, you have the possibility with any type of device that you've  
4 taken the patient who certainly has what may be a degenerative  
5 joint disease or something else, which is a clinically identifiable  
6 pathology, if you want to call it that, who also has underlying  
7 neurophysiological issues.

8 And I think that at least what I get that you're  
9 asking is once you made, you know, the surgery deals with the more  
10 overt clinical pathology, but then once you have addressed that,  
11 should you then turn around and try to address perhaps an underlying  
12 neurophysiological issue which in a sort of, you know, which came  
13 first, the chicken or the egg, but at that point in time perhaps,  
14 yes, they may need -- a person who failed surgical or non-surgical  
15 therapy and has a surgery may still be a candidate for some  
16 nonsurgical therapy which then may extend the life of their implant.

17 That would be my sort of professional opinion on  
18 it.

19 DR. BERTRAND: Dr. Quinn, is there any either  
20 pre-surgical or post surgical way of addressing that tendency that  
21 you made reference to?

22 DR. QUINN: I actually agree with Dr. Burton. There

1 is continuing nonsurgical therapy. It doesn't end with the  
2 implantation. I think the question is -- and I'm not sure I could  
3 answer it -- is the chicken or egg question. Do people brux because  
4 they have pain or do they have pain because they brux?

5 My anecdotal evidence is that if you reduce the pain  
6 levels, we do see a reduction. It wasn't a variable we followed,  
7 but it would be an interesting one to look at. My impression is  
8 that as the pain levels dropped we see less, but we still have  
9 people who continue to brux afterwards.

10 And I think to Dr. Li's point and your point, we  
11 will continue to use splints to theoretically unload the joint  
12 afterwards, which would theoretically decrease wear, but you know  
13 there are patients that no matter what we do, I've seen them brux  
14 right down to the pulp of the teeth. They're very difficult  
15 problems.

16 DR. BERTRAND: Thank you.

17 CHAIRMAN HEFFEZ: Dr. Runner.

18 DR. RUNNER: So this is Susan Runner.

19 Dr. Bertrand, are you suggesting that there could  
20 be a labeling issue regarding postoperative treatment of these  
21 patients in terms of addressing this issue specifically?

22 DR. BERTRAND: I'm not sure that the use of a

1 mouthguard is going to actually decrease the amount of loading  
2 over time on an appliance that has been surgically implanted.  
3 I think the way any type of cranial nerve mediated motor reaction  
4 occurs is neurochemically facilitated by incoming stimuli, but  
5 there are emerging ways to address that that is coming out in  
6 neuroscience which might enhance the longevity of any type of device  
7 placed into an area of the body that's controlled by cranial nerve  
8 reactions.

9 CHAIRMAN HEFFEZ: Dr. Schechter.

10 DR. SCHECHTER: Dan Schechter.

11 Dr. Burton, with respect to your concern about the  
12 number of sites and potential bias in there, how comfortable or  
13 what is your opinion with the sponsor's response regarding the  
14 population of available patients and available surgeons with  
15 appropriate patients?

16 DR. BURTON: I think that they're attempting, you  
17 know, to address that topic. My concern is a surgeon, and I'm  
18 one, you know, that exists in a, you know, university training  
19 environment where, again, we tend to see -- you know, there are  
20 certain procedures where we do -- and we're probably the only people  
21 in our state, and being a sparsely populated state that performed  
22 those, is that this appears to be something at least from what

1 Dr. Quinn was saying is probably more appropriate in a limited  
2 number of sites, hopefully more scattered about the country.

3 And I mean, that's not something we or I should say  
4 that I think that the FDA controls, but I think that you have to  
5 have some assurances that there is going to be an adequate training  
6 level because we have seen, looking back historically not only  
7 in oral surgery, but in certainly other areas that things work  
8 very well in certain surgeon's hands, and sometimes those are the  
9 individuals that develop that they have both the expertise and  
10 the experience to do that when, unfortunately, both devices and  
11 techniques get into less experienced hands.

12 You suddenly discover that complications that nobody  
13 dreamed of suddenly start to come out again, and we see other adverse  
14 effects and adverse outcomes from that, and again, you know,  
15 certainly the sponsor of the company can't guarantee that, but  
16 I think that as much as they can address that educational issue  
17 and how the devices are released to other surgeons at least can  
18 be examined.

19 And I think they've tried to address that, but that's  
20 my biggest concern, is when you have things that work well in certain  
21 people's hands and certain levels of experience that doesn't  
22 translate well to the general population of providers and



1 practitioners that are out there.

2 CHAIRMAN HEFFEZ: I'd like to move on to the next  
3 reviewer. Dr. Janosky.

4 DR. JANOSKY: Janine Janosky.

5 I have four primary issues that I wanted to spend  
6 some time talking about and discussing, and they are the issues  
7 that I primarily have been spending time talking about this morning  
8 also, as well as some other panel members have been talking about.

9 The number one issue is the issue of follow-up.  
10 If we look at the primary outcome measure, the primary outcome  
11 measure is a three-year measurement, and irrespective of how we  
12 measure that, we come down to about 45 people, and of those 45  
13 people, you have 11 of them that are noncemented. So you even  
14 have a subset of the 45 that is quite small, and that's actually  
15 that noncemented group is about ten percent of those that had  
16 started the study. The 45 is about 25 percent of those that have  
17 started the study.

18 So the issue then becomes: for primary outcome  
19 measures is 25 percent follow-up acceptable? Depending upon what  
20 criterion we will use, for the most part we would conclude that  
21 that would not be an acceptable level.

22 So then the issue becomes why is the follow-up so

1 low. Revolving enrollment, that's understandable, but then why  
2 are we looking at the PMA today as opposed to when most of that  
3 enrollment would be?

4 Some of the issues to try to get at why the enrollment  
5 was or why the follow-up is so small I tried to deal with in terms  
6 of hypotheses that the sponsor had presented to us, and one of  
7 those issues is: could you get some of the outcome measures, but  
8 not all of the outcome measures, given the fact that two of the  
9 outcome measures are paper and pencil, and we could ask the patients  
10 to respond on the VAS scales and send them back to their provider.

11 And the answer was that we don't have missing data  
12 irrespective of the type, and so there's some confusion as to  
13 whether there was, there wasn't. But I had taken a look at the  
14 data and the spreadsheet that was presented to us, and if someone  
15 is missing one of those measurements, they're missing all three  
16 of those measurements.

17 So that raises some concern to me as to why weren't  
18 they at least given the opportunity to provide the data for those  
19 that they can do using mail.

20 So the issue of follow-up, it encompasses all these  
21 other issues that I'm talking about, but for an event of 45 for  
22 three-year follow-up, which represents 25 percent, is that

1 reasonable or is that not reasonable?

2           The second issue is the one that we had just started  
3 talking about when Dr. Bertrand had brought it up and the one that  
4 we had talked about this morning, is that we're looking at two  
5 clinical sites, and I find it quite interesting that the sponsor  
6 refers to this as an efficacy study, which I would argue with two  
7 clinical sites it is, in fact, an efficacy study.

8           But we're not talking about efficacy when we're  
9 looking at the FDA. We're talking about effectiveness. So the  
10 question of whether two clinical sites with one practitioner at  
11 each of those sites is an issue for efficacy which is not our concern  
12 here or is it an issue of effectiveness which is our concern?

13           And the issue of whether it's an issue of  
14 effectiveness, I think, has been addressed by most of the panel  
15 members and leading in one direction.

16           The third issue is the one about outcomes, which  
17 we had talked about when I had talked about follow-up, and the  
18 final one is a pure statistical question which I had raised to  
19 the biostatistician at FDA in that the statistical assumptions  
20 are most likely not met for the statistical techniques that were  
21 done.

22           So then the question arises: would you have gotten

1 the same conclusions if you had used the appropriate statistical  
2 test?

3 I don't know the answer to that because the sponsor  
4 didn't provide the data analyses analyzed using other statistical  
5 techniques. So I'm left with as much confusion as I had this  
6 morning. I was hoping to get some feedback from the sponsor and  
7 from some other panel members as to how we deal with some of these  
8 issues and how we think through some of the issues.

9 So, again, the issues are the follow-up, the site  
10 selection, and the practitioners, one at each of the sites.

11 The outcome measures and why we don't have  
12 inconsistency in terms of that, why were the patients not given  
13 the opportunity to fulfill at least the paper and pencil  
14 assessments, and then the final one which is a purely statistical  
15 analytical question.

16 I'll stop at that point.

17 CHAIRMAN HEFFFEZ: Thank you. Thank you, Dr. Janosky.

18 Dr. Li.

19 DR. LI: You're right. You may have already answered  
20 this in a previous discussion, but I might have missed it. How  
21 long did you estimate or did someone estimate it would take for  
22 you to get to 80 percent of 180 cases to reach three years?

1 DR. JANOSKY: Yeah. If I take a look at 180, and  
2 we can deal with that issue of cases versus sides versus patients,  
3 but let's just give them the opportunity to say that cases is 180.

4 If you take 80 percent of 180, you get 144, and then  
5 have 143 measurements at six months.

6 DR. LI: So it takes two and a half years then to  
7 get to three years?

8 DR. JANOSKY: Approximately, right. So 80 percent  
9 of their data are available for six months worth of time. So on  
10 some level we can argue that there's six months worth of data  
11 available.

12 DR. REKOW: But can I?

13 CHAIRMAN HEFFEZ: Dr. Rekow.

14 DR. REKOW: Can I just go back? I agree with  
15 everything that you've said, but I also heard that the initial  
16 study was planned for only 68 patients, and I think we need to  
17 make sure we know what is the real basis that we're supposed to  
18 be using as our basis, and I don't know the answer, and it looks  
19 like Susan is anxious to tell us.

20 DR. RUNNER: Susan Runner.

21 I believe it was 89 -- 86. The initial IDE was  
22 approved with a projected number of 86, and that's the number that

1 the original statistics were based on.

2 DR. REKOW: And that was to be 86 patients with three  
3 years' worth of --

4 DR. RUNNER: Correct.

5 DR. REKOW: Eighty-six cases or 86 patients?

6 DR. RUNNER: I believe when we sent an IDE letter,  
7 we're talking about 86 patients. I mean, I think they interpreted  
8 it a little bit differently and changed it around, but we're talking  
9 basically about 86 people.

10 They then requested expansion of the study, and  
11 that's how we got to 300 approved, and they've gotten 180 operated  
12 at this point.

13 DR. JANOSKY: This is Janine Janosky.

14 I would postulate two things, Dr. Runner and Dr.  
15 Rekow, at that point. If that is the case, then what 86 are we  
16 going to take?

17 The sponsor didn't present to us data on only 86.

18 So I would expect to see the first 86 or the 86 meeting  
19 inclusion/exclusion criteria, and their data presented separately.

20 That would be the first concern.

21 The second concern, let's give them the fact that  
22 there was 86 and I'm assuming that that was based on statistical

1 power analyses in terms of estimates.

2 Then what is 80 percent of 86? That's in the 60s.

3 Do we have data on 60 patients for three years? And the answer  
4 is, no, we don't.

5 So even if you argue that there's 86 in there, that  
6 you should have three years' worth of data on and taking an 80  
7 percent rate, 20 percent attrition, you would expect 60-some  
8 patients with three years' worth of data, and we don't see those  
9 numbers.

10 CHAIRMAN HEFFEZ: Dr. Bertrand.

11 DR. BERTRAND: Peter Bertrand.

12 Simple question: were 86 people enrolled before  
13 January '99? I mean, that would give us a rough three-year  
14 follow-up.

15 How long did it take us to enroll those?

16 CHAIRMAN HEFFEZ: Would the sponsor come to the  
17 podium, please?

18 MS. VERSTYNEN: Mary Verstynen.

19 I believe that the first 86 patients enrolled will  
20 be out to three years in October of this year.

21 DR. BERTRAND: So it wasn't by January '99, January  
22 2002 that you had 86 people originally enrolled. It took longer

1 than '99 to get that many in.

2 MS. VERSTYNEN: Right, and so it would have been  
3 in October of '99 that we had the 86 patients enrolled, and they  
4 would be at three years.

5 DR. BERTRAND: So in three months?

6 MS. VERSTYNEN: Yes.

7 DR. BERTRAND: Okay. So from that standpoint with  
8 45, is there a way of figuring out how many of those 45 -- what  
9 date they were originally enrolled so that we could get an idea  
10 on that concept.

11 MS. VERSTYNEN: I can tell you in the first year  
12 of the study nine patients were enrolled, and then the study was  
13 enrollment stopped for a year's time period just to follow those  
14 first nine patients. So there was a real lag in the enrollment  
15 initially.

16 So I would say it probably took us -- I don't know  
17 that I could put an exact date, but enrollment started out very  
18 slow and has built tremendously in the last two years, and it  
19 actually built -- now, Dr. Sinn's patients first were at three  
20 years. I believe was it in -- I remember. I remember he did it  
21 at Easter time. It was April '99. Was that when?

22 Did your first patients come out to three years this



1 year or last year? Do you remember?

2 This year. Okay. So enroll really built then in  
3 April of 1999 when Dr. Sinn was added to the study.

4 DR. BERTRAND: So a lot more patients have been  
5 recruited since '99 than previously?

6 MS. VERSTYNEN: Yes, yes.

7 DR. BERTRAND: Okay.

8 MS. VERSTYNEN: I also want to state, too, as far  
9 as the sample size calculation that was originally in the IDE.  
10 Phyllis Silverman, we had worked with her in getting that sample  
11 size calculation, and at that point, looking at the literature,  
12 the outcome -- the delta of that calculation was based on a one  
13 centimeter improvement in pain, and clearly we see much more than  
14 that at the three-year time point.

15 CHAIRMAN HEFFEZ: Dr. Burton.

16 DR. BURTON: I guess my question, I guess, that Dr.  
17 Janosky -- at least what I have summarized in my mind what she's  
18 asking though is that given the fact that there appear to be an  
19 endpoint of when we would reach that number and we would have the  
20 three-year data for what was thought to be the original power or  
21 patient's number of studies, and we don't seem to be there, what  
22 prompted them?

1                   If it was going to be in October of this year, we  
2 would reach that number. Why is it August and we're at that point?

3                   And maybe Dr. Runner can answer that. What prompted  
4 the timing issue with this coming forward to the panel?

5                   DR. RUNNER: I think the company needs to answer  
6 that question.

7                   MS. VERSTYNEN: I can tell you exactly when that  
8 question was answered. It was at the last panel meeting in 2000,  
9 and at that point, both FDA and a Canadian official were there,  
10 and I had printed out the proposed follow-up that we would have  
11 in the next couple of years.

12                   Knowing that we had predetermined a cutoff of 86,  
13 I just showed them, okay, at this point we're going to have this  
14 many patients. At this point we'll have this many patients. At  
15 this point we'll have this many patients, and both FDA and the  
16 Canadian official said that when we had reached I think it was  
17 49 patients at three years, that that would be an appropriate time  
18 to submit it.

19                   CHAIRMAN HEFFEZ: Dr. Janosky.

20                   DR. JANOSKY: Janine Janosky.

21                   Ms. Verstynen, the number 49, what was that based  
22 on, the one that you just quoted, the number 49?

1 MS. VERSTYNEN: I went into our database and I picked,  
2 okay, cases that were done in a certain date. I just went back  
3 to the surgery dates just to see, okay, how many would I have at  
4 this time point. How many would I have at this time point?

5 DR. JANOSKY: Let me stop you for a second.

6 CHAIRMAN HEFFEZ: Dr. Janosky.

7 DR. JANOSKY: Janine Janosky.

8 DR. RUNNER: Can I just make one comment? And correct  
9 me if I'm wrong, Mary. I know PMAs are supposed to stand on their  
10 own, and I believe that -- and you correct me if I'm wrong -- that  
11 your desire to comment came about because of the history of the  
12 numbers that were associated with the two previous PMAs.

13 MS. VERSTYNEN: Exactly. I mean, I guess I was  
14 proposing and figuring out how many patients we had had at different  
15 time frames, and looking and having been at the two other panel  
16 meetings, our number that FDA and the Canadian office set of 40  
17 was far higher than the approved products.

18 DR. JANOSKY: Let me just follow up, please.

19 Janine Janosky.

20 Ms. Verstynen, typically we stopped studies based  
21 on criterion or criteria, depending upon how many we have, objective  
22 stopping rules so that if something is very effective, we might

1 stop it early because we can argue that we see much larger the  
2 effect that we possibly said.

3 So your number that you just said to us, that was  
4 not based on a specific stopping order; is that correct?

5 MS. VERSTYNEN: Correct.

6 Thank you.

7 CHAIRMAN HEFFEZ: Dr. Patters.

8 DR. PATTERS: Mark Patters.

9 A question for Dr. Janosky. You've used the number  
10 80 percent on several occasions, and I assume that that number  
11 is a number that one seeks in a clinical trial, but is that number  
12 necessarily fair given the nature of this trial, the nature of  
13 the patients, the nature of the multiple surgeries, and the  
14 psychological implications that go with patients suffering from  
15 this level of dysfunction? Is that fair to apply that number to  
16 this study?

17 DR. JANOSKY: I used the number based on a couple  
18 of things. One is typically what is the response level that we  
19 expect to see.

20 The second, always if we're estimating a point, how  
21 many subjects do we need for a point estimation? So if we're looking  
22 at a specific type of confidence interval for a point estimation,

1 how many subjects would we need based on a level?

2 So I'm sort of backtracking and giving them the  
3 benefit of the doubt.

4 DR. PATTERS: Let me then ask if --

5 DR. JANOSKY: So I actually would jack it up a little  
6 higher is what I'm saying.

7 DR. PATTERS: If we look at their patient  
8 accountability data which they provide on Table 8-7, they say that  
9 of the patients available at three years, theoretically available,  
10 82 and a half percent of them are included in the data, which is  
11 45.

12 If we go back for a year and a half, 89 of the  
13 theoretically possible 109 are available in the data. So if we  
14 assume that their losses don't change, you know, about roughly  
15 about 82 and a half percent of the patients are available. That  
16 would mean that we'd have approximately 85 patients available  
17 within a year and a half.

18 Would you read that the way I'm reading it?

19 DR. JANOSKY: I would probably come to the same  
20 estimates, although those are only estimates.

21 This is Janine Janosky speaking.

22 DR. BURTON: Yes, I understand that, but regardless

1 of how many they started with, 85 patients are a lot of patients  
2 for what they're doing. It may be only 50 percent of what they  
3 started, but it's a lot of patients.

4 Do you take that into account?

5 DR. JANOSKY: This is Janine Janosky again.

6 If you're going to argue that 50 percent is  
7 reasonable, then I would want to see data that shows me that those  
8 50 percent that completed were no different than the 50 percent  
9 that did not complete. I don't see those data.

10 So when I don't see data that I expect to see and  
11 I don't see a fair amount of data that I do expect to see, I need  
12 to wonder why. And since I don't have any basis to base anything  
13 on, say, okay, give me some hypotheses why I don't see this. Then  
14 I have to conclude that I don't know the answer.

15 So I can't conclude that 50 percent would be  
16 reasonable. So that's the quandary that I'm left with.

17 CHAIRMAN HEFFEZ: Dr. Burton?

18 DR. BURTON: I'm not sure this goes to Dr. Janosky  
19 or actually back to the sponsor, but in looking through this, it  
20 did state that you were starting marketing in Europe and obviously  
21 the PMA needs to stay and the IDE stands upon its own merits here,  
22 but also you've been marketing this device for at least greater

1 than two years.

2 And I notice I've been reading. It was in South  
3 Africa. Do you have any supporting or correlating data from its  
4 usage in areas outside the country or at least any comment upon  
5 that?

6 Because it's interesting. I just thought it was  
7 done and there's nothing saying numbers sold. Has there been with  
8 potentially less experienced people -- have you seen any other  
9 issues raised with that?

10 Because, again, I saw that at least that is  
11 occurring, but there is no reference beyond the fact that it is  
12 occurring.

13 DR. QUINN: Based on the Canadian approval and the  
14 CE approval, I have trained three surgeons, one in London, one  
15 in Sweden, and one in Toronto, who are well know, well experienced  
16 surgeons. I think the total number of cases among those three  
17 is approximately 75.

18 I don't have data on it, but that's the number of  
19 cases that's been done.

20 Might I comment on some of Dr. Janosky's? I think  
21 a few issues.

22 One, I appreciate your comment on partial data, and

1 maybe it was my assumption that since these follow-up visits were  
2 radiological and face to face, that was maybe my misinterpretation  
3 that we weren't looking for partial data, and we either got data  
4 or we didn't.

5 I think there's about nine patients who actually  
6 were seen by an oral surgeon in another part of the country who  
7 did the face to face, did the X-rays, and we accepted that. I  
8 did not pursue your concept of partial data, which may have been  
9 helpful.

