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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH 8466 '09 MAY 20 19 53  
OFFICE OF DEVICE EVALUATION

MEETING OF THE DENTAL PRODUCTS PANEL

OPEN SESSION - VOLUME I

Monday, May 10, 1999

10:30 a.m.

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

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P R O C E E D I N G S

**Welcome and Introductory Remarks**

MS. SCOTT: Good morning. Welcome to the Dental Products Panel Meeting for May 10 and 11, 1999. My name is Pamela Scott. I serve as the Executive Secretary for the Dental Products Panel. At this time, I would like to read into the record several administrative items.

The first item is the conflict of interest statement for May 11, 1999.

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

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

The agency determined that no conflicts exist. However, we would like to note for the record that the agency took into consideration a matter regarding Dr. Willie Stephens who reported an interest but no financial involvement in a firm at issue.

The agency has determined that Dr. Stephens may

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

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

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

22           For the record, these people are special  
23 government employees and are consultants to this panel under  
24 the Medical Devices Advisory Committee. They have undergone  
25 customary conflict of interest review. They have reviewed

1 the material to be considered at this meeting. Signed Dr.  
2 Elizabeth Jacobson, Acting Director, Center for Devices and  
3 Radiological Health, May 6, 1999.

4 The last administrative items is the appointment  
5 of temporary panel chairperson. I appoint Dr. Janine  
6 Janosky to act as temporary chairperson for the duration of  
7 the Dental Products Panel meeting on May 10 through 11,  
8 1999. For the record, Dr. Janosky is a special government  
9 employee and is a voting member of the Dental Products  
10 Panel.

11 Dr. Janosky has undergone the customary conflict  
12 of interest review and has reviewed the issues to be  
13 considered at this meeting. Signed, Dr. Jacobson, Acting  
14 Director, Center for Devices and Radiological Health, May 6,  
15 1999.

16 At this time, I would like to reintroduce our  
17 panel members for today. The panel members are listed in  
18 the back of the agenda.

19 As I stated previously, Dr. Janine Janosky is  
20 acting as our chair today. She is an assistant professor  
21 with the Department of Family Medicine and Clinical  
22 Epidemiology with the School of Medicine at the University  
23 of Pittsburgh. We also have with us Dr. Mark Patters who is  
24 the Chairman of the Department of Periodontology at the  
25 College of Dentistry at the University of Tennessee in

1 Memphis, Tennessee. He is a voting member to our panel.

2 Our consumer representative is Dr. Donald Altman  
3 who is the Chief of the Office of Oral Health with the  
4 Arizona Department of Health Services in Phoenix, Arizona.  
5 Dr. Alton Floyd is our industry representative. He is the  
6 President of Trigon Technology, Inc. in Edwardsburg,  
7 Michigan.

8 Our patient representative for today is Ms.  
9 Theresa Cowley who is the President of the TMJ Association  
10 in Milwaukee, Wisconsin. We also have with us today Dr.  
11 Peter Bertrand who is the Director of the Oral Facial Pain  
12 Clinic and a Specialty Advisor for Oral Facial Pain and TMD  
13 with the National Naval Medical Center in Bethesda,  
14 Maryland.

15 We have Dr. Richard Burton who is an assistant  
16 professor of oral and maxillofacial surgery with the  
17 Department of Hospital Dentistry at the University of Iowa  
18 Hospitals and Clinics in Iowa City, Iowa.

19 We have Gilbert Gonzales who is associate  
20 professor of neurology at the Memorial Sloan Kettering  
21 Cancer Center with Cornell University in New York, New York.

22 We have Dr. Leslie Heffez who is the professor and  
23 Department Head of Oral and Maxillofacial surgery at the  
24 University of Illinois at Chicago in Chicago, Illinois.

25 We also have Dr. Stephen Li who is a senior

1 scientist with the Department of Biomechanics and  
2 Biomaterials at the Hospital for Special Surgery in New  
3 York. We have Dr. Diane Rekow who is the Chairperson of the  
4 Department of Orthodontics at the University of Medicine and  
5 Dentistry of New Jersey in Newark, New Jersey.