10 The other one is in looking at the -- and I know  
11 you questioned the term "efficacy" -- but in looking at the three  
12 primary efficacy points that we looked at, we did feel strongly  
13 that the data does tend to plateau between three and six months,  
14 and we were hoping that would be taken into consideration when  
15 looking at the percent of follow-up at three years; that they would  
16 be similar.

17 It may not address the issues Dr. Li raised, and  
18 I think they're important ones, but in terms of the efficacy or  
19 whatever term you'd like to use, I do think that's an important  
20 factor to take into consideration.

21 The other one in terms of early in the study of  
22 broadening this to multiple investigators and multiple sites, it



1 was probably my reticence that stopped the company. I had some  
2 severe reservations. I think it was difficult enough to control  
3 this in a very controlled environment. I think it would have been  
4 more difficult because, as Dr. Rekow said, there was an evolution.

5 There were no events in this process, but it was an evolution,  
6 and I think that evolution was better controlled in a smaller  
7 environment.

8 CHAIRMAN HEFFEZ: Sometimes in studies such as this,  
9 data obtained from smaller sites is actually more valuable than  
10 data from bigger sites because you get to appreciate different  
11 indications, different surgeons' abilities, and that might end  
12 up sometimes judging the final usage, you know, of the instrument.

13 CHAIRMAN HEFFEZ: Any other questions? Dr. Li.

14 DR. LI: Can I -- Steve Li -- can I switch gears  
15 and ask a materials and mechanics question?

16 One question I forgot to ask earlier, you're using  
17 titanium screws on a cobalt chrome plate. In total joints we tried  
18 to list the last several years avoiding mixed metal contract because  
19 of crevice corrosion. For instance, we put a cobalt chrome head  
20 and a titanium stem. You'll actually find corrosion at the  
21 interface.

22 So my question is: do you see corrosion in these

1 locations of mixed metal contact or, better yet, have you actually  
2 looked for corrosion at any point where the mixed metals are in  
3 contact?

4 MR. ROMAN: I can't answer that question from a  
5 clinical standpoint. I have not visually seen any of the explants.  
6 It might be something that Dr. Quinn can answer.

7 But as far as looking for corrosion at an interface  
8 between the titanium and the cobalt chrome, that's not something  
9 that we've looked specifically for.

10 I did want to say however, that we are using the  
11 or that the titanium plasma spray coating that's on the mandibular  
12 components is also a Titanium 64 alloy, and we have quite a bit  
13 of experience with this in the orthopedic realm and have seen no  
14 problems with that.

15 DR. REKOW: This is Dr. Rekow.

16 Do you plasma spray the inside of the screw holes  
17 on the mandibular implant?

18 MR. ROMAN: No, no. It's limited to the ramal side  
19 of the plate.

20 DR. LI: Steve Li.

21 I would just suggest that you might want to look  
22 though where the screw holes and the screws interface because the

1 crevice corrosion is often dictated by the size of the space and  
2 the local pH. So it's quite possible on your coating the crevices  
3 are of a certain size where you won't get corrosion, but if you  
4 switch the joint space, if you will, around the mixed metals, you  
5 could get into an area where corrosion is possible.

6 CHAIRMAN HEFFEZ: Dr. Rekow.

7 DR. REKOW: This is Dr. Rekow.

8 Dr. Quinn, can I ask you and Dr. Sinn a question,  
9 please? When you do any of the tissue revisions in the joint space  
10 for whatever reason, do you as a matter of routine look at those  
11 histologically and immunologically, look for immunologic  
12 responses?

13 I know that that's an extra procedure. I know it's  
14 a lot of extra work, and I'm just wondering if you're doing that  
15 or not as a way to tease out whether or not you're getting any  
16 debris particles that could be an issue.

17 Because with some of your adverse events you're  
18 clearly going back into the joint space.

19 DR. QUINN: I think that has responded to Dr. Li's  
20 question this morning. We're doing histologic, standard histologic  
21 H&E staining. We haven't done specific immunologic testing, but  
22 I think it's not a bad idea.

1                   But I should say coming from a macroscopic point  
2 of view, what we tend to see is fibrous encapsulation. It looks  
3 like a healthy fibrous glistening encapsulation. We haven't seen  
4 multinucleated giant cells or any evidence of polymeric debris,  
5 which would be consistent with polyethylene debris as well.

6                   Again, the only foreign body reaction we did get,  
7 and it wasn't done, was the corn starch.

8                   There was one other question that I thought you  
9 raised and that I'd like to answer, and that was the difference  
10 between testing the bovine bone and testing on the human ramus.

11  
12                   We used 2.7 millimeter screws to secure the ramus.  
13 They come in eight and ten millimeters, and usually ten millimeters  
14 is beyond the bicortical width of the ramus. If anything, we have  
15 to back out a ten and put an eight in.

16                   You can actually palpate when the tip of the screw  
17 comes through immediately. So in most cases we know we're engaging  
18 bicortical bone.

19                   DR. REKOW: Thank you.

20                   CHAIRMAN HEFFEZ: I actually would like to move on  
21 to the questions, and when the questions are discussed, I'm sure  
22 some of these issues will be revisited.

1                   So all of the questions that are going to be asked  
2 to the panel are in your agenda book. We'll try to get it on Power  
3 Point so you'll appreciate the question, but it's in your agenda  
4 book.

5                   The first question was or is: can the results for  
6 jaw pain intensity, interference with eating, and maximum incisal  
7 opening for the cases presented with three-year data, which  
8 represent 25 percent of the implanted population, adequately  
9 represent the expected outcomes for the total study group at three  
10 years?

11                   Within this question, I think I'd like to ask the  
12 panel to consider that we're talking about cemented and noncemented  
13 cases. We have 11 noncemented cases at three years, but at this  
14 point in time the experienced surgeons are only placing noncemented  
15 prostheses.

16                   We'll have to ask ourselves is the cement an  
17 important variable, and is it -- it may not be an important variable,  
18 and it is a variable that is now excluded in the noncement cases,  
19 and that could be a positive thing.

20                   So I'd like to hear from the panel members how they  
21 feel regarding this question.

22                   Dr. Hewlett?

1 DR. HEWLETT: Actually related to this question I'd  
2 like to pose a question to Dr. Li if I could.

3 Dr. Li, you raised some concerns earlier about the  
4 creep or potential creep around the screw holes in the fossa  
5 component. My question is twofold.

6 One, if as the sponsor has described a superior part  
7 of the fossa is routinely abutted against temporal bone, does that  
8 then lessen your concern about potential creep around the screw  
9 holes?

10 And, number two, do you feel that obduration of any  
11 potential dead space with the polymethyl methacrylate cement and  
12 thereby perhaps an increased surface area of contact between the  
13 superior part of the fossa and the temporary bone, would that then  
14 further limit any possible creep around the screw holes in your  
15 opinion?

16 DR. LI: Well, I think the fact that it's supported  
17 superiorally helps, but the screws -- and I guess a minimum of  
18 four screws -- are placed because they're obviously felt that  
19 they're needed to hold the polyethylene in place.

20 But if there's no load on those screws, you then  
21 don't need screws, right? And the fact that you need a minimum  
22 of four tells me that either through empirical or through

1 calculations, that they figure they have needed four screws to  
2 hold that polyethylene staple in place.

3 So that tells me that that polyethylene left to  
4 itself is going to want to move away from the bone. Otherwise  
5 you wouldn't need four screws.

6 Now, stress obviously is lower the more supported  
7 the polyethylene is, but it clearly isn't zero because there is  
8 four or maybe five screws. So I don't think that removes my concern  
9 about the creep, although the more supported it is maybe the longer  
10 it will take for the creep to get to a level of where you'll cause  
11 a problem.

12 I'm sorry. What was the second part of the question?

13 DR. HEWLETT: Well, the other part is do you think  
14 there's a substantial benefit to using the cement inasmuch as it  
15 will increase the surface area contact between fossa element and  
16 the temporal bone.

17 DR. LI: Assuming that the gap or the space is --  
18 there really isn't like a whole gap where the whole back is, you  
19 know, unsupported, and they're just like little pockets of  
20 unsupported area.

21 The one saving grace about polyethylene, in fact,  
22 is that it does creep and deform. So even if you didn't use bone

1 cement, after a while the polyethylene I would suspect would kind  
2 of settle in eventually and kind of support itself.

3 So unless the gap is substantially large, I don't  
4 in my mind see why you would want to put cement in other than it  
5 looks better than it appears to be supported, which leads me to  
6 I don't have a great concern over the issue of whether or not the  
7 post was clipped off or not clipped off, unless you're going to  
8 think you're damaging the polyethylene somehow by the clipping.

9 But biomechanically in this particular application,  
10 I don't see a big influence of whether or not there's a post or  
11 no post.

12 CHAIRMAN HEFFFEZ: Dr. Burton.

13 DR. BURTON: Dr. Burton.

14 I'd like to sort of answer that as well. I would  
15 agree with Dr. Li. When I looked at it from looking at it from  
16 my clinical experiences, I didn't think that clipping off the post  
17 made any difference, and I actually personally from my experience  
18 with cement felt that actually the fact that you modified the  
19 technique with a surgical burr to seat the fossa more accurately  
20 without the need for cement, and I gather from Dr. Quinn what they  
21 found was when they adequately contoured the fossa, they had  
22 adequate bone contact, and the volume that they were filling was



1 so small that they were able to eliminate the cement, that I actually  
2 very candidly thought that was an improvement.

3 You know, you say, well, you have the earlier ones  
4 with cement versus noncement, and my guess is that probably  
5 eliminating the cement actually probably is an improvement unless  
6 from what Dr. Li sort of clarified, unless you felt that you needed  
7 the cement for support, but, again, adequately contoured to get  
8 good approximation it would be supported.

9 And by eliminating that cement I think you're just  
10 candidly just eliminating one more variable. I don't think that  
11 the cement itself has any truly saving grace properties that make  
12 you want to have it in there.

13 So my estimation, when I looked at this before coming  
14 here and hearing the other comments, was that that actually was  
15 an improvement, not a detractor to the change.

16 CHAIRMAN HEFFEZ: Dr. Cochran.

17 DR. COCHRAN: David Cochran.

18 I would reinforce exactly those comments based upon  
19 our experience in periodontal surgery as well, using a number of  
20 different agents, cements, infurcations. I felt the fact that  
21 they did away with that was probably an excellent move on the  
22 sponsor's part in keeping it simply and just the components.

1 Well, the bone is going to react obviously to the  
2 trauma of flattening. You're creating an acute wound, and I think  
3 that's where you get some of that hypertrophy of the bone tissue.

4 So I think that as it is without it, it's fine. Also the clipping  
5 of the post, I feel like that very little influence on the device  
6 as well.

7 CHAIRMAN HEFFFEZ: So let us just summarize this point  
8 then. We're saying that the data of cemented and uncemented can  
9 actually be combined. Is that the general feeling of this panel?

10 Okay. So let's come back to the question then.  
11 Do we feel that the data that's available is adequate, just to  
12 summarize the question? The question is up there.

13 Dr. Patters?

14 DR. RUNNER: Can I interrupt for just a second?  
15 You basically answered question number four. Is that -- you started  
16 with number one, but you sort of answered number four.

17 CHAIRMAN HEFFFEZ: Well, question one involves number  
18 four. So that's why I brought it. We're still on number one,  
19 but --

20 DR. PATTERS: Let me try to deal with question number  
21 one. I feel like using a percent to say this is only 25 percent  
22 of the data is not fair to the sponsor. I think the sponsor needs

1 to be complimented on conducting what I feel is an obviously  
2 scientifically valid clinical trial of which all the data is not  
3 presently in.

4 I think the real issue is are 45 cases at three years  
5 enough to conclude safety and effectiveness. I don't know the  
6 answer to that, but I don't think it's fair to take a percentage,  
7 like 25 percent, and say, well, they've only got a quarter of the  
8 data. So it's not enough.

9 The question is: they have 45 cases now. It appears  
10 that they should have 85 cases no less than a year from now, maybe  
11 a year and a half from now. How many is enough? I'm not prepared  
12 to say, but overall I think that sponsors have taken a very valid  
13 scientific approach, and I think they're to be complimented.

14 It would seem to me that most of the compliments  
15 go to Dr. Quinn for conducting what appears to be an excellent  
16 and unbiased trial.

17 CHAIRMAN HEFFFEZ: I think we shouldn't focus on the  
18 25 percent, but we still need to answer the question. Do we feel  
19 the data that is available at three years is adequate enough to  
20 predict an outcome?

21 Dr. Rekow.

22 DR. REKOW: This is Dr. Rekow.

1 I would like to have a little discussion about a  
2 little bit different spin on this. When I looked at all of the  
3 primary outcome assessments, I didn't see very much change after  
4 maybe six months and maybe even shortly after three months.

5 And so how much new information could we anticipate  
6 getting even if there were hundreds of more patients from what  
7 seems to be the trend at six months that continues to three years?

8 And I'd like to hear some conversations about that.

9 MR. SCHECHTER: This is Dan Schechter.

10 I know this application is supposed to stand alone,  
11 and of course, it does, but as the sponsor noted, similar devices  
12 have had less patients involved, and those were approved, and in  
13 a sense, if we consider more and more patients, other than the  
14 45 that have already reached the three years, we're in a sense  
15 penalizing the sponsor for extending their ID and getting more  
16 people involved.

17 Had they not extended it, the total study group would  
18 be much smaller and maybe we would be more willing to just accept  
19 the 45. So I think we should keep that in mind that the fact that  
20 they're extending this and that very few have gone beyond six months  
21 in some sense is a good thing. It means that it has so far been  
22 very successful, and FDA is willing to extend that.

1 But don't penalize the sponsor for that.

2 MS. HOWE: Elizabeth Howe.

3 My concern about the number and the amount of data  
4 is that there can be additional data collected fairly  
5 simplistically; that if we're talking about answers that could  
6 be generated by mail or if it could be done at another location  
7 and submitted to the researcher there, in fact, is more data out  
8 there.

9 The question is: would those numbers make a  
10 difference?

11 And with such small numbers, it in fact could make  
12 a difference.

13 CHAIRMAN HEFFEZ: Dr. Cochran.

14 DR. COCHRAN: David Cochran.

15 You asked the question what more would you gain,  
16 and my concern still is obviously Dr. Quinn is a very talented  
17 surgeon, and we're thinking about safety issues, and you've got  
18 one surgeon who's very gifted with a reasonable number of cases  
19 at 30 years, but the additional data I think you're going to get  
20 is the variability between surgeons, and clearly when the device  
21 is approved, there are going to be a lot of people that use it  
22 and hopefully a lot of people wont use it that shouldn't be using

1 it.

2 So I think that's where the additional data would  
3 come from, is can an average, if you will -- nobody wants to be  
4 called "average" -- but an average oral surgeon be able to use  
5 this device and have the same results as someone as gifted as Dr.  
6 Quinn?

7 The other is -- I lost my thought. Sorry.

8 CHAIRMAN HEFFEZ: May I say something? That's really  
9 addressing question number two. I think we should just specifically  
10 ask if this information that we have now available for three years  
11 can give us enough confidence that this outcome will be reproduced  
12 in the following years, and that's the biggest question for those  
13 issues.

14 Okay. So Dr. Patters.

15 DR. PATTERS: Mark Patters.

16 I'd like to address Dr. Rekow, who I think brought  
17 up a very valuable point. It is not necessary in my mind that  
18 the sponsor answer these questions at only the three-year data  
19 point, and the fact that there seems to be little change in the  
20 data after three to six months, to me the panel should consider  
21 that information.

22 As to whether that additional information had

1 shorter time periods give evidence towards safety and  
2 effectiveness, and I think Dr. Rekow's point is an important one  
3 and needs to be considered by the panel.

4 The three years is as arbitrary. It's an arbitrary  
5 number that FDA recommended in a guidance document, but that doesn't  
6 mean that the data that's not three years old should be ignored.

7 DR. REKOW: Can I clarify one point? I want to make  
8 sure that you --

9 CHAIRMAN HEFFEZ: Dr. Rekow.

10 DR. REKOW: I'm sorry.

11 I want to make sure that you understand that when  
12 I raised that point I was talking about these three parameters  
13 of the pain intensity, the eating, and the incisal opening. I  
14 clearly think there are some issues related to adverse effects  
15 that have other implications.

16 I wanted to focus the discussion on this from the  
17 data that we've seen, and that's where I wanted to have this  
18 conversation at this moment to go.

19 CHAIRMAN HEFFEZ: Dr. Li and then Dr. Burton.

20 DR. LI: Just a clarification question. For question  
21 number one, what are we supposed to consider the total study  
22 population?

1 DR. RUNNER: This is Susan Runner. We consider the  
2 total study population the 180 cases that have been implanted.

3 DR. RUNNER: Thank you.

4 CHAIRMAN HEFFEZ: Dr. Burton.

5 DR. BURTON: In response to that question about the  
6 data, I think that for the three presented items I think you probably  
7 can because it appears that at that three to six month point that  
8 they reach I would say a stable endpoint, but the numbers don't  
9 really seem to change.

10 I think the question is that not having an adequate  
11 number out. In looking at previous and other implant systems and  
12 other surgical techniques that involve things similar to this,  
13 many times we didn't start to see those.

14 The other problems, other than the pain and opening,  
15 started to appear; at least my experience was in that 18 to 36  
16 month point was when you started to see more of the other potential,  
17 quote, unquote, complications appear.

18 So, yes, for those particular outcomes it probably  
19 is adequate at this point because I think we can extrapolate that  
20 out. The real question is for the overall device. Does that give  
21 you the same confidence?

22 And I'm not sure I have quite the same confidence



1 for the shortness and the numbers relative to that as I do for  
2 those three variables.

3 CHAIRMAN HEFFEZ: Ms. Helms.

4 MS. HELMS: Yes, Elizabeth Helms.

5 I just want to make a comment. I would certainly  
6 like to see a higher percentage, and I certainly think that we  
7 as patients need to be more accountable especially when we're going  
8 to enroll in a study; that we should be following through all the  
9 way to the end.

10 But one of the points I wanted to make is you can  
11 be also assured that if the patients that have these surgical  
12 procedures done were having problems, you'd be hearing about them.

13 If their pain had increased, you'd be hearing from them because  
14 they don't pick up the phone, you know, when everything is good,  
15 but they sure do when everything is bad.

16 CHAIRMAN HEFFEZ: That's really not always the case  
17 in clinical practice unfortunately. Sometimes they don't want  
18 to hurt the doctor's feelings. Sometimes it's a financial reason.  
19 There's multiple reasons.

20 DR. BURTON: I guess having been involved with a  
21 number of studies and with both TMJ implants and TMJ surgery, I  
22 actually would agree with Dr. Hefez. I think it's almost the

1 opposite.

2                   There are a lot of people who when they become  
3 dissatisfied go to someone else, and I will be honest. I've had  
4 a couple of people in the last month who had had other implants  
5 done at other points. I said, "Well, have you contacted your  
6 original surgeon and discussed this, you know, these burning issues  
7 with them?"

8                   And the response is invariably candidly been, "No,  
9 I have not."

10                   And these patients candidly were 18 to 24 months  
11 out, and they said, "Yeah, I was doing really well. I moved.  
12 I haven't gotten back."

13                   Have you called and told them and discussed what's  
14 going on here?

15                   And the answer has been no. So I get a little antsy  
16 personally when I say, "Well, they're just gone," and so they're  
17 going for geographic success. The truth is that an equal number  
18 of those may be geographic failures.

19                   CHAIRMAN HEFFFEZ: So I'd like to bring back the panel  
20 to this question. Okay? So I'm going to -- you see the question  
21 up there, and we've got three things here: pain intensity,  
22 interference with eating, and maximum incisal opening.

1 I am going to try to summarize what the panel said,  
2 and I'd like to hear if the panel is comfortable with what I've  
3 said.

4 The data that is presented does and we do feel it  
5 can be extrapolated for these points and we can expect that the  
6 outcomes will continue. However, it would be satisfactory to us  
7 if the company made an effort to obtain the additional data that  
8 it can do through mailings, and that we may see some variability  
9 in there, and that the company should, of course, continue to  
10 collect data.

11 But given this, these three points, that the data  
12 that's been presented does adequately reflect expected outcomes.

13

14 Would this be acceptable to the panel? I'm not trying  
15 to put words in anybody. I'm trying to summarize it so the gastric  
16 juices get satisfied.

17 (Laughter.)

18 DR. BURTON: Richard Burton.

19 I would say yes. I think given the parameters as  
20 you presented them, I would say yes.

21 CHAIRMAN HEFFEZ: Dr. Patters.

22 DR. PATTERS: Mark Patters.

1 I concur with Dr. Burton and Dr. Heffez that, yes,  
2 it does.

3 DR. SUZUKI: Jon Suzuki.

4 I say yes.

5 CHAIRMAN HEFFEZ: Okay. Good. This is not a vote.  
6 We just sort of want to just get a general feeling.

7 I would like to jump to question four, and then we'll  
8 break for lunch. Okay? So let's go to question four.

9 The company plans to market the device that's  
10 noncemented or as a cemented fossa. In the clinical data set,  
11 some of the cases are with cement and some cases are without cement.  
12 Please discuss the data in light of these two different methods.  
13 Are there differences in outcomes?

14 So we previously discussed this issue, and that we  
15 did feel that we could consider the data of both the cemented and  
16 noncemented together, but I do think that I would like to ask the  
17 company. Mr. Pratt, is he in the room?

18 I'd like to ask Mr. Pratt: why does the company  
19 intend to market a cemented fossa when the two surgeons are not  
20 placing any cemented fossas anymore?

21 MR. PRATT: Joel Pratt with Lorenz Surgical.

22 The objective was to provide the surgeons as many

1 options, and if a surgeon felt that in a particular case cement  
2 was needed, they would feel comfortable doing so.

3 CHAIRMAN HEFFFEZ: Well, we have now two experienced  
4 surgeons who are teaching this technique which we will talk about  
5 later as far as teaching modalities, but teaching the technique,  
6 and they're not teaching the placement of the cement.

7 MR. PRATT: That's correct.

8 CHAIRMAN HEFFFEZ: I don't think I have to bring it  
9 any further.

10 Can you comment on that?

11 MR. PRATT: Dr. Quinn, would you tell us a surgeon  
12 not to use cement?

13 DR. QUINN: Peter Quinn.

14 I think this is more geared to the original  
15 application which used the term PMA cement or other media, and  
16 we were keeping in the possibility here, and I have strong hopes  
17 for this, that we will develop biologics and that sort of calcium  
18 phosphates with BMPs in them or something more biologic that  
19 ultimately might fit an application here.

20 That was some of the reasoning, but if that's not  
21 acceptable to the panel, my feeling is that we will continue to  
22 place these without cement.

1                   CHAIRMAN HEFFEZ: So there are specifics to what  
2 you just said, and I think Dr. Runner should address that from  
3 the FDA point of view.

4                   DR. RUNNER: I think the panel has to be reminded  
5 that we have to take the application on what is in the application.  
6 We cannot approve something on the possibility that something  
7 will be developed.

8                   So either you will cement with what you cemented  
9 or you will not cement with what you have not cemented.

10                   (Laughter.)

11                   DR. QUINN: My opinion strongly is that this should  
12 be cementless. That is what we're teaching. That's what's working,  
13 and if we come up with another application, we'll have to do another  
14 study in the future.

15                   CHAIRMAN HEFFEZ: Okay. Thank you, Dr. Quinn.

16                   I would like Dr. Sinn to come to the podium and also  
17 give us your opinion regarding this.

18                   DR. SINN: Well, my --

19                   CHAIRMAN HEFFEZ: Identify yourself.

20                   DR. SINN: Doug Sinn from Dallas.

21                   My experience showed that early on in the first six  
22 or seven patients that I did that the cement really didn't add

1 anything to the case from my standpoint, and I actually was more  
2 happy once I took one pin off and just tested it, that I increased  
3 the stability much more by removing the pin than I did by adding  
4 the cement.

5 So I empirically discussed that with Peter, and we  
6 decided that we would try and make that change.

7 CHAIRMAN HEFFEZ: So you're both on the same  
8 platform.

9 DR. SINN: Absolutely.

10 CHAIRMAN HEFFEZ: Thank you.

11 Okay. Other questions from the panel? Dr. Patters,  
12 you had an earlier question or no?

13 DR. PATTERS: Mark Patters.

14 Dr. Heffez, you expressed my concerns far more  
15 eloquently than I probably could.

16 CHAIRMAN HEFFEZ: Dr. Burton.

17 DR. BURTON: My question then back to Dr. Quinn or  
18 to the individual from Lorenz.

19 Is the intent then or would you be more amenable  
20 to marketing it? Because obviously you removed the pin as of  
21 February this year. To market the device as an endless device  
22 without a luting medium, if you want to try to call it, whatever

1 you would. Would that be your intent to market it that way rather  
2 than sort of as an either/or?

3 MR. PRATT: Joel Pratt, Lorenz.

4 I think we would be very comfortable marketing only  
5 for noncemented use based on the two clinicians' experience.

6 CHAIRMAN HEFFFEZ: Okay. So now let us just summarize.

7 Are there differences in outcomes? We feel that  
8 we can pool the data and that we're now talking only about a  
9 cementless fossa; is that correct?

10 Okay. Without any further comments, I think we can  
11 break for lunch and we would like to return precisely at two o'clock.

12 thank you.

13 (Whereupon, at 12:31 p.m., the meeting was recessed  
14 for lunch, to reconvene at 2:00 p.m.)

15

16

17

18

19

20

21

22



1  
2  
3  
4  
5

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(2:02 p.m.)

CHAIRMAN HEFFEZ: Okay. The second question that we need to address, I know we just finished lunch, but let's keep our attention to this. The second question is up there.

It's 132 of 180 cases were treated at site one, 40 of 180 cases at site two, and eight of 180 at site three and four and five. Does the fact that 96 percent, 172 of the 180 of the cases were treated only at two sites present a potential for bias in the clinical outcomes?

So I'd like to hear from the panel members. Dr. Patters.

DR. PATTERS: Mark Patters.

Of course it's potential for bias, but it works in both directions. It could bias the scientific nature of the project in a positive way and introduce far fewer variables. If there were ten sites and seven of the surgeons decided that in their hands they needed to put in two more screws than were in the protocol, then you'd be adding variable upon variable upon variable, and I think to be commended here are the two sites that only added one variable of taking the cement and cutting the post off.

1                   But, yeah, in ten sites there could have been ten  
2 variables added, and the scientific validity of the study  
3 compromised. So of course, it's a bias, but it works in both  
4 directions.

5                   DR. SUZUKI: Jon Suzuki.

6                   I wanted to comment also I agree with Dr. Patters.  
7 I think that the variables have been at least minimized. There's  
8 always variables in any clinical trial, but the fact that the vast  
9 majority of them were conducted at two sites I think minimizes  
10 those outside factors and probably for the statisticians' sake  
11 it makes things a lot more streamlined.

12                   And I also asked the question earlier today regarding  
13 a learning curve, and we were reassured that there would be a  
14 significant training period or training sessions for those surgeons  
15 that are going to be using thee particular products. So I don't  
16 think it's a problem.

17                   CHAIRMAN HEFFEZ: Let me introduce a factor that  
18 I think that we should take into account, is that if there are  
19 only two centers to train people, is that feasible? That's  
20 something I think I'd like to hear how the other panel members  
21 feel.

22                   Dr. Burton.

1 DR. BURTON: Richard Burton.

2 I think obviously that would be a significant thing,  
3 and the fact that you're not going to be on training might actually  
4 -- perhaps that should go back to Drs. Quinn and Sinn though.  
5 Do you have a feel I don't want to say what the demand is, but  
6 you know, are you going to be able to deal with the fact of being  
7 able to do that because, you know, again, what you were saying,  
8 Dr. Quinn, was that you were going to be or Dr. Sinn was going  
9 to be performing at least a surgery with these individuals when  
10 they started to utilize this system.

11 So, I mean, that's going to be sort of a rate limiting  
12 step, if you want to look at it that way, to any type of marketing  
13 attempt by the company.

14 CHAIRMAN HEFFEZ: I just wanted to touch upon that  
15 point, but it's going to be really addressed in question 6(b).  
16 So if we can just stay on track as far as whether it's presenting  
17 a potential for bias just in the clinical outcomes.

18 Dr. Li.

19 DR. LI: Steve Li.

20 I'd just pass along kind of a story from the VAS  
21 spinal cage panel that I was on in orthopedics. There was a  
22 multi-center; I think it was a ten or a dozen multi-centers, a

1 couple of dozen orthopedic surgeons involved in testing a spinal  
2 cage, and six of the two resident surgeons had a financial interest  
3 in the product, and the results from those six surgeons were about  
4 a 15 or 20 percent higher success rate than those that did not  
5 have a financial interest in the device.

6 Now, I don't think they were dishonest and the  
7 solution was not to give everybody a financial interest to improve  
8 the performance, but I think the message though is they had a level  
9 of expertise or knowledge about the device that was not passed  
10 on to the very next generation of surgeons. So that was probably  
11 a very close training situation where the first six trained the  
12 next two dozen, and yet there was still a very large difference  
13 in success rate.

14 Now, I don't know if that translates to this or not,  
15 but it certainly raises the issue that two centers done by two  
16 expert surgeons would probably reflect the best possible outcome.

17 CHAIRMAN HEFFFEZ: Well, we certain can ask Dr. Quinn  
18 and Dr. Sinn if they can come to the podium and do they have a  
19 financial interest in the selling of the product.

20 DR. LI: Well, again, that wasn't my point, I think.

21 CHAIRMAN HEFFFEZ: Yes.

22 DR. LI: Yes.

1 CHAIRMAN HEFFEZ: Go ahead.

2 DR. QUINN: I'd like to answer that question first.

3 I have no patent in this. I have not received any stock. I have  
4 receive consulting fees over the past nine years, all of which  
5 have been donated to the University of Pennsylvania School of  
6 Medicine, Oral Surgery Giving Fund.

7 I have full intentions of being remunerated for time  
8 spent training other surgeons and putting courses on as a clinical  
9 service agreement, but actually with some great difficulty with  
10 the University of Pennsylvania Technology Transfer Center. We  
11 convinced them that it would be in the best interest to have Biomet  
12 maintain the patent on this device so that it's not held by me  
13 or the university.

14 To the issue of sites, Dr. Burton mentioned rate  
15 limiting. I'm somewhat in favor of rate limiting. I don't want  
16 the gate opened wide on this. I do think that we will broaden  
17 the site. In fact, the next proposed site is the University of  
18 Florida under Dr. Dolwick, who once he has training would become  
19 a trainer himself.

20 We try to identify sites based on both the expertise  
21 of the surgeon and the geography because I think that's important  
22 for the patients involved.

1 I don't have a specific gating of how this would  
2 go, but to extend this from two to four to six gradually would  
3 be my preference and not to open this up widely immediately.

4 CHAIRMAN HEFFEZ: Thank you.

5 Dr. Sinn, could you answer the other question?

6 Identify yourself just before.

7 DR. SINN: Doug Sinn from Dallas.

8 I, too, have no financial interest, no patent, or  
9 no relationship with Lorenzo other than as a consultant, and have  
10 received compensation for reimbursement for training or for  
11 traveling and that's all.

12 CHAIRMAN HEFFEZ: Thank you.

13 Any other questions from the panel?

14 (No response.)

15 CHAIRMAN HEFFEZ: So if we could summarize this  
16 question, do we all feel or it appears to me that we all feel that  
17 it doesn't really bias the clinical outcomes, and that in some  
18 ways it could be beneficial. Everybody more or less concur with  
19 that statement?

20 DR. PATTERS: I concur.

21 CHAIRMAN HEFFEZ: Okay. Very good.

22 We'll go to the next question. Fifty-two patients

1 of the 168 implanted patients had reports of adverse events. Of  
2 these 52 patients, eight required permanent devise removal. Please  
3 discuss the rate of adverse events in this patient population.

4 So if we look carefully at the adverse list, you'll  
5 see that actually the reporting was quite generous, reporting  
6 things that weren't really directly related to the prosthesis  
7 itself, but related to the surgical approach, for example, to it.

8 So I'd like you to look at that adverse list as a  
9 panel, and do you feel this list of adverse events is inappropriate?

10 Dr. Cochran.

11 DR. COCHRAN: This is David Cochran.

12 I think given the population that we're dealing with,  
13 this is a very low rate, in fact, and I'm very comfortable with  
14 it.

15 (Pause in proceedings.)

16 CHAIRMAN HEFFEZ: Excuse the silence for just one  
17 moment.

18 Dr. Runner?

19 DR. RUNNER: I saw Dr. Burton and Dr. Eggleston nod  
20 their head. Could they make those nodded comments more verbal,  
21 please?

22 DR. BURTON: Richard Burton.



1 I as one of the oral surgeon consultants to the panel  
2 and having been involved with TMJ surgery for, I guess, 20 years  
3 now, actually I feel that both the rate and the reporting -- I'd  
4 have to agree. Actually Dr. Cochran was reasonably liberal in  
5 their approach to that because, again, many things that were worded  
6 as adverse events were actually what most of us as surgeons --  
7 and I'm not sure patients like that term -- but are part of the  
8 normal, accepted things that go along with just the surgical  
9 approaches to the joint or with any type of surgery whether it  
10 be infected, both the rates, the occurrence, and the resolution  
11 of those. We're certainly within the normal realms for this type  
12 of surgery, and in looking at the number of joints that had been  
13 lost within that time frame, with eight explanted joints out of  
14 that number, while certainly everybody wishes it was zero, it still  
15 is still historically looking probably a much lower number than  
16 most of us really would -- I candidly would have probably expected  
17 out of that population, even though the fact that this is not some  
18 ten or 15-year follow-up and in that amount of time, that is, again,  
19 both a reasonable number and a reasonable outcome.

20 CHAIRMAN HEFFEZ: Dr. Hewlett.

21 DR. HEWLETT: For me, in order to get a comfort level  
22 with this question, I tended to focus on the six reported cases

1 that were deemed by the investigators device related because of  
2 the generosity, if you will, in describing the other adverse events.

3 And even within those, there seemed to be some  
4 circumstances that, looking at it objectively, could perhaps even  
5 be not necessarily related to the device.

6 So given that, six cases, all but one of which appear  
7 to fall -- the adverse events occurred within that three-year  
8 period. I would tend to concur with the other sense of the panel  
9 so far that this is an acceptable level of adverse events.

10 CHAIRMAN HEFFEZ: Okay. Thank you.

11 Now, I'd like to tackle this issue which is related  
12 to two and three, and I'd rather tackle it now because we'll need  
13 to tackle it later.

14 Related to two and three I'd like to ask the panel  
15 regarding the indications because the indications are related to  
16 adverse events, and it's related to clinical outcomes.

17 We've discussed already previously that the  
18 indications are covered over approximately 11 rubrics, and the  
19 point has been made that the testing has been primarily in certain  
20 rubrics, and I'd like to know how the panel feels where the device  
21 has been properly tested, in which of those diagnostic categories.

22 So I enlist the panel members to look at the

1 indications and give me their comfort level.

2           During the silence I can help out and say at least  
3 there's osteoarthritis, and one of the points raised was the fact  
4 that many of these patients have multiple diagnoses and a primary  
5 diagnosis wasn't assigned.

6           But if you look at the numbers, you're looking at  
7 osteoarthritis, traumatic arthritis, total implant, avascular  
8 necrosis, ankylosis. Those are the big categories.

9           In a previous question, Dr. Quinn -- and I'll ask  
10 him to come to the podium just to confirm this -- did indicate  
11 that he felt that he agreed that the prosthesis had been tested  
12 better in certain cases, such as osteoarthritis and in other  
13 categories less well.

14           Do you want to respond to that?

15           DR. QUINN: Peter Quinn.

16           I would just like to make the point that I think  
17 in order to collect data we were trying to be very specific for  
18 the purpose of the study, to identify very specific diagnoses.

19           I think if you look at the two approved devices that  
20 are on the market, they both have the same indications, and I think  
21 there are five indications. They are much broader.

22           For example, one of the approved indications is loss

1 of vertical height of conduct. That would cover any of these  
2 indications. So I think in an attempt to collect more specific  
3 data, we may have painted ourselves into a statistical corner.

4 And I would suggest and maybe ask Dr. Runner if  
5 looking at indications of approved devices would actually be better  
6 guidance.

7 CHAIRMAN HEFFEZ: I'll ask Dr. Runner to help in  
8 the situation because we're not allowed to look at another -- you  
9 know, your PMA has to stand alone, but I'll ask Dr. Runner.

10 DR. RUNNER: I would suggest that the panel take  
11 into account this particular device and the indications that are  
12 listed on this device, and if you feel that there is not data,  
13 do you feel that you can extrapolate from the known condition to  
14 use of this device and whether that's appropriate or not?

15 CHAIRMAN HEFFEZ: Dr. Burton.

16 DR. BURTON: Richard Burton.

17 One question I had. I just noticed this because  
18 of going back and forth, but in our panel packets there's a summary  
19 of safety with respect to this, and it lists ten indications for  
20 use, and then the essential prescribing information, which is very,  
21 very similar lists 11, and the difference is that it lists a number  
22 eight, and to make it 11, but number eight says degenerated or

1 reserved joints with severe anatomic discrepancies, which the  
2 indications for use in the summary sheet doesn't list that one.

3 So, I mean, I'm not sure. The first question is,  
4 and I guess it's probably back to you, Dr. Runner, is why there  
5 is a difference between the two, but I think that, you know,  
6 sometimes trying to make a difference between whether it's  
7 avascular necrosis, a degenerative rheumatoid patients, or a  
8 degenerated or severely resorbed joint really are in reality all  
9 the same thing.

10 So, I mean, I would actually -- I think Dr. Quinn  
11 may be correct here, in the fact that the specificity may not really  
12 be the issue. I think it's the degree of deformity, the degree  
13 of disability that the patient has is really probably the driving  
14 factor in making the decision to move toward some kind of a joint  
15 replacement as opposed to a more conservative procedure and whether  
16 it fits one of those specific categories may not be the best system  
17 of classifying it for that.

18 But can you answer why there's a difference between  
19 those two lists?

20 CHAIRMAN HEFFEZ:

21 DR. QUINN: I apologize for the discrepancy. I wasn't  
22 aware.

1 DR. RUNNER: This is Susan Runner. In terms of our  
2 review of the PMA, we looked at the indications for use list.  
3 The summary of safety and effectiveness is typically a document  
4 that's submitted by the company and is substantially revised at  
5 the end of the review process. So that really was not reviewed  
6 in detail.

7 The indications for use that was submitted with the  
8 PMA would be the primary indications that we went through for our  
9 review.

10 CHAIRMAN HEFFEZ: I have, Dr. Quinn, a question.  
11 If you look at the indications, in general they are all similar  
12 in the sense of lots of vertical dimension. One of them always  
13 that stands out is the development abnormality, and how many cases  
14 actually were treated with developmental abnormality to your  
15 knowledge?

16 DR. QUINN: I can't recall any that actually fell  
17 into that, offhand that fell into that category.

18 CHAIRMAN HEFFEZ: Dr. Patters.

19 DR. PATTERS: Mark Patters.

20 It appears to me that Dr. Quinn has pointed out that  
21 there is no reason to believe that the device would behave  
22 differently in indications which were not studied, but I think

1 it's only appropriate that the sponsor indicate in the labeling  
2 that this use has not been studied, and there is no data. That  
3 would satisfy me.

4 There's no reason to think it would behave  
5 differently, but there is no data to say that it, indeed, does  
6 or does not.

7 CHAIRMAN HEFFEZ: How do the other panel members  
8 feel about Dr. Patters' statement?

9 You can sit down, Dr. Quinn. Thanks.

10 DR. BURTON: Richard Burton. I would agree with  
11 Dr. Patters on that. In our summary package, Table 2 was diagnosis,  
12 and it lists out 11 diagnoses some of which have been grouped within  
13 those surgical indications because the arthritides are grouped  
14 as one group, whereas they split out all three of the arthritides  
15 separately as part of their percentages, and it appears, at least  
16 looking at the diagnosis table, that there are listed indications  
17 in terms of surgical indications that thus far there have been  
18 no cases presented that fit that diagnoses.

19 But I think that what Dr. Patters and I would agree  
20 with is the fact that given the fact that these are all functionally  
21 equivalent in many respects, that you would not expect that this  
22 device or any other to perform any differently given the clinical

1 environment that they're in because clinically though the origin  
2 of the problem may be different. It probably would not affect  
3 the device itself once it was implanted.

4 CHAIRMAN HEFFEZ: So let me -- Dr. Runner?

5 DR. RUNNER: I just wanted to remind the panel that  
6 you can feel free to make recommendations about a more general  
7 indication for use or more specific as you see fit.

8 CHAIRMAN HEFFEZ: I'd like to maybe summarize the  
9 panel's position here and, please, I would like to hear from the  
10 panel how they feel.

11 We feel that the indications that the -- that the  
12 devices indicated for replacement of the temporomandibular joint  
13 and it has been well studied for perhaps loss of vertical dimension  
14 in osteoarthritic, traumatic arthritis, avascular necrosis,  
15 ankylosis, but additional studies need to be developed in order  
16 to study it in other diagnostic categories, to replace other  
17 diagnostic categories.