6 Dr. Harry Skinner will be with us tomorrow. He is  
7 professor and Chair of the Department of Orthopedic Surgery  
8 with the University of California at Irvine in Orange,  
9 California. And we have Dr. Willie Stephens who is an  
10 associate surgeon for the Division of Maxillofacial Surgery  
11 at Brigham and Women's Hospital in Boston, Massachusetts.  
12 He is also with the Harvard Oral and Maxillofacial Surgery  
13 Associates in Brookline, Massachusetts.

14 We would like to thank our panel for being present  
15 today with us. I would also like to state the FDA  
16 participants for today. We have Mr. Timothy Ulatowski who  
17 is the Director of the Division of Dental, Infection Control  
18 and General Hospital Devices with the Office of Device  
19 Evaluation, Center for Devices and Radiological Health, the  
20 Food and Drug Administration.

21 We also have Dr. Susan Runner who is the Branch  
22 Chief for the Dental Devices Branch within the Division of  
23 Dental, Infection Control and General Hospital Devices,  
24 Office of Device Evaluation, Center for Devices and  
25 Radiological Health.

1           We have Ms. Angela Blackwell who is a biomedical  
2 engineer also with the Dental Devices Branch within the  
3 Division of Dental, Infection Control and General Hospital  
4 Devices. And we have Dr. Murty Ponnappalli who is a  
5 mathematical statistician with the Division of Biostatistics  
6 in the Office of Surveillance and Biometrics.

7           Thank you very much.

8           Also, I would like to remind all of the  
9 participants for today and all the people who are attending  
10 the meeting today that if you have not signed in, please do  
11 so at the table at the front. Also, if you would like  
12 summary minutes or a transcript from today's meeting, there  
13 is a sheet on the front table that gives you the address and  
14 the phone number that you can contact to receive that  
15 information.

16           Also, if you have not received an agenda or some  
17 of the handouts that we have today, those are also at the  
18 front sign-in table.

19           At this time, I will turn the meeting over to Dr.  
20 Janosky.

21           DR. JANOSKY: Good morning. At this time, we are  
22 going to have an update of FDA activities. There are two  
23 items on the agenda. One is a Y2K update by Mr. Neil Ogden  
24 followed by a postmarket surveillance presentation by Dr.  
25 Tom Gross.



1 representing the year using only two digits or other date-  
2 related problems such as failure to recognize a leap year.  
3 Example; 00 leads to confusion between the Year 2000 and  
4 1900.

5           Definition of Year 2000 compliance. For the  
6 purpose of the database, Year 2000 compliance means with  
7 respect to medical devices and scientific laboratory  
8 equipment that the product accurately processes and stores  
9 date-time data including, but not limited to, calculating,  
10 comparing, displaying, recording and sequencing operations  
11 regarding date-time data during, from, into and between the  
12 20th and 21st Centuries and the Years 1999 and 2000  
13 including correct processing of leap-year data.

14           Request of the panel: to provide advice regarding  
15 problematic devices from panel's domain of expertise;  
16 identify types of devices which, because of their use of  
17 dates could present risks to patients if not addressed;  
18 suggestions to the Center for Devices and Radiological  
19 Health regarding actions to reduce risks from the Year 2000  
20 problems.

21           The FDA set up a database and there is the  
22 worldwide web address, [www.fda.gov](http://www.fda.gov). Just select on the Year  
23 2000 item under that address.

24           Other CDRH and FDA activities include letters to  
25 manufacturers, guidance to manufacturers, established

1 database of product information on Internet, monitoring and  
2 assessment activities, educational activities for  
3 manufacturers, clinicians and the public.

4           You can contact your panel executive secretary or  
5 you can contact Mr. Tom B. Shope at this address, phone  
6 number, e-mail address if you have further questions or  
7 issues or you know of devices that could be subject to this  
8 problem.

9           What has FDA done regarding Year 2000 date problem  
10 and medical devices? Internal assessment of potential  
11 impact and vulnerable devices. In June, 1997, a  
12 notification letter to manufacturers that advised of the  
13 problem, told how FDA will address this problem in premarket  
14 review. New submissions were not required for repairs which  
15 are only date-related. Repairs and updates before the  
16 impact would not be classified as recalls.

17           Participation in biomedical working group, federal  
18 users of devices and scientific equipment; a working group  
19 chaired by the Department of Health and Human Services;  
20 consolidated request for information in January, 1998;  
21 private and public healthcare organizations have the same  
22 information needs.

23           An FDA website was established in the spring of  
24 1998 and guidance on FDA's expectations was issued in June,  
25 1998.

1 Additional letters to manufacturers were sent out  
2 on June 29, 1998, September 2, 1998 and on September 21,  
3 1998 a letter on manufacturing process concerns was issued.  
4 Additional communications planned included speaking with the  
5 manufacturers, healthcare facilities and clinicians and  
6 consumers.

7 The biomedical equipment database is an FDA-  
8 operated worldwide website and includes data provided by  
9 manufacturers, voluntary submission of data, certification  
10 by manufacturers, continually updated, is searchable by the  
11 manufacturers and is downloadable for people to use the  
12 information.

13 It also includes manufacturers lists of products  
14 which are impacted, noncompliant, so people can search to  
15 see if a device they have may be noncompliant. The  
16 manufacturer certifies that all products, both current and  
17 past production are complaint. Manufacturer certifies that  
18 none of their products use dates and the manufacturer  
19 provides a worldwide web link to their website where  
20 requested information is provided.

21 Contained in the January 21, 1998 letter to  
22 manufacturers, based on a definition in the Federal  
23 Acquisition Regulations, comprehensive product information  
24 and non-compliant does not mean a risk to the public health.

25 What does the product database show? Many

1 companies have not yet recorded assessments in progress.  
2 Most noncompliant products involved date display or date  
3 recording--i.e., date stamping. A limited number of  
4 products with significant operational problems. PC-based  
5 products have PC-type problems. Manufacturers are providing  
6 solutions in a variety of approaches.

7           The FDA's role regarding recalls related to the  
8 Year 2000 problem. FDA can require recall of devices which  
9 present a significant risk to the public health. FDA will  
10 monitor reports of Y2K problems with emphasis on devices  
11 that could present significant risk to patients and  
12 investigate and take action where warranted.

13           CDRH and FDA future activities include  
14 establishment of a biomedical equipment clearing house and  
15 agreement with the Department of Veteran Affairs; expansion  
16 of the database; outreach communications with industry,  
17 clinicians and consumers; vigorous action on products which  
18 present significant risks; and increased inspection emphasis  
19 on Y2K problems.

20           Health-facilities issues; inventory and assess  
21 devices used; obtain information on device status; test  
22 devices for Y2K compliance; check interconnected or network  
23 devices; check device-information system connections; plan  
24 for or develop workarounds, upgrades or replacements; and  
25 develop contingency plans.

1           And that is the last slide. To conclude, I would  
2 just like to say that the FDA and the Center have taken the  
3 Y2K problem very seriously. We have been involved in a  
4 number of activities as you just heard about. We would like  
5 all of you to also take this issue quite seriously.

6           Thank you.

7           DR. JANOSKY: Thank you.

8           Are there any questions?

9           MR. ULATOWSKI: That slide for the panel, what the  
10 panel can do, is there a systematic means of interacting  
11 with the panel members? Who do they contact?

12           MR. OGDEN: They can contact the executive  
13 secretary, Pam Scott, or they can talk to Tom Shope at the  
14 numbers and information that was given there. Those are the  
15 two main people that we are supposed to focus the  
16 information through from the panel.

17           DR. JANOSKY: Any comments or questions from panel  
18 members?

19           Thank you.

20           The next is Dr. Tom Gross who is going to speak on  
21 postmarket surveillance.

22           DR. GROSS: I would like to take a few minutes  
23 today to talk to you about postmarket evaluation at CDRH.  
24 We in the Office of Surveillance and Biometrics believe that  
25 it is important that advisory panels are aware of postmarket

1 programs because these activities may directly affect your  
2 deliberations about the product's safety and effectiveness.