18 DR. RUNNER: Question. Are you stating that you  
19 feel additional studies need to be completed or you would prefer  
20 a labeling?

21 CHAIRMAN HEFFEZ: A labeling. I'm sorry.

22 DR. RUNNER: A labeling that would say that it has



1 not been studied in these conditions?

2 CHAIRMAN HEFFFEZ: Dr. Runner, I agree, a labeling  
3 saying that the device has not been studied adequately for those  
4 other rubrics.

5 How would the panel feel regarding that? Dr.  
6 Bertrand.

7 DR. BERTRAND: Peter Bertrand.

8 I think having a caveat that in certain conditions  
9 there's been some data and in other conditions there isn't enough  
10 patients with that diagnoses had that labeling, I think it would  
11 suffice.

12 CHAIRMAN HEFFFEZ: Okay. I've got a general consensus  
13 on that.

14 Now, there's one other point related to two and three  
15 that I want to cover, is that in some cases part of either the  
16 fossa, in most cases the fossa, but either the fossa or the condylar  
17 prosthesis was removed for reason X and that patient went through  
18 a certain period of time before receiving the other portion of  
19 the joint, prosthesis. In other words, they're walking around  
20 with a partial joint prosthesis. Is there a recommendation when  
21 that has to be replaced or is it adequate to let them function  
22 with a hemiprosthesis?

1 I'd ask Dr. Quinn or Dr. Sinn to address them.

2 DR. QUINN: We clearly don't believe in  
3 hemiarthroplasty as a general indication, but I think there are  
4 time periods that are determined by the cause for the initial  
5 removal. For example, in infection, and Dr. Sinn had a patient  
6 with MRSA that he can comment on, but we have reimplanted them  
7 up to two years later, and as short as three months later when  
8 the tissue condition improves to the point where it would be safe  
9 to reimplant it.

10 I'm not sure we could put a time period on it, but  
11 I think we could say there should not be permanent hemiarthroplasty  
12 indications.

13 CHAIRMAN HEFFEZ: So have you seen any adverse  
14 effects from waiting in a delayed fashion on those few cases prior  
15 to replacing the glenoid fossa, for example?

16 DR. QUINN: It was not a great n, but I think the  
17 biggest problem is deviation of the mandible to the side of implant  
18 removal. If there isn't gross deviation and, again, in  
19 multioperated patients where they're scarred, they tend not to  
20 deviate as much as somebody who has a de novo fractured condyle.

21 If there was gross deviation, and based on the  
22 deviation there was malocclusion and pain, I would tend to replace

1 it sooner than later, but we have replaced them up to two years  
2 later.

3 CHAIRMAN HEFFEZ: Thank you.

4 DR. QUINN: Can I ask Dr. Sinn to comment on his  
5 patients?

6 CHAIRMAN HEFFEZ: Dr. Sinn.

7 DR. SINN: Dr. Sinn.

8 The explants that I was involved in, one patient,  
9 as Peter mentioned, was a methicillin resistant Staph. infection,  
10 and that particular patient was a nurse in an emergency room and  
11 probably a MRSA carrier, and the explant was done both top and  
12 bottom on one side. The opposite side was left to function. It  
13 was not infected.

14 It was replaced three months later when we had tag  
15 white blood cell scans that were negative, and it got infected  
16 a second time and, in fact, explanted on the same side a second  
17 time., and it remains out to this day, and it's been about six  
18 or eight months since I took it out, and the patient is begging  
19 me to have it put back in because of the dysfunction that's  
20 associated with it.

21 But I've had no explants where I did partial  
22 removals. So all of mine have been complete. If I did, I did

1 three.

2 CHAIRMAN HEFFFEZ: Okay. Thank you.

3 So I'd like to have a consensus from the panel that  
4 this device is -- as far as labeling is concerned, that we should  
5 consider not recommending it for partial joint replacement. How  
6 does everybody feel about that?

7 DR. PATTERS: Excuse me, Dr. Heffez. Mark Patters.

8 In the labeling that I see in all capital letters  
9 they say, "Do not use the individual components for partial joint  
10 reconstruction. So it's quite clear that they're insisting that  
11 it be used only as a total prosthesis.

12 CHAIRMAN HEFFFEZ: All right. I'd like to move now  
13 on to question five.

14 The sponsor has provided engineering test data and  
15 a protocol for testing on both the new fossa design without a post  
16 and the fossa with a post removed using a rongeur. Do the  
17 engineering test data and protocol as presented given adequate  
18 safety and effectiveness information on the device?

19 Now, I understand that the information regarding  
20 the post being removed is to be forwarded to the FDA, but we haven't  
21 received that as of yet. If we presume that that information concurs  
22 with the data with the post -- I'd like to ask the question that

1 way -- is the data providing adequate safety and effectiveness?

2 I'd like to hear from Dr. Li.

3 DR. LI: Steve Li.

4 Actually I'm not sure the test is meaningful in  
5 either case. It seems to be unidirectional loading that doesn't  
6 really place the post anywhere in a biomechanically important  
7 function. So I think this particular test is not effective  
8 evaluating the device.

9 Secondary to that is as I said earlier I don't really  
10 think the presence of post, removing that post actually has serious  
11 or actually any biomechanical effect.

12 As long as I'm talking, can I raise things about  
13 testing or is this not the time to do that?

14 CHAIRMAN HEFFEZ: No, that would be a good time.

15 DR. LI: I guess I would rather see them test the  
16 things that I think are the big question marks in my mind. That  
17 would be obviously the wear issue, the polyethylene wear issue.

18 I'd like to test this concept of creep of the  
19 polyethylene around the screws that fits the polyethylene to the  
20 glenoid area. I just can't believe that those don't loosen in  
21 time. Maybe the amount of loosening is not clinically detrimental,  
22 but I would be very surprised if this happened at all.

1                   And a third, much less important, I think we should  
2 at least check whether or not there's any chance of mixed metal  
3 crevice corrosion by using titanium screws against a cobalt chrome  
4 plate.

5                   I think those three would be important features.

6                   Also I think the screw pull-through test with the  
7 polyethylene also is not a clinically meaningful test. I think  
8 if you want to do that test, you might do it in conjunction with  
9 a pre-test. That would be the load to the flange, to the  
10 polyethylene flange and see if that actually causes creep because  
11 that's how it's going to pull through and loosen.

12                   Once it gets to a loosened point, it's going to be  
13 loose. It will probably never really pull all of the way off the  
14 screws, but it could become loose to the point that it would be  
15 either poorly functional or nonfunctional.

16                   So those would be my suggestions for additional  
17 testing.

18                   CHAIRMAN HEFFEZ: While we're discussing this I'll  
19 ask Mr. Mulry or Dr. Mulry -- I apologize -- to circulate the device  
20 around the panel so that they can actually touch and feel it.

21                   MR. SCHECHTER: This is Dan Schechter.

22                   I don't know if anybody with the sponsor can answer

1 this question, but can anyone comment on how the testing done on  
2 this device compares to the similar devices, namely knee joint  
3 or hip point that has been mentioned a couple of times here today,  
4 how the testing compares at all specifically in terms of the  
5 specific tests that were done, pull through, et cetera.

6 MR. ROMAN: Shawn Roman.

7 Just to make sure I understand the question here,  
8 you want to know how the test results are --

9 MR. SCHECHTER: Not necessarily the test results,  
10 but the battery of tests needed in terms of a pull-through test,  
11 a T test. It was mentioned before that there was no or that you  
12 don't have a good fixture model to simulate TMJ motion. Are there  
13 fixtures like that for a knee joint that you use, just as an example?

14 DR. BERES: Ken Beres from Biomet.

15 I think in terms of the testing that was done, it's  
16 really a look at failure models, and we particularly ought to take  
17 fracture or failure modes.

18 And so you run it through the T tests and see does  
19 this flange break or does that break? And those tests are done,  
20 and these obviously and HIPS for a situation that mimics their  
21 use. Similarly, when we did a T test, we put it in a mock-up of  
22 a TMJ and you cycle it through ten cycles, which are really for

1 just breakage.

2 The idea of wear testing is a very good one, and  
3 we do that with hips and knees where there are simulators especially  
4 designed for those joints, to give you an answer. TMJ, I'm not  
5 aware of anything close to a simulator that could get us that data.

6 It's a great idea, but I don't know of a machine that exists that  
7 would be capable of giving that data.

8 CHAIRMAN HEFFEZ: As far as the mechanical testing,  
9 I raised the point and asked if you had a comment on it before  
10 as far as many times you're testing all of this in vitro with the  
11 parts perfectly mated, but the value of testing it with them not  
12 perfectly mated, which would probably be a more realistic test.

13 How do you feel about that? Would those tests be of value?

14 PARTICIPANT: I think that's an exceptionally  
15 important point. Even in the total hip joint where the contact  
16 stress and perfectly aligned, there may be only ten or 15 percent  
17 yield strength of the polyethylene. If you put the cut at a high  
18 induction angle and you look close to the rim, the contact stress  
19 gets up over the yield strength of the material.

20 So that the alignment and how the mandibular point  
21 would contact the fossa would greatly influence the contact stress  
22 and resulting failure mode of the polyethylene.



1                   And just as a follow-up to Mr. Schechter's question,  
2 I think in general my general feel is that your in vitro testing  
3 should mimic what's going to happen in vivo. At least two or three  
4 of the cases of the test that provided by the applicant a reasonable  
5 materials test, but even they realized that they are not in vivo  
6 related tests.

7                   So they're kind of a good material engineering thing,  
8 but they don't really help the patient, and so my suggestions are  
9 to try to point the testing and direction so that a result will  
10 give you some clinically meaningful predictive bound.

11                   There's almost none of that as relates to the  
12 polyethylene.

13                   CHAIRMAN HEFFEZ: Dr. Runner.

14                   DR. RUNNER: Susan Runner.

15                   Correct me if I'm wrong. The company did set up  
16 their fatigue test model in a worst case scenario with the  
17 mandibular portion canted; is that correct?

18                   PARTICIPANT: That's correct. As mentioned in my  
19 presentation, we incorporated three different conditions into the  
20 fatigue testing which were used to simulate worst case scenarios,  
21 one of those being angling the mandibular component at ten degrees  
22 with respect to the fossa.

1 DR. LI: Steve Li.

2 Wasn't that a worst case scenario for the mandibular  
3 component? Wasn't it still aligned on the fossa side?

4 PARTICIPANT: Well, the nature of the design is for  
5 the spherical head of the mandibular component to align with the  
6 spherical head and --

7 DR. LI: I understand, but my point is that the worst  
8 case scenario, the way I read their test description, the worst  
9 case referred to the mandibular side.

10 For instance, if you work perfectly -- I haven't  
11 handled the components, but I think Dr. Quinn said not perfectly  
12 performing. So there's a little bit of possible motion of the  
13 mandibular.

14 DR. QUINN: Actually the spherical head of the  
15 mandibular component has a smaller spherical radius than the --

16 DR. LI: Correct. So that gives the mandibular point  
17 of contact a range of places it could be, and some of those places  
18 are higher contact stress than others.

19 DR. QUINN: And that's why we had angled the --

20 DR. LI: But it wasn't clear to me that they were  
21 not mutually exclusive, but you could put you component at ten  
22 degrees and get contact with the fossa component at the exact same

1 place, or did you when you moved the mandibular component change  
2 the location of the contact point to the fossa?

3 DR. QUINN: I guess for the testing the center lines  
4 from the spherical radii that made the components work were aligned.

5 DR. LI: That's your interpretation. So it was the  
6 worst case for the mandibular side, but not necessarily for the  
7 fossa side.

8 DR. QUINN: Again, I don't see the difference there  
9 between them. You definitely would have a smaller surface contact  
10 between the mandibular component and the fossa component. So it  
11 would be a worst case scenario for the fossa component.

12 CHAIRMAN HEFFEZ: To come back to that, what did  
13 you test for? What are the tests?

14 DR. QUINN: All of the T tests were done with that  
15 angulation.

16 CHAIRMAN HEFFEZ: Thank you.

17 PARTICIPANT: As I understand, maybe just to clarify,  
18 it sounds to me like Dr. Li's concern, which I think would be well  
19 founded, is that the test occurred and produced some pressure and  
20 did not try to replicate any sort of either rotation or  
21 translational movement between the components.

22 DR. LI: That's correct.

1 PARTICIPANT: And I think that's the concern that's  
2 being raised.

3 DR. LI: And that -- I'm sorry. Steve Li -- that's  
4 exactly right, and also the location and the contact. In other  
5 words, as Dr. Rekow just handed me the components, if I could use  
6 my hands as the components, the mandibular component is here or  
7 it could be here, and the closer it gets to the edge, the higher  
8 the stresses get on the polyethylene.

9 So I would keep this contact area constant and change  
10 my mandibular component a long way, but yet if I don't move the  
11 location of contact, my contact stress on the polyethylene is the  
12 same.

13 So unless they specifically move the contact points  
14 as they move the mandibular component, they're putting the  
15 mandibular component in the worst case scenario, but not  
16 necessarily the polyethylene.

17 CHAIRMAN HEFFEZ: Yes.

18 MS. HELMS: Can I answer that?

19 CHAIRMAN HEFFEZ: Please identify yourself.

20 MS. HELMS: Elizabeth Helms.

21 I can answer that worst case scenario because this  
22 would be one of my questions and my key scenario. Ankylosis of

1 the right side, healthy joint on the left side. The ankylosis  
2 caused the left side to take the entire load, and the condyle went  
3 up into the fossa of the bone until it broke through the disc and  
4 then broke through the bone of, you know, the fossa.

5 I can't tell you the excruciating pain that's  
6 involved when you lose, you know, both sides like that, and so  
7 Dr. Li's question, I think, is really valuable because if you have  
8 a case scenario where you have one side that has a loss, what's  
9 going to happen to the condyle as it hits up into what is it,  
10 polypropylene? Is that right?

11 What will happen to that with that, and that's an  
12 intense load on the site, and you know, would it be fair to say  
13 that that kind of test has been done so that you would have a response  
14 because that is something that can happen in many cases.

15 CHAIRMAN HEFFEZ: Any further comments from the  
16 group?

17 DR. FAULK-EGGLESTON: This is Dr. Faulk.

18 We don't have a comment. We just had a question  
19 now that we've seen the device: why the indentation is on the  
20 top surface even on the site that doesn't have the little indented  
21 letter P or Y is there?

22 MR. ROMAN: All right. That is an undercut groove

1 of those included in the design to give an area for securing a  
2 bone filler or bone cement that does not extend above the top surface  
3 of the fossa component.

4 DR. FAULK-EGGLESTON: But now you're not putting  
5 in a bone filler.

6 MR. ROMAN: That's correct.

7 DR. BURTON: So Richard Burton.

8 So my question is, you know, it may not make a  
9 difference, but wouldn't you just have a smooth surface up there?

10 It looks like it was an undercut obviously for retention, and  
11 you know, you eliminated the post offer here, but retained that.

12 MR. ROMAN: Yeah, I agree. Since we've discussed  
13 offering it as a cementless device, that undercut groove does seem  
14 unnecessary at this point.

15 CHAIRMAN HEFFEZ: However, these devices have been  
16 marketed and used and studied; is that correct, the cementless  
17 devices, since February?

18 MR. ROMAN: Yes.

19 CHAIRMAN HEFFEZ: Dr. Hewlett. I'm sorry.

20 DR. HEWLETT: I was just going to say or suggest  
21 that given Dr. Li's concern and the ensuing discussion that perhaps  
22 we've identified a potential condition for approval that might

1 be the appropriately discussed further during the voting.

2 CHAIRMAN HEFFFEZ: Yes, but I think that if we could  
3 address this question right now specifically, I think we could  
4 say, if I can summarize what I'm hearing, that additional test  
5 data should be done in order to demonstrate adequate safety and  
6 effectiveness.

7 There were certain questions that were raised  
8 regarding where creep and mixed metals. Those were the -- now,  
9 how does the panel feel?

10 Dr. Runner?

11 DR. RUNNER: This is Susan Runner.

12 The question would be if the panel could discuss  
13 whether this testing needs to be done pre-market or post market.

14 CHAIRMAN HEFFFEZ: All right. We could discuss that  
15 during the voting, but I guess we could ask: do the engineering  
16 test data and protocols presented give adequate safety and  
17 effectiveness information on the device as it stands?

18 How do people feel about that? Dr. Patters?

19 DR. PATTERS: Dr. Patters.

20 It appears so in my mind, and since they report no  
21 failures of the device in the 180 cases that it has been planted  
22 in, I feel pretty confident that the device is safe.

1 CHAIRMAN HEFFEZ: Dr. Bertrand?

2 DR. BERTRAND: Peter Bertrand.

3 Is that over a three-year period or longer, or are  
4 we restricted to a three-year period?

5 I know that Dr. Quinn's group and Dr. Sinn's group  
6 are continuing to collect data in three and four years. So we  
7 really don't know long-term effects yet, but over three years it  
8 does appear that it's fairly safe, but are we looking at it as  
9 far as making a judgment at three years?

10 DR. RUNNER: This is Susan Runner.

11 I think that for the purposes of this panel meeting  
12 we should look at it in terms of how the study was designed for  
13 three years.

14 CHAIRMAN HEFFEZ: So, Dr. Patters, you're --

15 DR. ANSETH: Dr. Anseth.

16 I just had a quick question for Dr. Li.

17 I think you had brought up some of your experience  
18 with the hip and knee implants, and based on the long history of  
19 using the ultra high molecular weight polyethylene and the cobalt  
20 chromium alloys, could you comment on if there were excessive wear,  
21 would they have seen anything, any other indications after three  
22 years of this study?



1 DR. LI: It's possible had they looked more  
2 carefully, for instance, with a more focused or more specific idea  
3 on the histological sections, perhaps closer view of the retrieved  
4 polyethylene components, perhaps even further analysis of the in  
5 vitro tests, had they made some more measurements on the laboratory  
6 test specimens. I think all of those were three potential sources  
7 of getting some idea of how much wear and damage is occurring.

8 But my concern is none of these measurements were  
9 made. So they may or may not be a problem. I guess that's my  
10 question or that's my concern.

11 DR. ANSETH: But in general, if wear becomes a problem  
12 is it seen later, so after? So would three years be on a very  
13 short time scale?

14 DR. LI: Three years would be on a very short time  
15 scale for something like osteolysis. You would have to have an  
16 enormous amount of wear, but we have unfortunately on the orthopedic  
17 side, I can think of three instances of devices that look great  
18 at three years, and there was a line for revisions at five because  
19 we just don't understand the wear rate. We just didn't see the  
20 wear rate at three.

21 CHAIRMAN HEFFEZ: Dr. Rekow.

22 DR. REKOW: Dr. Li, I want to ask you another

1 question.

2 I agree that wear is a potential tremendously  
3 important concern. I don't know enough about the orthopedic  
4 literature to know if you get wear data and you can characterize  
5 the wear patterns and you can characterize the size of the  
6 particles, is the state of the science sufficiently well defined  
7 that we would know what those imputations are likely to be?

8 I have no trouble asking people to do more studies,  
9 but if we don't know what the outcomes of the studies are, I'm  
10 reluctant to impact their business for something we might not have  
11 anymore information other than some esoteric answers.

12 DR. LI: Steve Li.

13 An excellent question. I think all I can tell you  
14 quite honestly, in the laboratory, in vitro testing side is we've  
15 got tests that will tell you if you're going to be in really bad  
16 trouble. We don't really have a test to say if you're going to  
17 be okay. So therein lies the problem.

18 So at this point though, it's possible to be kind  
19 of in a not okay situation at two and three years and not really  
20 know it unless you actually go out of your way and look a little  
21 harder.

22 So I'm just worried that, in fact, it looks great.

1 In fact, the data looks great at three, but you run into things  
2 we've seen before that all of a sudden at four and five you've  
3 got a large revision business because of osteolysis.

4 Now, I'm not saying that's the case here. I just  
5 don't know.

6 DR. REKOW: As a follow-on question -- this is Dr.  
7 Rekow -- now I've forgotten the question. Are there any ways that  
8 you can effectively accelerate the test so that in vitro you could  
9 accomplish more cycles with heavier loads or something that gives  
10 you the same sort of things at least in the knees and hips in a  
11 shorter time span, that essentially gives you a worst case, but  
12 you could extrapolate a different time span than the three-year  
13 clinicals?

14 DR. LI: Those are really the descriptions of NIH  
15 grants actually.

16 To be fair to the sponsor, as far as I know, there  
17 is no, in fact, currently available TMJ simulator. However, the  
18 device has been around since the early '90s. In the early '90s  
19 there were no knee simulators either.

20 So for some reason this particular area has not  
21 devoted their attention to building one, but certainly there are  
22 no more degrees of freedom in a TMJ than there are in a knee.