3 The objectives of this presentation are threefold;  
4 one, to describe a few of the key methods of device  
5 postmarket evaluation at CDRH; two, to present challenges in  
6 better accomplishing postmarket evaluation; and, three, to  
7 describe the pivotal role that advisory panels can play in  
8 this arena.

9 This slide entitled, "From Design to  
10 Obsolescence," makes three key points. One, it emphasizes  
11 the fact the medical devices have a definable life cycle  
12 from initial design to lab and bench testing, clinical  
13 testing, FDA review and, importantly, postmarket evaluation.

14 Two, that there are life cycles, that there are  
15 feedback loops throughout this life cycle leading to  
16 continuous product improvements. Postmarket evaluation and  
17 its related programs have an important part to play in this  
18 process.

19 The third point is that the clinical community,  
20 including the advisory panel, has a very important part to  
21 play in this process, not only on the premarket side but on  
22 the postmarket side as well.

23 As products move into the marketplace, questions  
24 of public-health interest may arise in the postmarket  
25 period. There may be questions about the long-term safety

1 of a product, about the performance of a device in community  
2 practice as it moves out of the narrow confines of clinical  
3 trials.

4           There may be questions about the effects of change  
5 in user setting; for instance, moving devices from a  
6 professional setting to home-use settings. There may be  
7 questions about the effects of incremental changes in  
8 technology which may bring to question the performance of  
9 the device. Lastly, there may be unusual adverse events or  
10 patterns of adverse events which may present public-health  
11 questions.

12           Now, let's talk about some of these programs that  
13 are related to these public-health questions. The first  
14 program I would like to discuss is the medical-device  
15 reporting program. This is a nationwide surveillance system  
16 of voluntary or mandatory reports of adverse events related  
17 to device use.

18           Beginning in 1973, CDRH started receiving  
19 voluntary reports. In 1984, manufacturers were required to  
20 submit reports of death and serious injury if a medical  
21 device may have caused or contributed to that event to the  
22 FDA. They were also required to report malfunctions to the  
23 FDA as well.

24           Beginning in 1990, all user facilities,  
25 principally nursing homes and hospitals, had to report

1 deaths to the FDA and serious injuries to the manufacturer.

2 All told, we have received about 1 million reports  
3 since its inception and, beginning in the early '90's, FDA  
4 continues to receive about 100,000 adverse-event reports per  
5 year. These are submitted on standardized forms and data  
6 are collected on device-specific event description,  
7 pertinent dates, and patient characteristics.

8 Unfortunately, many of the reports often have very  
9 limited information. Even basic demographic information  
10 such as age and gender is missing from the majority of  
11 reports. Nonetheless, they can provide FDA with critical  
12 signals about potential public-health problems.

13 There may be several actions that are prompted by  
14 the MDR program. When we investigate adverse events, this  
15 may lead to a directed inspection of a manufacturer  
16 facility. These investigations may ultimately lead to  
17 product injunction or seizures. It may lead to product  
18 recalls, as in the case of dental cements or endodontic  
19 probes.

20 It may also result in patient and physician  
21 notifications as in the '94 notification about Proplast.  
22 And they may also prompt additional postmarket studies.

23 Now let's turn to the two postmarket authorities  
24 that we at CDRH have. One is entitled postmarket  
25 surveillance or section 522 and the other is the

1 postapproval authority under the PMA regulation. Section  
2 522 originally mandated in SMDA 1990 was changed in FDAMA  
3 1997.

4 Now, in 1990 version, the statute had lists and  
5 categories of devices the manufacturers of which were  
6 required to do postmarket-surveillance studies on. In the  
7 '97 version, there are no longer those lists and categories.  
8 However, FDA has the discretionary authority to impose  
9 postmarket-surveillance studies on devices that have  
10 particular public-health questions.

11 Now, postapproval refers to class III PMA  
12 products. These studies are better known as "condition of  
13 approval" studies. Again, they are reserved strictly for  
14 PMS products. 522 extends its coverage to class II and III  
15 510(k) products whose failure may present a public-health  
16 problem.

17 Now, both authorities are seen as a complement to  
18 the premarket process in continually assuring the safety and  
19 effectiveness of products in the marketplace.

20 In implementing the statute, the 522 provisions,  
21 we publish criteria in the form of guidance to help us in  
22 our considerations of when to impose postmarket surveillance  
23 on class-II or class-III products. The principal criteria  
24 is that we feel there should be a critical public-health  
25 question.

1           This may be driven by a for-cause event, an  
2 adverse event that is worthy of further investigation. It  
3 may be linked to new or expanded conditions of use such as  
4 moving from professional to home use. It may be linked to  
5 the evolution of technology. There may be questions about  
6 the durability of the product as it changes in its  
7 technology.

8           The second criterion is that there should be  
9 consideration of other postmarket strategies, that imposing  
10 question 522 to address this particular public-health  
11 question may not be the most appropriate tool. Perhaps the  
12 question could answered through the MDR program or through  
13 other mechanisms such as the quality-systems mechanism.

14           Thirdly, the study should be practical and  
15 feasible and a related question should be how will the data  
16 be used. This becomes particularly relevant when we deal  
17 with rapidly changing technology. By the time the studies  
18 are done, the data may be obsolete.

19           Lastly, what is the priority of this particular  
20 public-health question? What is the magnitude of the risk  
21 and the benefit, the extent of population exposure, the  
22 seriousness of the outcome at hand. This should all be  
23 taking into account to help us prioritize these studies.

24           Once we decide to impose postmarket surveillance  
25 under section 522, we should make sure that the study design

1 is best matched to the public-health question. There are  
2 lost of study designs to choose from aside from going the  
3 route of clinically rigorous studies.

4 I have listed a few possible study designs. It  
5 may be as simple as doing a detailed review of the complaint  
6 history or literature, doing non-clinical testing of the  
7 device, using the existing databases, doing something simple  
8 such as telephone or post-care follow-up of patients, and  
9 then doing something more sophisticated such as use of  
10 project registries, case-control studies and, in rare  
11 events, turning to randomized trials to answer these  
12 questions.

13 These are some of the frustrations we have  
14 experienced in the postmarket period in terms of  
15 implementing postmarket surveillance under 522. These are  
16 challenges that face us today.

17 I mentioned previously the rapid evolution of  
18 technology can make studies obsolete. There may be lack of  
19 incentives for industry. Doing a postmarket study for  
20 industry, they may only see the downside of doing these  
21 studies because it may only bring bad news about their  
22 product. We have to change that paradigm and make it of  
23 interest to industry to participate in these postmarket  
24 studies.

25 There may be lack of interest in the clinical

1 community. Clinicians may be more interested in studying  
2 cutting-edge technology as opposed to addressing public-  
3 health issues related to mature technologies.

4           Lastly, there may be a lack of a clearly specified  
5 public-health question. We ran into this situation in the  
6 1990 version of section 522 in studying standard vascular  
7 grafts. These are mature technologies. Industry and  
8 ourselves felt that many of the questions had already been  
9 addressed. So, in that particular instance, it was a device  
10 looking for a public-health question.

11           What is the challenge to the advisory panel? It  
12 is really a challenge to us all. That is when considering  
13 postmarket studies, whether postapproval or 522, we need to  
14 make sure that this is of primary importance. We can  
15 envision, in the future, coming to you, the advisory panel,  
16 for your input on potential 522 studies.

17           We need to clearly specify the public-health  
18 question and we need to note the clinical and regulatory  
19 relevance of answering the question. In other words, what  
20 will we do with that data? Are the data there to reassure  
21 us that the postmarket experience is similar to the  
22 premarket experience?

23           Is it there to address residual questions? Can it  
24 be done in a timely fashion?

25           Lastly, what is the future of MDR and postmarket

1 surveillance? Well, with regard to medical-device  
2 reporting, we are moving more towards summary reporting and  
3 away from individual reporting for efficiency sake. We are  
4 exploring the opportunities of using a sentinel reporting  
5 system using a subset of user facilities to report to us  
6 rather than the universe in an attempt to get high-quality  
7 reports.

8 We are moving into the electronic age and we hope  
9 that reports could be submitted electronically as opposed to  
10 hard copy. We hope to integrate more with the quality-  
11 systems regulation especially in trending requirements of  
12 adverse-event reports. And we are beginning a process of  
13 exchanging adverse-event reports internationally.