1 So it is a possible thing to construct, but you might not have  
2 to go that far.

3 I mean, certainly looking with 180 devices out there,  
4 there might be enough clinical information from retrievals,  
5 histological sections, maybe pick a subset of groups to do a more  
6 close radiological study.

7 There are options where you can get a clinical sense  
8 for how much wear is going on. I guess I would like to see some  
9 measure of that, if not right away in the laboratory, at least  
10 some program to try to determine what level of wear they've got.

11 CHAIRMAN HEFFEZ: In the in vitro testing that was  
12 done, would you have expected to see where?

13 DR. LI: No, that's one of my concerns. I saw none  
14 of the in vitro tests that would actually, or at least the way  
15 they conducted the tests, that give me any indication of wear or  
16 creep results in there.

17 So it's possible had they done a similar work and  
18 made extra measurements they could have answered some of these,  
19 but the testing done so far, I think it's kind of an odd thing.

20 The testing says the device is okay. The clinical results say  
21 at three years the device is okay. But I don't think they really  
22 had anything to do with each other

1                   In other words, I don't think a laboratory test  
2 really dictated or predicted the clinical situation.

3                   CHAIRMAN HEFFEZ: Dr. Cochran.

4                   DR. COCHRAN: David Cochran.

5                   I think one of the things we have to keep in mind  
6 though is the function on these particular joints. As was pointed  
7 out in the data, a lot of these patients have had five surgical  
8 procedures before this, and you've got 45 cases at three years  
9 with, as Dr. Patters pointed out, no indication of failure in any  
10 sort of way.

11                   So although some of the in vitro testing would  
12 certainly be nice to see, I don't see that as a real necessity  
13 for us to go and make a decision in this case.

14                   CHAIRMAN HEFFEZ: Dr. Burton.

15                   DR. BURTON: Richard Burton.

16                   I would agree with Dr. Cochran on that. I mean,  
17 I think that it's interesting. I can tell you that there's a  
18 bioengineering group at our institution who has looked actually  
19 for three or four years now trying to come up with a simulator  
20 with numerous attempts at things, none of which have been very  
21 successful.

22                   I mean, I think it can be done, again, if you're

1 looking for grant money to try to do something like that, but again,  
2 trying to correlate what you might find in vitro with what we have  
3 at least found thus far in the clinical population doesn't appear  
4 that we're going to gain enough certainly at this juncture that  
5 would aid us making a decision either way.

6 I think, you know, we probably all hope that we will  
7 find some method where we can provide more adequate testing, and  
8 unfortunately at this juncture it doesn't exist, and I can't see  
9 how we can ask the sponsor to sit there and say, "Yeah, we ought  
10 to come up with a test, but we're not really exactly sure what  
11 it is and we're not really sure what we're going to find, and we're  
12 not sure what the correlation is going to be with what we find  
13 with the clinical presentation.

14 CHAIRMAN HEFFEZ: I will leave this question, but  
15 I want to just leave one statement, which is that the question  
16 is addressing the engineering test data. It's really not addressing  
17 engineering test data and its relationship to clinical data. It's  
18 specifically addressing the engineering test data.

19 So I just leave that, and then we'll come back to  
20 it when we look at conditions.

21 Six (a), draft labeling has been submitted by the  
22 sponsor and reviewed by the FDA. Please discuss the draft labeling

1 as presented.

2 Labeling is in -- everybody familiar where it's  
3 located? It's located in the back of -- the industry rep. and  
4 the patient rep. do not have this, but it's in -- for the panel  
5 members, it's located in the panel packet, one of the orange tabs.

6 It's tab number three.

7 For industry rep. and patient rep., tab two.

8 The labeling from the sponsor describes a  
9 description of indications, contraindications, warnings,  
10 precautions, adverse events, clinical studies, how it's supplied,  
11 sterility, and it has a second section that describes patient  
12 information

13 So let's look at the first section, which is the  
14 actual prescribing information. I'd like to hear from the panel  
15 members.

16 DR. BURTON: Dr. Burton.

17 I have a question for Dr. Runner. You know, it made  
18 the comment in the question that these have been reviewed I would  
19 assume by your staff. You don't state much of an opinion, but  
20 the indications, like I said, are listed out being reasonably  
21 specific.

22 From a labeling standard perspective, would it be

1 better to perhaps maybe reduce the number and broaden them,  
2 including those particular areas, but I mean do we need to be or  
3 should we be this specific?

4 DR. RUNNER: This is Susan Runner.

5 I believe that the sponsor has developed the  
6 indications that it wishes to market the device as, and if you  
7 feel that there should be some changes, you should recommend it.

8 But these are the indications that they started the study with,  
9 and these are the indications that they've presented to us to  
10 evaluate.

11 CHAIRMAN HEFFEZ: Dr. Bertrand.

12 DR. BERTRAND: Peter Bertrand.

13 I thought earlier we addressed that. We had data  
14 for some of the indications, and we were going to make the  
15 recommendation that for labeling that we don't have enough data  
16 on some of these other indications as part of the labeling process.

17 Did I misunderstand that?

18 CHAIRMAN HEFFEZ: That is correct.

19 DR. BERTRAND: So I think that applies to what we're  
20 looking at in 6(a) as far as indications.

21 DR. BURTON: Richard Burton.

22 Would we then, Dr. Heffez, would we then take that



1 existing list of 11 indications, look at the existing patients  
2 that meet those indications, and for those say that it is approved  
3 for those indications, and then for the ones for which there's  
4 insufficient data to show correlation, then sort of make them a  
5 subset?

6 I'm not sure. How would that be worded?

7 CHAIRMAN HEFFFEZ: Dr. Runner.

8 DR. RUNNER: I think at this point in time the panel  
9 could defer that to FDA for a more complete review after the panel  
10 meeting, if you so choose. I think it would be laborious to go  
11 over specific numbers at this point in time.

12 I do think that for this question though there was  
13 some discussion earlier about potential labeling for treating the  
14 patient for potential bruxes and more tooth contact, and that might  
15 be an addition that you might want to further discuss.

16 As I recall, Dr. Bertrand had mentioned that issue.

17 DR. BURTON: Dr. Burton.

18 I would agree with that, Dr. Bertrand, but in the  
19 contraindications, actually the last one, number nine, states that  
20 it is contraindicated in patients with severe hyperfunctional  
21 habits, e.g., clinching, grinding, et cetera.

22 So I'm not sure how we address it because they have

1 sort of already said that you really -- you know, their  
2 contraindications say that you really shouldn't put them in those  
3 patients to begin with.

4 CHAIRMAN HEFFEZ: Dr. Runner.

5 DR. RUNNER: However, we've heard from Dr. Quinn  
6 that their patients had between 18 and 24 hours a day tooth contact.

7 So that to me indicates some degree of bruxism.

8 DR. BURTON: Actually I think that regarding this  
9 item it should probably be moved up into the warnings as opposed  
10 to being in the paragraph. It should be listed numerically.

11 How do the panel members feel about that?

12 You have listed warnings, but I think one warning  
13 would be that emplacement of this device in patients with severe  
14 hyperfunctional habit, an undesirable outcome may occur, and I  
15 think that would be item number 617 in the one.

16 DR. RUNNER: I think there's some very specific  
17 literature about what's a warning, what's a contraindication, and  
18 we can --

19 CHAIRMAN HEFFEZ: Look at that.

20 DR. RUNNER: -- work at that.

21 CHAIRMAN HEFFEZ: Okay, but at least leaving this,  
22 we can suggest that we should look at where it's localized in the

1 document.

2 DR. RUNNER: Right.

3 CHAIRMAN HEFFEZ: The hyperfunctional habits.

4 DR. RUNNER: Right.

5 CHAIRMAN HEFFEZ: Yes?

6 DR. ANSETH: Kristi Anseth.

7 Also on the precautions, the number nine that talks  
8 about use of the system with filler material, and I thought that  
9 we had discussed this being a cementless system.

10 CHAIRMAN HEFFEZ: Correct. So that's something we  
11 should look at removing. Thank you.

12 I'd like to move to the second part of that, which  
13 would be the patient information, if we could look at that.

14 In the patient information, I notice the term glenoid  
15 fossa in one place and then fossa in another place. When it says  
16 what is a Walter Lorenz TMJ implant? It says, number two, fossa  
17 implant, and then when you go to what are the possible  
18 complications, it talks about glenoid fossa.

19 I think probably the patient might feel better with  
20 a diagram, for example, indicating what is the glenoid fossa and  
21 let them know it is a glenoid fossa. They may think it's two  
22 different terms.

1                   Also, if you look at contraindications, you list  
2 active infection, but in the material for the physician, it says  
3 active or chronic infection, which is what are the  
4 contraindications for Walter Lorenz, patients with active  
5 infection, but contraindication for the physician is active or  
6 chronic infection. Just to be consistent.

7                   I'll ask the company to consider maybe active foreign  
8 body reaction. I don't see that really listed there, but it is  
9 a concern with people with current prostheses undergoing foreign  
10 body reaction, that that should be treated before implanting a  
11 new device.

12                   So I'm suggesting active infection, chronic  
13 infection, or foreign body, active foreign body reaction. I made  
14 those suggestions, but I'd like to hear from the panel how they  
15 feel.

16                   Dr. Cochran.

17                   DR. COCHRAN: It looks like the foreign body issue  
18 is addressed in number four and the possible complications under  
19 I believe that's the patient, under the patient information. It's  
20 not exactly what you said, but it at least addresses it.

21                   CHAIRMAN HEFFFEZ: That refers to the foreign body  
22 reaction to the material that they implanted.

1 DR. COCHRAN: Right.

2 CHAIRMAN HEFFFEZ: But I'm referring to foreign body  
3 material on another implant that they're removing to put in.

4 Anybody else have any comments?

5 (No response.)

6 CHAIRMAN HEFFFEZ: Okay. The foreign body reaction  
7 I think should be placed also in the physician information.

8 All right. We'll move on then to 6(b). Please  
9 discuss the need for training and the type of training protocol  
10 that may be necessary for safe and effective use of this device.

11 If I could just summarize what's been said up to  
12 now, that the principles involved feel that training at one or  
13 two sites and expanding those sites as people are properly trained  
14 is necessary.

15 I think that they have an audiovisual tape that has  
16 not been furnished to the FDA, and that they will have a protocol  
17 through probably continuing education programs that they will  
18 offer.

19 I'd like to hear from the panel how they feel in  
20 general regarding this. Also, perhaps we should think about is  
21 it possible, that it is very easy to do this early on in the course  
22 of a product. Sometimes as the product gets distributed it becomes

1 more and more difficult from the company's point of view, from  
2 a financial point of view from the company, financial view from  
3 the physician to do.

4 One minute. I see your hand.

5 I think that I'd like you to, panel and perhaps the  
6 sponsor, to consider that.

7 The other issue regarding training is a registry.

8 Is the company -- will the company maintain a registry of all  
9 the devices that are implanted?

10 Dr. Runner.

11 DR. RUNNER: Susan Runner.

12 TMJ devices are tracked devices, and it's required  
13 to be tracked by the company.

14 CHAIRMAN HEFFEZ: Dr. Rekow.

15 DR. REKOW: I think that I -- this is Diane Rekow  
16 -- I think that I heard that you were not going to make product  
17 available unless the clinician had been trained. Did I hear that  
18 properly?

19 Dr. Quinn is saying yes, and so I would like to make  
20 sure that that is explicitly included someplace because I really  
21 think that the points that we've made a number of times already  
22 today suggest the overwhelming need for careful, thoughtful

1 training and some hands-on experience probably before it just  
2 becomes available.

3 So that kind of requirement, I think, is an important  
4 one to include.

5 CHAIRMAN HEFFEZ: I think you have to take it one  
6 step further because with time everything gets diluted.

7 What is adequate training, you know? And are there  
8 only going to be approved sites, or can you go to someone who has  
9 already placed several and be trained by that individual even though  
10 it's not an approved site?

11 I think those things end up getting all muddled.

12 Dr. Runner.

13 DR. RUNNER: This is Susan Runner.

14 I think that if the training requirements are  
15 specific enough in the approval, I suppose approval order, any  
16 changes in that would have to come through a PMA supplement. So  
17 they would be required to maintain the training that's approved  
18 initially.

19 CHAIRMAN HEFFEZ: So the company should be careful  
20 in stipulating what should be the adequate training for this device.

21 DR. RUNNER: That's correct.

22 DR. BERTRAND: Question.

1 CHAIRMAN HEFFEZ: Dr. Bertrand.

2 DR. BERTRAND: Peter Bertrand.

3 Based on the data we have right now, it almost seems  
4 like the labeling should say that there's only two places to be  
5 trained, the two major members of the study.

6 CHAIRMAN HEFFEZ: I think from a practical point  
7 of view you can't have the company coming here every time they  
8 want to add a site. So I think that they have to entertain how  
9 the training would be done so that it satisfies the panel, but  
10 at the same time doesn't box them into a corner.

11 Can I hear from maybe the President of Walter Lorenz?  
12 Mr. Pratt.

13 MR. PRATT: Joel Pratt.

14 This is really an important issue to us in that we  
15 want to certify surgeons before they're trained and train them  
16 and limit the distribution to doctors that are trained with this  
17 product.

18 However, in the long term, you know, if we look at  
19 three and four and five years down the road, Dr. Heffez makes a  
20 very good point of continuing the rigid training program three  
21 and five, as you said, may get diluted over the years and will  
22 depend on the ongoing results of the product.



1 I mean, I would envision that if we continued to  
2 train doctors and add doctors using the device and the clinical  
3 results are very good, we will continue to do that level of training.

4 It's important for us to have obviously a very successful product  
5 clinically.

6 At the same time, and I guess I shouldn't address  
7 market issues, but -- well, I won't go there.

8 CHAIRMAN HEFFEZ: Actually, I think it's important  
9 if you could address them.

10 MR. PRATT: Well, there are two other companies that  
11 sell TMJ devices, and I don't know if they're regulated in how  
12 they train doctors.

13 CHAIRMAN HEFFEZ: Dr. Runner.

14 DR. RUNNER: I don't recall the specific label of  
15 either of the two devices. However, if you were going to require  
16 training for this device as one of the conditions of approval,  
17 again, if you're going to change that in any substantive way, you're  
18 going to have to come in with a supplement, which is not impossible,  
19 but you're going to have to justify why it should be changed.

20 CHAIRMAN HEFFEZ: Yes.

21 DR. FAULK-EGGLESTON: Yes, this is Dr. Faulk.

22 Yes, you need a lot of training, and I'm not

1 disagreeing with that, but if you make it so difficult that no  
2 one can get to the training, you've limited the product but you've  
3 also limited how you can help the patient.

4           So if somebody has okayed another device and you  
5 make it impossible for the individuals to get training, that's  
6 not fair to the patient either. So there has to be a medium between  
7 training and between availability.

8           CHAIRMAN HEFFEZ: Dr. Burton.

9           DR. BURTON: Richard Burton.

10           I would agree with Dr. Faulk on that. My question,  
11 although I've listened to this and I think probably harkening back  
12 to the days of dental implants when you couldn't buy them if you  
13 weren't blessed by the company and how that evolved, and I'm sure  
14 that that's sort of what Dr. Heffez is, is that over time as there  
15 is greater and broader understanding and use those things became  
16 diluted down.

17           And I think I certainly would agree with the sponsor  
18 in the fact that you have to avoid that because my memory -- and  
19 it's probably certainly no better than Dr. Runner's -- I'm not  
20 sure in the past that we ever recommended that or that there was  
21 ever any training contingency with that.

22           But I guess that, you know, your company and Dr.

1 Quinn and Dr. Sinn at least made comments on the fact that it was  
2 necessary or they felt it was necessary to have that. So you know,  
3 we need to reach some kind of an agreement here on what's an  
4 acceptable initial limitation that will be broad enough that will  
5 allow that to grow within the framework as we approve it at this  
6 point in time.

7 CHAIRMAN HEFFFEZ: I think it's important, that we  
8 don't need to come to an agreement. We, the panel members, have  
9 to feel comfortable whether the device can be utilized or what  
10 level of training should be instituted to feel comfortable with  
11 this device being marketed. I think that's the question.

12 MS. HELMS: Elizabeth Helms.

13 Yes, I agree. I mean, the quality of the training  
14 is essential because if the quality isn't there, the patient is  
15 going to be put at risk again by somebody else, and we've seen  
16 this far too often happen to patients that have had or didn't get  
17 the quality of care because the education of the provider wasn't  
18 to the highest level or that they were rushed.

19 So the quality is very important. At the same time,  
20 how the patients access it. My question would be, you know, if  
21 there's only two sites that are training sites and a provider wants  
22 to come into the training site, does his patient come with him

1 there? And at whose cost is that going to be?

2 CHAIRMAN HEFFEZ: Dr. Runner.

3 DR. RUNNER: I think that we're getting a little  
4 tied up in specifics of this training program. I think that the  
5 panel should recommend the level of training that you feel  
6 necessary, and the agency can negotiate with the company about  
7 the specifics of the training program.

8 CHAIRMAN HEFFEZ: So if I could summarize discussions  
9 that occurred previously -- thank you, Mr. Pratt.

10 MR. PRATT: May I make one more point? And that  
11 is that we do intend to expand the number of sites for training.  
12 Because of the burden that it would pose on Dr. Quinn and Dr.  
13 Sinn, we would like to have geographically around the United States  
14 and around the world centers where doctors can go and be trained  
15 prior.

16 So that would maybe address Dr. Faulk's question  
17 about access.

18 CHAIRMAN HEFFEZ: Thank you.

19 So if we could just summarize the comments made now  
20 and previously, I feel that I'm correct in saying that some training  
21 regarding this device is important, and that level of training,  
22 the specifics of it will be worked out between the FDA at another

1 time; is that correct?

2 DR. RUNNER: If that's what the panel feels  
3 comfortable with, unless they want to make more specific  
4 recommendations about the level of training.

5 CHAIRMAN HEFFEZ: I think we all -- and I'd like  
6 to have everybody say if they concur with me -- but they all feel  
7 that some level of training is required in order to put this device  
8 in.

9 There was multiple nodding for the tape recorder.

10 Yes.

11 MS. HELMS: Elizabeth Helms.

12 I'd like to say a high level of training.

13 CHAIRMAN HEFFEZ: Okay. With qualitative terms,  
14 it's extremely difficult to know what that means, but I think  
15 restated that we all feel that they require training regarding  
16 the actual surgical instrumentation and surgical technique.

17 DR. BERTRAND: Just one last comment. Peter  
18 Bertrand.

19 Dr. Dolwick, who is going to be the next person that  
20 you're going to train, thereafter with the degree of training of  
21 one or two surgeries, he then becomes eligible to train others,  
22 right?

1                   Okay, and so is that the way it's going to be? Can  
2 we make that decision kind of right now? You have to be trained  
3 by someone already trained and that's the way it would expand in  
4 order to get centers at other areas?

5                   CHAIRMAN HEFFFEZ: I think those particulars we can  
6 let go for here and have the FDA detail with.

7                   Ms. Scott was kind enough to tell me that if the  
8 panel feels that certain specific recommendations, such as you  
9 have made --

10                  DR. BERTRAND: Well, I think that's a decision I  
11 was kind of asking the panel to say.

12                  DR. RUNNER: Okay. We will take that under  
13 advisement.

14                  CHAIRMAN HEFFFEZ: So one recommendation would be  
15 that whatever test site the person doing the training should have  
16 at least been trained at least at one of these two sites or have  
17 had training on its own.

18                  Yes, Dr. Li.

19                  DR. LI: Steve Li.

20                  Can I ask Dr. Quinn or Dr. Sinn? Are the  
21 biomechanical consequences part of your training? Like the  
22 biomechanical consequences of malalignment or off position or

1 having the joint too tight or too loose, is that part of the  
2 training, just out of curiosity?

3 DR. QUINN: Peter Quinn.

4 Maybe I could suggest some language that might be  
5 helpful, that we intend to do both hands on and didactic training.

6 It should not be site specific though because I've gone elsewhere.

7 It's more difficult with medical legal implications these days,  
8 but I've gone elsewhere. So I wouldn't want to limit it to sites.

9 But I do think if we use the term both "hands on"  
10 and "didactic" it would cover the high level that I think Ms. Helms  
11 is trying to get to.

12 To Dr. Li's question, yes, we intend to have a lab  
13 session where we can set up the prosthesis and best case/worst  
14 case scenario and discuss the biomechanical implications of the  
15 fit of the prosthesis.

16 CHAIRMAN HEFFEZ: Okay. Thank you.

17 I'd like to move on to 6(c). The sponsor intends  
18 to complete the pivotal PMA study following all patients for three  
19 years. Please discuss the need for any additional post market  
20 studies and issues that should be addressed were those studies  
21 to be required -- where those studies are to be required.