14 What is on the front for postmarket surveillance?  
15 As I have alluded to previously, we need to have at our  
16 disposal a wider variety of design approaches. There needs  
17 to be more collaboration with industry and the clinical  
18 community, and we need to have expanded access to different  
19 data sources to help address these important public-health  
20 questions.

21 Thank you.

22 DR. JANOSKY: Thank you.

23 Are there any comments or questions from the  
24 panel? Again, thank you.

25 At this time, we will move into the open public

1 hearing. At issue today is a review of a premarket approval  
2 application by the sponsor TMJ Concepts.

3 For the open public hearing, we have five  
4 presentations. The order in which we will go through these  
5 presentations is as follows: the first will be by Ms. Lisa  
6 Brown from the TMJ Association. The second will be by Mr.  
7 Kevin Clark from the TMJ Association. The third will be by  
8 Diana Zuckerman from the National Women's Health Network  
9 followed by two letters which will be read into the record  
10 by Ms. Pamela Scott.

11 Each of the presenters are given ten minutes and I  
12 ask the speakers to state whether or not they have any  
13 involvement included, but not limiting to, financial  
14 involvement with manufacturers of the products being  
15 discussed today or with their competitors.

16 Before we hear from Ms. Lisa Brown from the TMJ  
17 Association, Dr. Susan Runner has some comments for us.

18 DR. RUNNER: Just briefly, it was brought to our  
19 attention that the terminology for these different devices  
20 today can be confusing because of the use of the word TMJ  
21 implants, et cetera, in many of these devices.

22 So, for the purposes of this meeting, when we  
23 refer to TMJ implants, we are talking about the generic  
24 device type. When we are referring to the TMJ Concepts  
25 device, we will refer to it as the TMJ Concepts device.

1 When we are referring to the TMJ Implants Inc. device, we  
2 will refer to that as the Christensen device.

3 I have checked this with the sponsors and they are  
4 all in agreement with that. So we have TMJ implants is the  
5 generic device type, TMJ Concepts is the device we are  
6 considering today. And the Christensen device is the third  
7 device type.

8 Thank you.

9 DR. JANOSKY: Thank you.

10 Ms. Lisa Brown from the TMJ Association.

11 **Open Public Hearing**

12 MS. BROWN: Good morning. My name is Lisa Brown.  
13 I am a TMJ patient and board member of the TMJ Association.  
14 I have no involvement with manufacturers or products being  
15 discussed today, financially or otherwise, or with their  
16 competitors.

17 I would like to thank the FDA for the opportunity  
18 to testify before you today. The TMJ Association was  
19 founded by two women who were experiencing problems with  
20 their TMJ implants. In the thirteen years of its existence,  
21 the Association has grown from a local to a national  
22 organization in touch with thousands of TMJ patients.

23 With the advent of our website, newsletters, e-  
24 mail and other contacts, we have heard from many thousands  
25 more nationally and internationally. We are here today to

1 speak for over 10 million people in America, the majority  
2 women, who suffer pain and dysfunction in and around the  
3 temporomandibular joint.

4 Not all of these women need implants. But for  
5 those who do, it is the responsibility of the FDA and the  
6 panel to assure them that safe, reliable and effective  
7 devices are available, ones that will give them back the  
8 proper use of their jaws, ideally allowing them to bite,  
9 chew and swallow food, to smile and kiss, to laugh, talk and  
10 sing and to do so without pain or discomfort.

11 I have with me samples of letters and comments we  
12 have received from people within the last several years  
13 describing their experiences with TMJ implants. We feel  
14 there is no better way of communicating these patients'  
15 perspectives than to let you hear them in their own words.

16 I will start by quoting a woman who called the  
17 Association. The bilateral devices she received were her  
18 first implants. She said, "The implants hurt so bad I cry  
19 all of the time. My surgeon told me these implants work  
20 97 percent of the time."

21 Like so many others, this lady thought she would  
22 be rid of TMJ problems after she received these devices,  
23 cured so to speak. She had the devices implanted in order  
24 to regain her quality of life and thought that a 97 percent  
25 chance of being cured was almost a guarantee of success. In

1 reality, what she received was increased destruction of her  
2 jaw joints and her life. She wanted to know if she was the  
3 only one.

4           What is sad about this is the only comfort we  
5 could offer her was that she is not alone and that there are  
6 many others. We desperately need safe and effective devices  
7 and we desperately need a solid scientific base that goes at  
8 the heart of the problem of what cause TMJ diseases and  
9 disorders and how best we can treat them.

10           Now let me turn to the letters. From Missouri: "I  
11 have piercing pains in my jaw joints since the most recent  
12 implants were put in. I called the implant manufacturer and  
13 they won't send me anything. I have also called the FDA. I  
14 hear the implants cracking."

15           From Pennsylvania: "I continue to work because I  
16 don't want this to conquer me. I am in very bad physical  
17 condition since my implants and my coworkers see it. My  
18 eyes are black and blue and I have lymphoma. When I see a  
19 doctor or surgeon now or go to the pain clinic, they tell me  
20 it is all in my head. If I add up what I have spent on  
21 treatments, it is over a million dollars."

22           From South Carolina: "I developed a massive lump  
23 when my first implants were put in. When I called the  
24 surgeon, he blamed me for flying in an airplane and then  
25 abandoned me. I have had to have my parotid gland removed

1 and my eyes sown shut for a year. My most recent implant  
2 failed, had to be removed and they left my jaw with nothing  
3 for more than a year. I now have a rib graft and I am going  
4 to a pain clinic."

5 From Mississippi: "My doctor now has me on shark  
6 cartilage and magnets for pain. Is that a good idea around  
7 my implants? I have severe pain 24 hours a day and I can't  
8 hold my head still. It bobs up and down from spasms."

9 From Delaware: "I am now on two seizure medicines.  
10 I had to have the implants removed because the screws came  
11 out. The hip cartilage didn't work at all and now I have a  
12 new set of the same implants again. I am now having  
13 problems with the hip that they took the cartilage from."

14 From West Virginia: "I have excess bone growth and  
15 scar tissue after my implant. The surgeon placed a bite  
16 block in my mouth during surgery and I woke up screaming.  
17 The surgeon said it was the drugs and put me in detox the  
18 day after surgery. Now no one will listen."

19 From Michigan: "My vision is blurred terribly, but  
20 the surgeon told me there is nothing wrong, the implants  
21 look fine. The implants I have now are loose. They are not  
22 holding so I can't eat anymore. Physical therapy just makes  
23 things worse."

24 From California: "I am not doing good after these  
25 implants. Doctors and surgeons want nothing to do with me

1 now. I need a competent physician. I want to know how  
2 victims of the lack of standard of care can protect  
3 themselves. How am I supposed to get insurance coverage  
4 now?"

5 From Florida: "Since I had these implants put in,  
6 I am still having four more seizures per day and terrible  
7 double vision even though I am taking dilantin. Now, I have  
8 no money for the doctor and don't know what to do."

9 From Hawaii: "My surgeon tells me that the Vitek  
10 implants I had are eating away at my current implants. I am  
11 getting a lot of adhesions. My ears burn and ring and I am  
12 constantly tired. I have no energy."

13 From Ohio: "I keep getting a spiel about the  
14 false-positive/false-negative results on my test. Since my  
15 implant is failing, my oral surgeon thinks I need a new  
16 condyle part of the same implant. My neurologist says not  
17 to have any more surgeries because of the neurological  
18 damage that already exists. Then my oral surgeon says, 'You  
19 need surgery.' What do I do?"

20 From Georgia: "My surgeon told me, "You all have  
21 this disease. It is not the device. It is the disease.  
22 Then he told me that there is wear on my current implants,  
23 but he only puts them in; he doesn't take them out."

24 From Canada: "Since these implants, I am unable to  
25 work and have a constant fever. I have to take Demoral for

1 pain. Now my joints are coming out through my skin and I am  
2 not sure what to do."