22 I'd like to hear from the panel. Any post market

1 studies that should be continued or should be instituted?

2 Dr. Li.

3 DR. LI: I'm agreeing that there might not be an  
4 appropriate in vitro test for wear, but I think as long as you  
5 have a metal on polyethylene, highly loaded joint, I don't think  
6 you could dismiss the possibility of osteolysis at a five-year  
7 or a six-year period.

8 So I'm not quite sure how we get our hands around  
9 following that up to make sure we just don't --

10 CHAIRMAN HEFFEZ: Well, we can --

11 DR. LI: I'm sorry.

12 CHAIRMAN HEFFEZ: Can't we request the company, I  
13 believe, Dr. Runner, to continue further than three years, to  
14 provide data up to five years? Is that correct or not?

15 DR. RUNNER: That is correct.

16 DR. LI: Also, while I have the microphone for a  
17 second, could I ask the sponsors who provide the example pieces,  
18 were those pieces tested or what was the source of those devices?

19 Can anybody tell me?

20 DR. RUNNER: Those devices were provided to F --  
21 this is Susan Runner -- those devices were provided to FDA as  
22 examples of the devices.



1 DR. LI: Right, but were they tested before they  
2 got to you?

3 DR. RUNNER: I don't know.

4 DR. LI: Were these as new devices?

5 DR. RUNNER: I don't know the status of those devices.

6 MR. ROMAN: Shawn Roman.

7 To be honest with you, I'm not sure what the status  
8 of those devices were either.

9 DR. LI: Okay. The only reason I'm asking is the  
10 articular surfaces show signs of wear very much like a retrieved  
11 knee component.

12 MR. ROMAN: Okay.

13 DR. LI: And it's difficult to manufacture those  
14 surfaces with those particular features. So wherever those came  
15 from, they appear as if they were worn.

16 So whatever you did to get them, you did some sort  
17 of wear, and wear is occurring. So that's the only reason I ask.  
18 I'm sorry to get off the track.

19 CHAIRMAN HEFFEZ: I'd like to ask a corollary  
20 question. If the company has followed up to now 40 -- sorry.  
21 The number has escaped me -- 40-odd cases for three years; is that  
22 correct?

1 DR. RUNNER: Forty-five.

2 CHAIRMAN HEFFEZ: Forty-four. If that's all that  
3 would ever be followed up because of lack of follow-up, would that  
4 be adequate to the panel? Does the panel feel that would be adequate  
5 without any additional post market studies?

6 So just those cases because the statement is "follow  
7 all patients for three years." Assume no other patients get into  
8 that category. Would this information be adequate, that you would  
9 feel comfortable, that no additional post market studies would  
10 be issued or there were no outlying issues?

11 Dr. Runner.

12 DR. RUNNER: You're talking about the 180.

13 CHAIRMAN HEFFEZ: Yeah.

14 DR. RUNNER: All 180 would be followed to three years.

15 CHAIRMAN HEFFEZ: Right, but they didn't have any  
16 data to provide even for those 180.

17 Dr. Quinn.

18 DR. QUINN: A comment. Peter Quinn.

19 I believe pivotal PMA means the original 86.

20 DR. RUNNER: Well, we increased your study to  
21 300-some odd entrances. If you have 180 patients enrolled at this  
22 time, we would expect them all to be followed through three years.

1 DR. QUINN: We expect to do that. I'm just  
2 questioning what "pivotal PMA" means.

3 DR. RUNNER: I meant the application as it stands  
4 now.

5 DR. QUINN: Okay, and at the risk of getting my  
6 statistical ears boxed by Dr. Janosky, we should realize that we  
7 closed the study March 31st. So there is further three-year  
8 follow-up already that's ongoing that can be provided because it  
9 is continuing.

10 CHAIRMAN HEFFFEZ: So I'm not hearing anything from  
11 the panel. Dr. Rekow.

12 DR. REKOW: I'm comfortable if we ultimately could  
13 see the information that you're in the process of accumulating,  
14 but I wrestle with this whole wear issue, and I agree with Dr.  
15 Li that it needs to be done, and the paradox that I have is how  
16 to do it in a realistic and cost effective way.

17 And I'm really having a lot of trouble with that  
18 because that has been such a tremendous burden to the patients  
19 in terms of those systems that don't fail, and I personally suspect  
20 that your stuff is pretty good from what we've seen, but there's  
21 no data to assure that, and that's the real troublesome part.

22 And that's where I agree with Steve, and I don't

1 know that I can give you some really terrific guidance in terms  
2 of that, but it is an issue that I think needs to be addressed  
3 somehow.

4 CHAIRMAN HEFFEZ: Dr. Bertrand.

5 DR. BERTRAND: Peter Bertrand.

6 Looking at your data, you have collected data on  
7 six years in some patients and five years and four years. Is that  
8 just something you're continuing to do naturally? Is it an  
9 intention to continue to do it regardless?

10 PARTICIPANT: Yes.

11 DR. BERTRAND: So you have beyond the confines of  
12 the study an intention to look beyond three years. That's great.

13 DR. FAULK-EGGLESTON: This is Dr. Faulk.

14 So what you're saying is it's no added burden or  
15 anything else to say that we would like to see the data through  
16 five years.

17 (Laughter.)

18 CHAIRMAN HEFFEZ: Dr. Quinn.

19 DR. QUINN: Peter Quinn. I'm sorry.

20 It's a tremendous burden, and I don't want to bring  
21 economics into this in a large part, but there is. This is a burden  
22 because this is all uncompensated care. If you understand how

1 insurance companies work, visits after 90 days are within the global  
2 period unless the gatekeeper or primary physician sees a reason  
3 why you have to go visit your doctor.

4 None of these are approved or reimbursed. So it  
5 is a burden that we have to take into consideration. It shouldn't  
6 drive this. We will continue to collect data.

7 I agree with collecting data on the original patient  
8 group. Whether we collect it at the same landmarks, I would continue  
9 to at least try to get yearly data after that, but it is a large  
10 burden.

11 CHAIRMAN HEFFEZ: Dr. Runner.

12 DR. RUNNER: In regards to the wear issue, I do  
13 believe in some of our previous implant applications where this  
14 same issue has been raised, there was a condition of approval that  
15 indicated that retrieved implants should be further evaluated for  
16 wear, and that was one of the ways that we addressed that problem.

17 So that could potentially be a condition that could be placed  
18 on this application.

19 CHAIRMAN HEFFEZ: From a practical point of view,  
20 Dr. Runner, who does that testing? Is it the company?

21 DR. RUNNER: The company does that testing.

22 CHAIRMAN HEFFEZ: Okay. I would like to close this

1 session and open up the public hearing. I'd like to ask if there's  
2 anybody from the audience who would like to comment.

3 This public hearing is being held before the panel  
4 actually has a discussion and votes.

5 Would you please identify yourself?

6 MS. COWLEY: I'm Terry Cowley.

7 The discussion of long-term follow-up I think is  
8 critical to the TMJ patient population, and our contention is that  
9 not only should you be following patients long after explanation  
10 because we've learned that the repercussions of implants seem to  
11 manifest throughout the life of the patient.

12 I understand the financial burden on the  
13 manufacturer, but it's an even greater financial and fiscal burden  
14 on the patient when the device fails.

15 Something which might be taken into consideration  
16 is that the NIH is going to hopefully fund through a contract an  
17 implant patient registry, and perhaps this is not the place to  
18 talk about it, but it would be one of the vehicles by which  
19 manufacturers would have the capability of having their devices  
20 assessed, the patient assured their device would be analyzed and  
21 their condition monitored.

22 So so much.

1 CHAIRMAN HEFFEZ: Thank you. Any other comments?

2 (No response.)

3 CHAIRMAN HEFFEZ: Okay. I'd like then to move to  
4 the next session, which would be open committee discussion and  
5 voting.

6 I'd like to proceed in this section in the following  
7 manner. There are three ways that we can vote for this PMA:  
8 approval, approval with conditions, and not approval.

9 I'm going to, based on the discussions that have  
10 been held, I would like to go around the table and see how people  
11 feel regarding these options. Based on the discussion, it looks  
12 like there would be approval with conditions. That's based on  
13 the discussion.

14 If I'm incorrect, please let me know, but I'd like  
15 to hear from each panel member how they feel.

16 To assist us in understanding what each definition  
17 means, Ms. Scott will assist us.

18 MS. SCOTT: If the panel will look in their packets,  
19 there is a document entitled "Panel Recommendation Options for  
20 Pre-market Approval Applications."

21 And I will read the options for the vote, and the  
22 definitions outlined in this document.

1                   The medical devices amendment to the Food and Drug  
2 and Cosmetic Act required that the Food and Drug Administration  
3 obtain a recommendation from an outside expert advisory panel on  
4 designated metal device PMAs that are filed with the agency. The  
5 PMA must stand on its own merit as we have stated before, and your  
6 recommendation must be supported by safety and effectiveness data  
7 in the application or by applicable publicly available information.

8                   Safety is defined in the act as reasonable assurance  
9 based on valid scientific evidence that the probable benefits to  
10 health under the conditions of use outweigh any probable risk.

11                   Effectiveness is defined as reasonable assurance  
12 that in a significant portion of the population, the use of the  
13 device for its intended uses and conditions of use will provide  
14 clinically significant results.

15                   Your recommendation options for the vote as stated  
16 previously are as follows:

17                   Approvable. Definition for approvable, there are  
18 no conditions attached.

19                   The following agency action would be if the agency  
20 agrees with the panel recommendation, an approval letter will be  
21 sent to the applicant.

22                   Your second option: approvable with conditions.



1 You may recommend that the PMA be found approvable subject to  
2 specific conditions, such as resolution of clearly identified  
3 deficiencies which have been cited by you or by FDA staff.

4 Prior to voting, all of the conditions are discussed  
5 by the panel and listed by the panel chair. You may specify what  
6 type of follow-up to the applicant's response to the conditions  
7 of your approval recommendation you want. For example, FDA  
8 follow-up or panel follow-up?

9 Panel follow-up is usually done through homework  
10 assignments to the primary reviewers of the application or to other  
11 specified members of the panel.

12 A formal decision of the application at a future  
13 panel meeting is not usually held.

14 If you recommend post approval requirements to be  
15 imposed as a condition of approval, then your recommendation should  
16 address the following points: the purpose of the requirement,  
17 the number of subjects to be evaluated, and the reports that should  
18 be required to be submitted.

19 Agency action following this type of option. If  
20 FDA agrees with the panel recommendation and approvable with  
21 conditions letter will be sent.

22 Your next option, not approvable. Of the five

1 reasons that the act specifies for denial of approval, the following  
2 three reasons are applicable to panel deliberation.

3 (a) The data do not provide reasonable assurance  
4 that the device is safe under the conditions of use prescribed,  
5 recommended or suggested in the proposed labeling.

6 (b) Reasonable assurance has not been given that  
7 the device is effective under the conditions of use described,  
8 recommended or suggested in the labeling.

9 (c) Based on fair evaluation of all the material  
10 facts and your discussions you believe the proposed labeling to  
11 be false or misleading.

12 If you recommend that the application is not  
13 approvable for any of these stated reasons, then we ask that you  
14 identify the measures that you think are necessary for the  
15 application to be placed in an approvable form.

16 The agency action following this type of  
17 recommendation is as follows. If FDA agrees with the panel's not  
18 approvable recommendation, the agency will send a not approvable  
19 letter. This is not a final agency action on the PMA.

20 The applicant has the opportunity to amend the PMA  
21 to supply the requested information. The amended application will  
22 be reviewed by the panel at a future meeting unless the panel

1 requests otherwise.

2           Lastly, tabling. In rare circumstances the panel  
3 may decide to table an application. Tabling an application does  
4 not give specific guidance from the panel to FDA or the applicant,  
5 thereby creating ambiguity and delay in the progress of the  
6 application. Therefore, we discourage tabling of an application.

7           The panel should consider a not approvable or  
8 approvable with conditions recommendation that gives clearly  
9 described corrective steps.

10           If the panel does vote to table a PMA, the panel  
11 will be asked to describe which information is missing and what  
12 prevents an alternative recommendation.

13           CHAIRMAN HEFFEZ: All right. So I'd like to hear  
14 from the panel how they feel. I summarized the discussions looking  
15 that we had some items that we needed to say and, therefore,  
16 approvable with conditions.

17           Am I correct in making that statement? So I see  
18 some nodding, and to make it easier, I will ask for a motion from  
19 the panel members that it be approved as approvable with conditions.

20           DR. HEWLETT: So moved.

21           CHAIRMAN HEFFEZ: Dr. Hewlett.

22           DR. HEWLETT: Dr. Hewlett.

1 So moved.

2 CHAIRMAN HEFFEZ: Second?

3 DR. SUZUKI: Second.

4 CHAIRMAN HEFFEZ: Seconded by Dr. Suzuki.

5 Okay. So in the future, whoever makes the motion,  
6 state your name first and whoever seconds it, state your name first.

7 Now, is there any further discussion on it?

8 (No response.)

9 CHAIRMAN HEFFEZ: Prior to the vote I will ask the  
10 opportunity for the FDA to make any comments before the vote.  
11 I will ask the sponsor if they have anything they want to say before  
12 the vote.

13 DR. PATTERS: Don't the conditions have to be decided  
14 before the vote?

15 CHAIRMAN HEFFEZ: Yes, that's true. I apologize.

16 Well, going around the table we all agree with  
17 conditions. Now we'll just go with each condition.

18 One condition, we'll try to -- so I will look for  
19 different conditions, but to keep it organized I'm going to suggest  
20 certain conditions, and if I leave any out, please let me know.

21 One of the conditions was regarding labeling. We  
22 felt that the labeling should be altered to reflect foreign body

1 reaction as a warning in both patient and physician information.

2 We mentioned severe hypermobility habits should be  
3 looked at as far as where its location is in the document and  
4 outlining it.

5 And we looked at the indications whereby we felt  
6 that some indications -- that there should be some statement saying  
7 that certain conditions had been well tested, but others adequate  
8 documentation is still acquired.

9 So I will ask you on this labeling issue for a motion.

10 If I've left something out, please feel free to say, but I'd  
11 entertain a motion from the panel regarding the labeling condition.

12 Please, Dr. Bertrand.

13 DR. BERTRAND: Peter Bertrand.

14 Was part of our labeling part of the clinician  
15 education also?

16 CHAIRMAN HEFFEZ: No. That's a separate issue.

17 DR. COCHRAN: David Cochran.

18 I'll make that as a motion.

19 CHAIRMAN HEFFEZ: So could you state the motion?

20 DR. COCHRAN: No way.

21 (Laughter.)

22 DR. COCHRAN: As you read them.

1                   CHAIRMAN HEFFFEZ: Okay. So I will restate the motion.  
2           The motion is that the labeling should be modified to reflect  
3           foreign body reaction in a warning in both physician and patient  
4           information; that the hypermobile patient or the hypermobile  
5           condition should be more clearly described and located  
6           appropriately in the document; and that the indications should  
7           reflect which of those indications have been adequately studied  
8           and in which indications require additional information

9                   DR. REKOW: This is Diane Rekow.

10                   And I'll second it, but I want to strike the  
11           discussion if I may.

12                   CHAIRMAN HEFFFEZ: Well, hold on just a second. I  
13           want to make sure that that motion is -- Dr. Cochran, if you agree  
14           with that motion.

15                   DR. COCHRAN: Actually, all but the last part when  
16           you said about the indications requiring more data. I don't think  
17           we want to say requiring more data. I think we just say has not  
18           been evaluated.

19                   CHAIRMAN HEFFFEZ: Okay. So just to repeat the  
20           indication section, that the prosthesis has demonstrated efficacy  
21           in certain of these indications, but that it has not been  
22           demonstrated in the others. Fine.

1 So do you agree with that motion?

2 DR. COCHRAN: Yes.

3 CHAIRMAN HEFFEZ: Dr. Rekow, do you second that  
4 motion?

5 DR. REKOW: Absolutely. Second it.

6 CHAIRMAN HEFFEZ: Okay. Now, discussion. Dr. Rekow.

7 DR. REKOW: My discussion is taken care of. Thank  
8 you.

9 CHAIRMAN HEFFEZ: Dr. Bertrand.

10 DR. BERTRAND: Peter Bertrand.

11 By hypermobility, do you mean excess in function?

12 CHAIRMAN HEFFEZ: Yes. We can qualify the motion.

13 Are you --

14 DR. BERTRAND: I would rather be more specific as  
15 to nonfunctional contacts in voting versus hypermobility.

16 CHAIRMAN HEFFEZ: So we're going to dismiss the  
17 motion. We're going to maintain a new motion. The new motion  
18 is that labeling should address foreign body reaction in the  
19 physician and patient information; that indications should  
20 indicate that -- that a phrase should be written to indicate that  
21 certain conditions have been -- that the efficacy and safety of  
22 the prosthesis have been demonstrated in certain conditions but

1 not in others; and hypermobile conditions reflects hyperfunctional  
2 habits, including hyperfunctional habits such as bruxes and  
3 clinching, should be addressed in a different location in the  
4 document.

5 Do you accept that motion?

6 DR. COCHRAN: Yes.

7 CHAIRMAN HEFFEZ: Dr. Rekow?

8 DR. REKOW: Yes.

9 DR. JANOSKY: Dr. Rekow seconds it.

10 Any further discussion?

11 (No response.)

12 CHAIRMAN HEFFEZ: The FDA, any comments?

13 (No response.)

14 CHAIRMAN HEFFEZ: And the sponsor, any comments?

15 (No response.)

16 CHAIRMAN HEFFEZ: So now we're ready for the vote.

17 I'd like to go around the table, always starting from the same  
18 spot.

19 We are only voting on that particular condition.  
20 We're going to go through condition by condition, and then we're  
21 going to vote the whole thing after each condition. Okay? It  
22 will make it a lot easier.



1                   So with this condition I'd like to go around the  
2 table. Industry rep. and patient rep. do not vote, and consumer  
3 rep. as well.

4                   So Dr. Suzuki is the first one.

5                   DR. SUZUKI: Jon Suzuki, yes.

6                   DR. JANOSKY: Janine Janosky, yes.

7                   DR. HEWLETT: Ed Hewlett, yes.

8                   DR. BERTRAND: Peter Bertrand, yes.

9                   DR. FAULK-EGGLESTON: Jane Faulk, yes.

10                  DR. BURTON: Richard Burton, yes.

11                  DR. REKOW: Diane Rekow, yes.

12                  DR. PATTERS: Mark Patters, yes.

13                  DR. ANSETH: Kristi Anseth, yes.

14                  DR. COCHRAN: David Cochran, yes.

15                  DR. LI: Steve Li, yes.

16                  CHAIRMAN HEFFEZ: Okay. Thank you.

17                  So now we're going to go to condition number two.

18                  Again, just for simplicity's sake, I'm going to throw out a  
19 condition.

20                  We discussed that physician education was of  
21 paramount importance. So I'm going to make a suggested motion  
22 and then we'll see how the panel feels. Okay?

1 I'm going to make the motion that one condition would  
2 be that all physicians placing these devices should be adequately  
3 trained according to -- no, that all physicians placing these  
4 devices should receive adequate surgical training prior to  
5 utilizing or implanting these devices.

6 DR. FAULK-EGGLESTON: This is Dr. Faulk.

7 Can you make that physicians and dentists.

8 CHAIRMAN HEFFFEZ: Sure, although I understand the  
9 term "physician" at least refers to dentists.

10 DR. FAULK-EGGLESTON: Don't worry about it then.  
11 It's okay.

12 CHAIRMAN HEFFFEZ: So I need someone to make a motion  
13 or they can obviously discuss the motion.

14 DR. COCHRAN: Could we have "didactic and hands-on  
15 training"?

16 CHAIRMAN HEFFFEZ: Certainly. So the motion now reads  
17 that all surgeons who would be implanting these devices should  
18 receive adequate didactic and surgical or hands-on training for  
19 implanting the device.

20 DR. SUZUKI: This is Jon Suzuki.

21 I so move.

22 DR. BURTON: Richard Burton.

1 Second.

2 CHAIRMAN HEFFEZ: So I need any discussion. Dr.  
3 Patters?

4 DR. PATTERS: Yes. I'm Mark Patters.

5 Did you say "should" or "are required to"?

6 CHAIRMAN HEFFEZ: Are required. So let's repeat  
7 the motion. That all surgeons utilizing these devices are required  
8 to be trained didactically and hands on prior to utilizing the  
9 devices.

10 That's the motion. Dr. Suzuki?

11 DR. SUZUKI: Jon Suzuki, yes.

12 CHAIRMAN HEFFEZ: Dr. Burton, do you second?

13 DR. BURTON: Second. Richard Burton.

14 CHAIRMAN HEFFEZ: Any further discussion? Any  
15 further discussion?

16 (No response.)

17 CHAIRMAN HEFFEZ: I'd like to ask the FDA if they  
18 have anything to say regarding this motion?

19 DR. RUNNER: No.

20 CHAIRMAN HEFFEZ: No? And sponsor?

21 DR. BERES: Ken Beres.

22 I'm not a regulatory attorney nor a panel expert,

1 but maybe I could ask FDA. Is it the purview of the panel or FDA  
2 to regulate certification, accreditation, in that area?

3 I'm wondering if we're biting off more than we need  
4 to at this point.

5 DR. RUNNER: I'm going to defer to Dr. Schultz, our  
6 office director, deputy, soon to be office director.

7 DR. SCHULTZ: I'm going to address the question of  
8 should or required is a difference and has a legal term to it.

9 CHAIRMAN HEFFEZ: Let me try to --

10 DR. SCHULTZ: I'm sorry. My name is Dan Schultz.  
11 I'm Deputy Director of the Office of Device Evaluation.

12 This is something that comes up quite a bit in terms  
13 of the difference between accreditation and a requirement for the  
14 company to provide adequate training, and you're absolutely right.

15 The issue of accreditation is something that the states and  
16 hospitals and other bodies are required to do, and that's their  
17 mandate. That's not our mandate.

18 But our mandate is to make sure that adequate  
19 training is provided when necessary for newly marketed medical  
20 devices. So I think that the wording needs to be somewhat to the  
21 effect which I think is pretty close to what I heard you say, and  
22 certainly we can modify it appropriately, but I think the idea

1 being that there needs to be a training program which includes  
2 both didactic and hands-on experience provided by the company for  
3 every user, every potential user of this device.

4 And I think we can work with the company to make  
5 sure that that is worded appropriately.

6 Does that answer your question?

7 Without talking about accreditation because I think  
8 that that's another issue.

9 CHAIRMAN HEFFEZ: So maybe let's redo the motion.  
10 Please, if you're going to address it, come to the podium.

11 DR. SCHULTZ: If I could answer that question, the  
12 training program will be required as a condition of approval.  
13 That's not "should." That is a requirement as a condition of  
14 approval that such training will be provided.

15 The issue of accreditation is another issue. So  
16 the training needs to be provided. As far as who does the  
17 accreditation, that's something that will be addressed elsewhere.

18 CHAIRMAN HEFFEZ: So I'd like to suggest another  
19 motion. The company must provide a hands-on and didactic training  
20 program for the surgeons who intend to use this device.

21 Dr. Suzuki, will you?

22 DR. SUZUKI: This is Jon Suzuki. I withdraw my first

1 motion and I make the second motion.

2 DR. BURTON: Richard Burton.

3 Second it.

4 CHAIRMAN HEFFEZ: Does the FDA have any other further  
5 comment?

6 (No response.)

7 CHAIRMAN HEFFEZ: And now the sponsor.

8 DR. QUINN: Dr. Quinn.

9 And I may have introduced the term and I apologize.

10 I prefer if the use the term "clinical and didactic." We may  
11 have some credentialing medical legal issues in terms of how we  
12 allow physicians to enter other hospitals and actually touch  
13 patients in this current.

14 So clinical and didactic would mean that they would  
15 observe surgeries, participate in them to the degree, but "hands  
16 on" may be too far based on the different jurisdictions that we'd  
17 have to do it, but I think "clinical and didactic" would cover  
18 it.

19 CHAIRMAN HEFFEZ: Well, hands-on training does  
20 include laboratory work.

21 DR. QUINN: If that's understood, I agree.

22 CHAIRMAN HEFFEZ: Yes. So it does include laboratory

1 work. It's not patient hands on necessarily.

2 Do you want me to qualify that in the motion?

3 DR. QUINN: I think that would be helpful unless  
4 it's just understood that hands on could include both observational  
5 and laboratory.

6 CHAIRMAN HEFFEZ: Dr. Runner.

7 DR. RUNNER: This is Dr. Runner.

8 I think that these are recommendations from the panel  
9 to FDA, and FDA will work out the specifics of how it will be worded  
10 in the approval order.

11 CHAIRMAN HEFFEZ: Thank you.

12 So we have no further discussion. Now if we can  
13 have a voting around the table starting with Dr. Suzuki.

14 DR. SUZUKI: Jon Suzuki, yes.

15 DR. JANOSKY: Janine Janosky, yes.

16 DR. HEWLETT: Edmond Hewlett, yes.

17 DR. BERTRAND: Peter Bertrand, yes.

18 DR. FAULK-EGGLESTON: Jane Faulk, yes.

19 DR. BURTON: Richard Burton, yes.

20 DR. REKOW: Diane Rekow, yes.

21 DR. PATTERS: Mark Patters, yes.

22 DR. ANSETH: Kristi Anseth, yes.

1 DR. COCHRAN: David Cochran, yes.

2 DR. LI: Steve Li, yes.

3 CHAIRMAN HEFFEZ: Okay. We're now going to move  
4 to another condition. From our discussions, I'm going to suggest  
5 the following condition: that additional post market in vitro  
6 study be done to study the wear characteristics, the creep in  
7 relationship to the polyethylene, ultra molecular weight  
8 polyethylene, and the combination of metals, titanium, chrome,  
9 cobalt, and that these are post market studies.

10 There's sort of a motion that's waiting for a fish  
11 to catch.

12 DR. REKOW: This is Diane Rekow.

13 I'll propose the motion.

14 DR. LI: Steve Li.

15 Clarification. You suggested those as post market  
16 approval studies? Is that what --

17 CHAIRMAN HEFFEZ: That's what I'm suggesting. Just  
18 so the panel understands, certainly we could make it a pre-market  
19 study as well. I'm suggesting post market study. I'm trying to  
20 glean the information that we had. Some people felt comfortable  
21 with the clinical data having been -- you know, we have a certain  
22 amount of clinical data for three years.



1                   That information would be helpful, and so that's  
2 why I suggested post market studies. Certainly the motion does  
3 not have to be seconded.

4                   DR. RUNNER: This is Susan Runner.

5                   You said in vitro, I believe.

6                   CHAIRMAN HEFFEZ: Yes.

7                   DR. RUNNER: I was wondering if the creep study would  
8 be in vitro and the wear and corrosion studies would be from  
9 explants. Is that correct or would the corrosion also be in vitro  
10 and that only the wear be from explants?

11                  CHAIRMAN HEFFEZ: I'd like to actually if I can ask  
12 Dr. Li how he feels regarding those studies.

13                  DR. LI: Well, I guess given the excellent clinical  
14 results for three years I would be comfortable making it a post  
15 market test. I guess if I could clarify, on the creep test I would  
16 be looking specifically essentially for the preservation of the  
17 fixation of the polyethylene with the screws. So I'm really looking  
18 for whether or not that fixation of the polyethylene to bone is  
19 going to maintain its original stability, if you will.

20                  As far as the wear test goes, if it's post market,  
21 I would be in favor of developing some type of wear test, certainly  
22 after I've seen these that appear to have wear to them, both an

1       in vitro and an in vivo assessment of wear if it's going to be  
2 post market. I see no reason not to develop even some kind of  
3 evaluation for wear.

4                   And I guess I would add in there actually as long  
5 as it's post market the effects of malposition or nonoptimal  
6 position of the components.

7                   CHAIRMAN HEFFEZ: What Dr. Runner was trying to  
8 indicate -- do you feel those studies should be in vitro or in  
9 vivo?

10                   DR. LI: Well, I think the wear needs to be both.  
11       Going down the line, I think all those things have to be evaluated  
12 on any retrievals that come out.

13                   CHAIRMAN HEFFEZ: That's clear. How about in vitro?

14                   DR. LI: Okay. In vitro I think you should do the  
15 wear test. I think you should do the stability of the fixation  
16 with time. I don't think the corrosion test is a big enough issue  
17 to develop a laboratory test for. I think analysis of retrievals  
18 would give you sufficient information for that.

19                   CHAIRMAN HEFFEZ: Okay. Dr. Rekow, did you want  
20 to say something before Dr. Li spoke?

21                   DR. REKOW: No. We're on the same page.

22                   CHAIRMAN HEFFEZ: So let's look at the motion again.

1       That one condition would be that all explants would be retrieved  
2 and studied for wear, creep of the ultra molecular weight  
3 polyethylene, and possible corrosion, and in vitro testing to be  
4 performed to study wear and creep.

5                   DR. LI: As far as the wear assessment, I'm including  
6 in that like a histological evaluation of collected tissue on  
7 retrieved implants as well as looking at the implants.

8                   CHAIRMAN HEFFEZ: So the wear issue would involve  
9 microscopic and macroscopic debris.

10                   DR. LI: Right, and an in vitro test includes  
11 nonoptimal positioning of the components.

12                   CHAIRMAN HEFFEZ: So let's try another motion. The  
13 motion would be that all explants would be studied in regards to  
14 wear, microscopically and macroscopically, creep of the ultra  
15 molecular weight polyethylene, and possible corrosion at mixed  
16 metal sites.

17                   In addition, that we're recommending in vitro  
18 testing in which there would be microscopic/macroscopic testing  
19 of wearing, including optimal mating and suboptimal mating of the  
20 devices, as well as a study of creep of the ultra molecular weight  
21 polyethylene.

22                   That's the motion. How do people feel?

1 DR. LI: Steve Li.

2 So moved.

3 CHAIRMAN HEFFEZ: Looking for a second.

4 DR. BURTON: Richard Burton.

5 Second.

6 CHAIRMAN HEFFEZ: Okay. Any discussion?

7 MR. SCHECHTER: This is Dan Schechter.

8 I'm not sure how the panel feels, but with respect  
9 to the suggested test in vitro for creep, even Dr. Li indicated  
10 that an indication of some creep in screw holes may have no clinical  
11 significance. So I'd want to put the caveat to FDA in formulating  
12 an actual requirement that it be something that they could actually  
13 get meaningful data in vitro.

14 Given that there is no TMJ model existing in vitro,  
15 the fact that they may have some small creep could mean nothing.

16 So I know I don't have a vote here, but I'm a little uncomfortable  
17 with that requirement.

18 The other comment, on the requirement for testing  
19 the bimetal junction, there may be existing test data from other  
20 products or other research done since these are common metals used  
21 in implants, and if that is done, perhaps that would satisfy the  
22 panel.

1 CHAIRMAN HEFFEZ: It's not common to combine those  
2 two metals.

3 MR. SCHECHTER: Okay.

4 CHAIRMAN HEFFEZ: But as far as the creep is concerned  
5 -- it's not. Did you wish to?

6 MR. MILLER: Dane Miller from Biomet.

7 And, in fact, it is common to combine those two  
8 metals.

9 CHAIRMAN HEFFEZ: You're referring to titanium and?

10 MR. MILLER: Titanium and cobalt chrome. In fact,  
11 they are probably used, by our best estimates, around the world  
12 250,000 times per year, combination of hips and knees.

13 CHAIRMAN HEFFEZ: I stand corrected.

14 Is there data regarding corrosion on that?

15 MR. MILLER: There is a good bit of both in vivo  
16 and obviously or in vitro and obviously in vivo results that support  
17 the suitability of those two materials in combination.

18 CHAIRMAN HEFFEZ: What is the data regarding  
19 corrosion? Is there corrosion?

20 MR. MILLER: They are galvanically very similar and  
21 typically a combination of cobalt chrome femoral head and a titanium  
22 stem. There were early concerns, but those were not -- they did

1 not turn out to be an issue clinically, and that combination has  
2 been used, along with several other combinations of titanium and  
3 cobalt chrome, for something approaching 20 years.

4 CHAIRMAN HEFFEZ: And is that material used -- how  
5 long has it been used for the temporomandibular joint? Just  
6 curious.

7 MR. MILLER: I believe we were the first application  
8 of it there.

9 CHAIRMAN HEFFEZ: Okay. Thank you.

10 I stand corrected.

11 As far as the creep is concerned, Dr. Li, are we  
12 really looking at the creep for loosening of the device; is that  
13 correct? That's the important portion of it?

14 DR. LI: Correct. So I would be looking for some  
15 signs of loosening of the device. It could be actually in the  
16 existing test that we already give them that information if they  
17 would just assess it. So I'm not necessarily asking for development  
18 of a new test.

19 I just want some measure if it's going to be something  
20 I'm going to have to worry about or not, and I guess my question  
21 to Mr. Miller on the corrosion is: does the use of the screws,  
22 titanium screws in a titanium plate of this relatively thin

1 thickness compared to what's used in the hips and knees give you  
2 any concern?

3 In other words, a micro crack is something that's  
4 20 millimeters thick. It is not the same as a micro crack in  
5 something that's a couple of millimeters thick. Do you have any  
6 sense for that?

7 MR. MILLER: This is Dane Miller again.

8 I hadn't intended for this to get into a long  
9 discussion about the characteristics of the surfaces and how they  
10 interact, but to answer your question, yes, certainly the thinner  
11 the surface, the smaller the component, the more concerning a crack  
12 is.

13 However, we apply the titanium plasma spray coating  
14 in a fashion that it's attached to, but not mechanically bonded  
15 completely to the substrate. Therefore, any notch sensitivity  
16 may occur because the characteristics of the titanium coating is  
17 not expected to propagate into the material itself, into the cobalt  
18 chrome substrate.

19 DR. LI: Steve Li.

20 I was more concerned about where the screw contacts  
21 the plate rather than the coating, where you have a titanium screw  
22 through the cobalt chrome plate.

1                   Would you expect to see corrosion there and would  
2 you expect it to be a problem with the relatively thin titanium  
3 plate?

4                   MR. MILLER: I wouldn't expect there to be any more  
5 a corrosion problem there than at the junction between a cobalt  
6 chrome head and a titanium femoral stem or the combination of plasma  
7 spray coating of titanium on a cobalt chrome substrate. I wouldn't  
8 expect there to be any differences, and in fact, titanium screws  
9 have been used in combination with cobalt chrome plates, especially  
10 in revision surgery where complicated revision has to take place.

11                  DR. LI: Just one more. I don't mean to beat a dead  
12 horse in this relatively small issue, but, again, those are  
13 relatively thick components relative to the mandibular plate.  
14 So given that crevice corrosion occurs, for instance, on a femoral  
15 add against the titanium stem, that amount of corrosion is small  
16 relative to the size of the stem.

17                  But if you have the same amount of corrosion in this  
18 particular case with a much thinner plate, would you expect there  
19 to be a problem where you don't have it with a large fracture  
20 fixation plate or a femoral neck?

21                  MR. MILLER: This is all very subjective, but number  
22 one, I'm not aware in the case of a cobalt chrome femoral head



1 or any combination of cobalt chrome and titanium that it has led  
2 to crevice corrosion cracking that led to any gross failure of  
3 product, number one.

4 Number two, I would expect with smaller components  
5 that that amount of corrosion to be smaller, but we're talking  
6 in very qualitative terms right now. That could all be quantified  
7 with testing, but I wouldn't anticipate any greater a problem.

8 DR. LI: Thank you.

9 MR. MILLER: Thank you.

10 CHAIRMAN HEFFEZ: So this motion. Anybody like to  
11 vote on it? Dr. Suzuki?

12 DR. SUZUKI: Jon Suzuki, yes.

13 DR. JANOSKY: Janine Janosky, yes.

14 DR. HEWLETT: Ed Hewlett, yes.

15 DR. BERTRAND: Peter Bertrand, yes.

16 DR. FAULK-EGGLESTON: Jane Faulk, yes.

17 DR. BURTON: Richard Burton, yes.

18 DR. REKOW: Diane Rekow, yes.

19 DR. PATTERS: Mark Patters, yes.

20 DR. ANSETH: Kristi Anseth, yes.

21 DR. COCHRAN: David Cochran, yes.

22 DR. LI: Steve Li, yes.

1 CHAIRMAN HEFFEZ: Okay. And from our previous  
2 discussions there appear to be one concern that some information  
3 could still be obtained from following patients to a mailing to  
4 complete VAS, visual analog scores or scales.

5 How does the panel feel regarding entertaining a  
6 motion that the company should try to complete as much of the missing  
7 data, even if it's only partial data, if the patients can't come  
8 for follow-up using mail-in instruments?

9 Dr. Cochran first.

10 DR. COCHRAN: David Cochran.

11 Can we incorporate into that the fact that we're  
12 going to follow the 180 patients up to three years as well?

13 CHAIRMAN HEFFEZ: Okay. Dr. Patters.

14 DR. PATTERS: I was going to suggest that, and I  
15 would suggest further that what we state is that they seek full  
16 or partial data on all 180 patients, 180 cases. I'm sorry. Full  
17 when available, and partial when full is not available.

18 DR. REKOW: Can I?

19 CHAIRMAN HEFFEZ: Dr. Rekow.

20 DR. REKOW: I just want to know how you feel about  
21 this. The study was approved for 300 patients. They've started  
22 180. Do you want the whole study or do you want the 180 that have

1 already started to be completed?

2 DR. PATTERS: I think that that's all --

3 CHAIRMAN HEFFEZ: Dr. Patters?

4 DR. PATTERS: Well, I would ask FDA. The fact that  
5 it's approved for 300, that's a maximum. That's not a minimum,  
6 is it?

7 DR. RUNNER: That's correct, and we would expect  
8 at this point in time the 180 that have been enrolled to be followed  
9 for three years, and if additional patients are enrolled, for them  
10 to be followed for three years. Any patients enrolled in the study  
11 would need to be followed for the full three years.

12 DR. PATTERS: And that is what I suggest the motion  
13 be, but add to the fact that those patients who they are unable  
14 to get full data, that they should seek partial data.

15 DR. LI: Clarification.

16 CHAIRMAN HEFFEZ: Yes, Dr. Li.

17 DR. LI: Steve Li.

18 When you say follow the 180 cases for three years,  
19 does that mean some of them then will be followed up for five and  
20 six years? In other words, you don't stop following patients once  
21 they get to three years, right?

22 DR. RUNNER: Well, for the purposes of the study

1 in terms of following the study protocol, after each patient has  
2 reached the three-year point, they are no longer in the study.  
3 That's it.

4 Now, whether the surgeon elects to follow the patient  
5 in a different fashion, that's another issue, but for purposes  
6 of the study, they're done at three years.

7 DR. LI: Just to say something controversial, Steve  
8 Li again. If it's a money thing, I personally would rather see  
9 them pay the money to follow those 45 patients out to six years  
10 rather than another 140 for another three.

11 DR. RUNNER: I think to be realistic for FDA, we  
12 can't have an open ended study. We have to have some parameters  
13 on a study.

14 DR. LI: Could I say -- Steve Li -- could I say I  
15 would want to follow those 45 patients until they reach a five-year  
16 endpoint?

17 DR. RUNNER: If that's your recommendation, you can.

18 DR. LI: So that's a possible recommendation?

19 DR. RUNNER: That certainly is.

20 DR. COCHRAN: David Cochran.

21 Just as a clinical investigator, if you're going  
22 to change the way the study is done, you bring up a lot of IRB

1 issues, and you're going to have to go back to the IRB, and so  
2 I think we had better consider all the ramifications, not just  
3 financial, but also on the investigators for the study.

4 CHAIRMAN HEFFEZ: Dr. Janosky.

5 DR. JANOSKY: Yeah, Janine Janosky.

6 I would like to separate the two issues of one is  
7 following for effectiveness and one is following for safety, and  
8 I think what you're talking about, Dr. Li, is following for safety.

9 Within the following for effectiveness, there were  
10 three parameters that were set forth, and that study was to close  
11 at the end of three years. So I think it is reasonable for us  
12 to put forth one of the conditions that that study remain open  
13 until closure date when that last enrolled patient had reached  
14 three years.

15 Now, the issue of whether we want to follow them  
16 longer for safety, that's another issue, and I would suggest that  
17 we discuss that separately from completing that study for n equals  
18 180.

19 CHAIRMAN HEFFEZ: Question to the FDA. Do you  
20 separate safety and effectiveness?

21 DR. RUNNER: Well, for purposes of the approval,  
22 you should be looking at both. However, if you feel that after

1 the three-year point you would like additional long-term data,  
2 then potentially a different type of study or an additional with  
3 fewer points or different types of endpoints could be entertained  
4 by the company.

5 CHAIRMAN HEFFEZ: Dr. Janosky.

6 DR. JANOSKY: Janine Janosky again.

7 I'm not suggesting that we separate safety and  
8 effectiveness for those first three years. I'm elongating this  
9 study in the arm of the safety arm also based on some panel members'  
10 comments that what actually happens, and I think Dr. Burton at  
11 some point says that you expected to see a lot of failures 18 months  
12 and out.

13 DR. BURTON: Well, speaking from experience, with  
14 most devices it was really in that two to three-year point. So  
15 I don't know if it was a honeymoon period or whatever else, but  
16 that it took wear components or something else because, again,  
17 certain other situations -- there was more wear debris, but it  
18 seemed to me in what I have looked at in the past it's at 24 to  
19 36 month point is when you started to see those failures really  
20 start to occur.

21 And up until you got to about two years, it was sort  
22 of like, yeah, just about everything works at that point. And

1       whether it's cumulative effect, wear, debris, whatever factor you  
2       might want to focus in on, it seemed to be that period where you  
3       start to have those issues come forth or later, and that's what  
4       Dr. Li was saying, was the fact that maybe there are changes that  
5       are occurring at 36 months. Unfortunately we're not really capable  
6       to detect them, that might become more apparent at a four or  
7       five-year point.

8                       I'm just personally, when I'm listening to this  
9       back-and-forth, I'm just a little uncomfortable, you know, having  
10      done investigatory work and having done work with -- I'm a little  
11      uncomfortable with we're still sort of changing horses here in  
12      the middle of everything, and I'm not sure exactly how or why we're  
13      going to be able to effectively do that and do it in a fair manner.

14                     CHAIRMAN HEFFEZ: Okay. So let us do --

15                     DR. JANOSKY: Can I just add one thing, please?  
16      This is Janine Janosky again.

17                     For the long term safety issue, the registry might  
18      take care of that. AE event reporting might take care of that.

19      I just want to separate the issue that was brought up by many  
20      panel members, is what is the long-term effect in terms of safety  
21      profile.

22                     DR. REKOW: And if I could add one more thing.

1 CHAIRMAN HEFFEZ: Dr. Rekow.

2 DR. REKOW: This is Diane Rekow.

3 If the sponsor is required to do analysis on the  
4 retrieved devices, we'll be able to glean some of that data at  
5 any rate.

6 CHAIRMAN HEFFEZ: Okay. So here's the motion. For  
7 safety and effectiveness, all 180 cases should be followed for  
8 three years to completion of the study, revealing all partial  
9 and full data. This should include retrieving visual analog scores  
10 from patients who or from long distance patients.

11 That's the motion. How does everybody feel?

12 DR. LI: Steve Li.

13 Could I ask a question, I guess, on the registry?

14 What information is in the registry? Is it just like they're  
15 still on the patient; they're not on the patient?

16 DR. RUNNER: The registry doesn't exist at this point  
17 in time. That's a proposed grant that NIH is working on.

18 However, from FDA's purposes, all patients that  
19 receive these implants will be tracked. Therefore, the company  
20 will know where these patients are.

21 CHAIRMAN HEFFEZ: Could we stick to the motion that  
22 I am suggesting? I need somebody to --



1 DR. REKOW: I so move. Diane Rekow.

2 DR. SUZUKI: Jon Suzuki.

3 Second.

4 CHAIRMAN HEFFEZ: Okay. Any further discussion on  
5 it?

6 DR. LI: I'm sorry. Steve Li.

7 Can I add something and you can all vote it down  
8 if you don't want it?

9 CHAIRMAN HEFFEZ: Sure.

10 DR. LI: But I would like to follow at least those  
11 45 patients or whatever the number is that are at three years to  
12 a five-year period in addition to finishing the 180.

13 CHAIRMAN HEFFEZ: Dr. Patters?

14 DR. PATTERS: Mark Patters.

15 I feel if Dr. Li would like that as a condition,  
16 that's a separate condition and he should raise that after this  
17 motion.

18 DR. LI: Okay. Fair enough.

19 CHAIRMAN HEFFEZ: Sponsor, did you have something  
20 you want to say?

21 MS. VERSTYNNEN: Mary Verstynen.

22 I want to go back to the original study protocol

1 and the sample size calculation where we statistically justified  
2 a patient population of 86 years (sic) that we would follow out  
3 to three years, and that calculation was based on a delta of a  
4 one centimeter improvement in pain, which we have far surpassed.

5 And we were more than willing to follow the 86  
6 patients. As the study advanced and Dr. Quinn and Dr. Sinn started  
7 enrolling more patients, we did an IDE supplement and bumped the  
8 population up to 200 to make sure that they could serve the needs  
9 of their patients.

10 We could have stopped it at 86 and this discussion  
11 would be going on of 180. The 180 is an arbitrary number based  
12 on when we submitted our PMA.

13 The next thing is that then we did an IDE supplement,  
14 and we asked for 300 because we were approaching the 200 mark.  
15 It seems reasonable to me that -- it seems like as a company and  
16 a study sponsor we are being penalized because we allowed this  
17 device to be implanted into more patients than what we originally  
18 anticipated.

19 CHAIRMAN HEFFEZ: Dr. Runner.

20 DR. RUNNER: Despite the fact that you had 86 patients  
21 originally, you have enrolled 180 patients in this study. We would  
22 expect all 180 to be followed through.

1 MS. VERSTYNEN: And I guess the other thing, too,  
2 is -- and I agree with that -- I believe this is a device that  
3 requires post market surveillance. So it seems to me that what  
4 we should be discussing is what the post market surveillance  
5 requirements will be, not the completion of the IDE.

6 MS. SCOTT: May I interject at this point?

7 This is a recommendation by the panel. If the panel  
8 believes that the information presented is acceptable, they can  
9 make that determination. If the panel believes that there is  
10 additional information that should be added as a condition, they  
11 can make that determination based on their agreement or  
12 disagreement with how the study was designed and things of that  
13 sort.

14 FDA works with the sponsor in the IDE, but the panel  
15 can agree or disagree with what FDA has worked with the sponsor  
16 and what the sponsor has presented, and it is a recommendation  
17 to the FDA, and then following that, the FDA and the sponsor can  
18 work together.

19 But at this point, it's the panel's recommendation  
20 to FDA as what they believe is appropriate to approve the device  
21 at this point. The motion is approvable with conditions.

22 DR. FAULK-EGGLESTON: Jan Faulk.

1           The other issue is you went from one device that  
2 was cemented, and then now you have a device that you don't use  
3 the cement, which needs, I would suspect, different follow-up.  
4 So you can't just drop with the cemented items and then not get  
5 data on the ones that aren't cemented.

6           CHAIRMAN HEFFEZ: Dr. Burton.

7           DR. BURTON: Richard Burton.

8           Like I said, I guess I'm sympathetic with what the  
9 company is saying, but in my opinion, when you requested and  
10 expanded that, the IDE refers to 200 and then I guess eventually  
11 into three. Certainly you don't have to enroll further patients  
12 at this time and continue it to 300 patients, but when you accept  
13 this responsibility and the ability to continue the study to that  
14 180, it seems to me that you would accept to some degree the decision  
15 then to follow at least that group out to the three-year study  
16 point as you would have any of the other patients.

17           And I guess I'm a little uncomfortable with then  
18 suddenly deciding, well, we're going to go to that 86 on out, but  
19 the other, you know, 94 patients at this juncture we'll sort of  
20 disenroll them and abandon what data that may represent, which  
21 again, as Dr. Faulk pointed out, includes a large number or the  
22 bulk of the number which had the noncemented fossa as well.

1                   So I think to walk away from that also would limit  
2 the potential ability to evaluate the product.

3                   CHAIRMAN HEFFEZ: There's a motion on the floor,  
4 and it's been seconded. Any other discussion?

5                   (No response.)

6                   CHAIRMAN HEFFEZ: So let us go. Dr. Suzuki.

7                   DR. SUZUKI: Jon Suzuki, yes.

8                   DR. JANOSKY: Janine Janosky, yes.

9                   DR. HEWLETT: Ed Hewlett, yes.

10                  DR. BERTRAND: Peter Bertrand, yes.

11                  DR. FAULK-EGGLESTON: Jane Faulk, yes.

12                  DR. BURTON: Richard Burton, yes.

13                  DR. REKOW: Diane Rekow, yes.

14                  DR. PATTERS: Mark Patters, yes.

15                  DR. ANSETH: Kristi Anseth, yes.

16                  DR. COCHRAN: David Cochran, yes.

17                  DR. LI: Steve Li, yes.

18                  CHAIRMAN HEFFEZ: There's another condition that  
19 probably should be labeled as Label 2 condition, but the condition  
20 would be that we would remove all reference to cementing the  
21 prosthesis and the item should be marketed only as a cementless  
22 prosthesis.

1 Any comments on that?

2 DR. PATTERS: So moved.

3 CHAIRMAN HEFFEZ: So Dr. Patters made the motion.

4 Anybody second it?

5 DR. FAULK-EGGLESTON: Jan Faulk.

6 I second.

7 CHAIRMAN HEFFEZ: Any discussion?

8 (No response.)

9 CHAIRMAN HEFFEZ: Okay. Let's vote on it. Dr.  
10 Suzuki.

11 DR. SUZUKI: Jon Suzuki, yes.

12 DR. JANOSKY: Janine Janosky, yes.

13 DR. HEWLETT: Ed Hewlett, yes.

14 DR. BERTRAND: Peter Bertrand, yes.

15 DR. FAULK-EGGLESTON: Jane Faulk, yes.

16 CHAIRMAN HEFFEZ: Dr. Burton.

17 DR. BURTON: I'm sorry.

18 CHAIRMAN HEFFEZ: We're voting where we're moving  
19 cementless prosthesis.

20 DR. BURTON: I'd like to hear the motion again,  
21 please. I'm sorry.

22 CHAIRMAN HEFFEZ: The motion is that we would be

1 removing any reference to marking the item as a cement --

2 DR. BURTON: Richard Burton, yes.

3 DR. REKOW: Diane Rekow, yes.

4 DR. PATTERS: Mark Patters, yes.

5 DR. ANSETH: Kristi Anseth, yes.

6 DR. COCHRAN: David Cochran, yes.

7 DR. LI: Steve Li, yes.

8 CHAIRMAN HEFFEZ: Okay.

9 DR. RUNNER: Could I ask a question, please?

10 CHAIRMAN HEFFEZ: Yes.

11 DR. RUNNER: Just for clarification, the fourth  
12 motion was to continue to follow all 180 patients to three years  
13 with full or partial data post market.

14 CHAIRMAN HEFFEZ: Yes.

15 Another condition was the FDA has yet to receive  
16 the report regarding the mechanical testing of the device without  
17 the post. So it is conditioned that the data regarding mechanical  
18 testing and engineering testing on this device without the post  
19 be provided to the FDA and does not demonstrate substantial  
20 difference between the engineering data on the device with the  
21 post.

22 Any comments? Anybody wish to make that motion?

1 DR. REKOW: Diane Rekow.

2 I so move.

3 CHAIRMAN HEFFEZ: Second?

4 DR. SUZUKI: Jon Suzuki.

5 Second.

6 CHAIRMAN HEFFEZ: Any discussion?

7 (No response.)

8 CHAIRMAN HEFFEZ: I guess we can go for voting.

9 Dr. Suzuki.

10 DR. SUZUKI: Jon Suzuki, yes.

11 DR. JANOSKY: Janine Janosky, yes.

12 DR. HEWLETT: Edmond Hewlett, yes.

13 DR. BERTRAND: Peter Bertrand, yes.

14 DR. FAULK-EGGLESTON: Jane Faulk, yes.

15 DR. BURTON: Richard Burton, yes.

16 DR. REKOW: Diane Rekow, yes.

17 DR. PATTERS: Mark Patters, yes.

18 DR. ANSETH: Kristi Anseth, yes.

19 DR. COCHRAN: David Cochran, yes.

20 DR. LI: Steve Li, yes.

21 CHAIRMAN HEFFEZ: Okay. Now, Dr. Li, you raised

22 a question about safety, want to follow patients up to five years.



1           Would you like to make a motion?

2                         DR. LI:  No, I withdraw that motion.

3                         CHAIRMAN HEFFEZ:  Are there any other conditions  
4           that the panel feels should be discussed?

5                         DR. BURTON:  Richard Burton.

6                         Dr. Heffez, they had earlier made a comment about  
7           whether the panel makes any recommendations regarding the post  
8           market surveillance.  Dr. Runner, do you feel there's any need  
9           for any recommendations from the panel regarding post market  
10          surveillance items?

11                        DR. RUNNER:  I feel that the recommendations that  
12          you've already made are post market surveillance items.  If you  
13          feel there's some additional things that you would like the company  
14          to do, they should be added at this point because all of these  
15          are things that we will get from the sponsor, particularly the  
16          clinical data on the 180 patients up to three years.

17                        DR. BURTON:  Let me ask a question then.  You know,  
18          you made reference to the fact that this item really just tracks  
19          the patients.  There does not exist a patient registry, and what  
20          obviously Dr. Li was alluding to or at least my interpretation  
21          was that the fact is that what occurs in that three to five-year  
22          point, is there any place that that data would ever come back to

1 as we currently stand?

2 DR. RUNNER: Well, the adverse event data on patients  
3 post any marketing of any device should come to us through MDR  
4 and MedWatch reports, tracked items, as well as other devices that  
5 are on the market.

6 So it's incumbent on the surgeon and/or the patient  
7 to report adverse events to the agency post market, and there's  
8 methods in place for that to happen.

9 CHAIRMAN HEFFEZ: This appears to conclude all of  
10 the conditions unless another panel member has a condition that  
11 they would like to raise.

12 (No response.)

13 CHAIRMAN HEFFEZ: Not hearing any, I'm going to now  
14 entertain a motion that we approve this as approvable with  
15 conditions, and the conditions that have all been -- each of us  
16 have heard. If we want, we want repeat those or I think -- no.

17 So then we can go ahead and vote on approval with  
18 each of the conditions that have been outlined.

19 DR. BURTON: Would you need a motion?

20 Richard Burton.

21 CHAIRMAN HEFFEZ: We can discuss this. Yeah, go  
22 ahead.

1 DR. BURTON: I go ahead and move then. I guess I  
2 move the question because I think we had actually made that  
3 recommendation before.

4 CHAIRMAN HEFFEZ: Yeah, and you can second it if  
5 Dr. --

6 DR. BURTON: Okay. Richard Burton.

7 Second.

8 CHAIRMAN HEFFEZ: And for the record, who moved?  
9 Who made that motion? I need somebody to make that motion.

10 DR. HEWLETT: I believe I did.

11 CHAIRMAN HEFFEZ: I think Dr. --

12 DR. HEWLETT: Ed Hewlett.

13 CHAIRMAN HEFFEZ: Okay. Now, any further discussion?

14 (No response.)

15 CHAIRMAN HEFFEZ: So could we vote, just to change  
16 the pattern?

17 (Laughter.)

18 CHAIRMAN HEFFEZ: Before we vote, Ms. Scott was kind  
19 enough to indicate to me if the consumer representative, industry  
20 representative want to make some comments prior to this final vote.

21 MR. SCHECHTER: Dan Schechter.

22 Nothing at this time.

1 CHAIRMAN HEFFFEZ: Sponsor has anything?

2 (No response.)

3 CHAIRMAN HEFFFEZ: Okay. So then let's proceed to  
4 the vote.

5 Dr. Li.

6 DR. LI: Steve Li, yes.

7 DR. COCHRAN: David Cochran, yes.

8 DR. ANSETH: Kristi Anseth, yes.

9 DR. PATTERS: Mark Patters, yes.

10 DR. REKOW: Diane Rekow, yes.

11 DR. BURTON: Richard Burton, yes.

12 DR. FAULK-EGGLESTON: Jan Faulk, yes.

13 DR. BERTRAND: Peter Bertrand, yes.

14 DR. HEWLETT: Edmond Hewlett, yes.

15 DR. JANOSKY: Janine Janosky, yes.

16 DR. SUZUKI: Jon Suzuki, yes.

17 CHAIRMAN HEFFFEZ: Okay. So that's a unanimous vote.

18 So I'd like to go from each panel member who voted  
19 and have a specific reason why you voted the way you did on record.

20 So Dr. Li.

21 DR. LI: Steve Li.

22 I think the clinical record that you've reported

1 is excellent as far as you've reported it. My only concerns are  
2 those things that were essentially not tested, for which we don't  
3 have a clear assessment, but then time will tell if those things  
4 and if the post market approval tests are conducted.

5 DR. COCHRAN: David Cochran.

6 I felt that the material that was presented to the  
7 panel members, as well as the discussion during the day, fit the  
8 requirements as defined for both safety and effectiveness as  
9 defined for both safety and effectiveness for the device.

10 DR. ANSETH: Kristi Anseth.

11 I also thought that the results show and demonstrated  
12 safety and effectiveness and the conditions associated with the  
13 approval fill in some of the extra information about follow-up  
14 and labeling and some of the wear tests that weren't conducted.

15 DR. PATTERS: Mark Patters.

16 I believe the sponsor and their clinicians should  
17 be commended for the high scientific quality of the study and  
18 introducing minimal variables, and I feel that they've shown safety  
19 and efficacy.

20 However, I feel that conditions that require that  
21 they follow the subjects through three years as originally agreed  
22 is appropriate.

1 DR. REKOW: This is Diane Rekow.

2 I don't have anything to add, but I wanted to say  
3 the same things that Mark has just said because I really compliment  
4 you on the quality of the study, and I can't wait to see the papers  
5 that are coming out.

6 DR. BURTON: Richard Burton.

7 As an individual that's dealt a number of years with  
8 this patient population, which is a difficult population to deal  
9 with, and not the individuals personally, but their disabilities  
10 and the problems that grow forth from that, like was said, it's  
11 a very well done study, and I was certainly convinced by the data  
12 that was presented and the presentations that it is a safe and  
13 efficacious product.

14 And I think that, you know, the only questions that  
15 really I saw running around the table was looking at the long-term  
16 issues because most of us who have been in this particular arena  
17 for any length of time realize that sometimes the amount of time  
18 you have to study these kinds of issues, sometimes they don't come  
19 up to us within that time frame.

20 And I guess it's incumbent upon not only just the  
21 company but the surgeons that are utilizing it, and that's sort  
22 of, I guess, what I'm speaking actually to Dr. Quinn and to Dr.

1 Sinn, and that as you educate these people that they understand  
2 to be vigilant for those long-term issues as well.

3 Thank you.

4 DR. FAULK-EGGLESTON: This is Jan Faulk.

5 And my opinion is one as a clinician. You need  
6 increased modalities to help these patients. They are out there.

7 They need help, and you need to do it in a better, more efficacious  
8 way than we've done previously.

9 DR. BERTRAND: I'm Peter Bertrand.

10 I voted yes for approval because I thought the data  
11 was tremendously well presented. I believe the company is following  
12 up and Dr. Quinn and Dr. Sinn are following up with an incredible  
13 patient compliance rate.

14 I also want to applaud them on their perceived need  
15 to sustain education long term both for clinicians and for patients.

16 DR. HEWLETT: This is Ed Hewlett.

17 I'm pleased to see that such a well conducted study  
18 is going to benefit a population of Americans who suffer from a  
19 malady with particularly high morbidity, as well as complexity  
20 and difficulty in treatment. So congratulations on that.

21 And I'd like to concur with the rest of the panel  
22 members that I'm quite satisfied within the limits of the additional

1 information that would be collected as a result of the conditions  
2 that safety and efficacy standards have been met.

3 DR. JANOSKY: Janine Janosky.

4 I view the ratio for effectiveness and safety to  
5 be a positive one for the intermediate data points, and I think  
6 the conditions that we applied to the motion will let us see whether  
7 that holds true for the final data point.

8 DR. SUZUKI: Jon Suzuki.

9 I voted yes because I feel the clinicians are  
10 outstanding; the protocol is scientifically sound; and the results  
11 are very satisfactory.

12 CHAIRMAN HEFFFEZ: At this time I would like to thank  
13 all of the panel members, all of the consultants, patient  
14 representative, consumer representative, industry representative,  
15 certainly the FDA for all of the background work and effort.

16 And I certainly want to thank the sponsor for having  
17 the people here to answer all of the questions and all of their  
18 hard work.

19 At this time, this concludes this meeting, and again,  
20 I appreciate all of your efforts.

21 Dr. Runner?

22 DR. RUNNER: Excuse me. Before we go to the closed



1 session, I think Ms. Scott wanted me to present some plaques of  
2 appreciation to two panel members who are serving today as  
3 consultants, but who have officially gone off as permanent panel  
4 members.

5 And I have a letter and plaque for Dr. Mark Patters,  
6 who has been on our panel for a number of years, and this is a  
7 certificate of appreciation and recognition of your service.

8 (Applause.)

9 DR. RUNNER: A similar plaque of appreciation to  
10 Dr. Janine Janosky who has been stolen away by other panels for  
11 her excellence.

12 (Applause.)

13 CHAIRMAN HEFFEZ: So thank you very much for  
14 everybody, and I will ask everybody to clear the room when the  
15 FDA enters a closed panel, closed session.

16 (Whereupon, at 4:25 p.m., the meeting in the  
17 above-entitled matter was concluded.)

18

19

20

21

22

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12