3 The TMJ Association was begun when problems were  
4 occurring from Vitek and Silastic TMJ implants. To quote  
5 the late Congressman, Ted Weiss, "These devices fail  
6 100 percent of the time." When Vitek implants were finally  
7 recalled by the FDA in December, 1990, the disaster for  
8 patients was swept under a rug, a rug of denial,  
9 abandonment, mistrust and abuse.

10 The recall was not the end of the disaster,  
11 however, as Silastic became a big seller along with a dozen  
12 other devices. Many of these devices slipped through the  
13 FDA approval process by being called "custom devices," or  
14 qualified as being substantially equivalent to the devices  
15 already on the market.

16 The TMJ Association has been asking for valid  
17 clinical data for years now. We, the patients, need hope  
18 and reassurance that there are safe and effective devices to  
19 restore jaw function, but we have been burned before and we  
20 are twice shy. We do not know whether the devices under  
21 consideration today are safer or more effective than the  
22 Vitek or Silastic devices.

23 No one can even tell us how many of these devices  
24 have been implanted. No one can tell us why we have  
25 received hundreds of calls from patients who say they are

1 failing. The problem is especially tragic for people  
2 originally injured by Vitek and Silastic devices. Their  
3 lives are a constant torment. They need replacement  
4 devices, but continue to experience implant failure after  
5 failure in a pattern that increases complications and  
6 diminishes the quality of their lives.

7 For the patients who have had no prior implants,  
8 and who need devices, a potential for disaster exists.  
9 Members of the panel, it is no exaggeration to say that  
10 lives are at stake. We respect the science and clinical  
11 experience you bring to the issues before you. The  
12 decisions you make in the course of the meeting are critical  
13 to us and to the millions of TMJ patients we represent.

14 Thank you.

15 DR. JANOSKY: Thank you.

16 Mr. Kevin Clark representing TMJ Association.

17 MR. CLARK: Good morning. My name is Kevin Clark.

18 I have no involvement, financial or otherwise, with the  
19 companies here today and tomorrow or any of their  
20 competitors.

21 By profession, I am a stock trader and a partner  
22 in Hartland Advisors, a Milwaukee-based money-management  
23 firm. By marriage, I am Heidi Clark's husband. Heidi is a  
24 beautiful 35-year-old woman who had a promising career which  
25 was nipped in the bud by multiple surgical procedures

1 involving multiple types of implants.

2 Heidi, as many TMJ patients, is in desperate need  
3 of her fourth and fifth surgical implants, total joints,  
4 because the last three have failed. Perhaps it was the many  
5 evenings when I returned from work to find Heidi writhing in  
6 pain, begging me to help her take her life or when I visited  
7 her in locked word after the total joints were implanted,  
8 but, at some time, I knew something needed to be done to  
9 change the TMJ system.

10 Two years ago, I became a member of the board of  
11 the TMJ Association. I joined this patient-advocacy  
12 organization because it is fighting valiantly and against  
13 incredible forces to change the face of TMJ by demanding the  
14 science to explain the etiology and pathogenesis of this  
15 disease as well as the science underlying the many  
16 treatments being recommended to the patients.

17 In short, our motto is, "Show us the science."  
18 This philosophy has evolved from being sold hope along with  
19 the treatment only to have it shattered time and again with  
20 the lives of the patients and we who love them.

21 Lisa Brown has given you a picture of what life  
22 can be like as a result of implantation of a TMJ device.  
23 Needless to say, we believe there are some patients which  
24 these devices have helped and improved their life, but we  
25 have heard from only a few or a handful of them.

1           The ones we have heard from are those whose lives  
2 and health have been increasingly compromised, worsened, or,  
3 in some cases, even resulted in death. This panel meeting  
4 is a monumental event in the lives of TMJ patients. TMJ  
5 devices, some on the market since the early 60's, are being  
6 implanted a fourth of an inch from one's brain, fell through  
7 the cracks of the FDA classification process.

8           It was only in 1992, during the Congressional  
9 hearing entitled, "Are FDA and NIH Ignoring the Dangers of  
10 Jaw Implants?" that the late Congressman, Ted Weiss,  
11 relentlessly asked the FDA, "When will you classify these  
12 devices?"

13           Upon the third time, Mr. Benson responded, "This  
14 month." A month short of seven years, and ten years after  
15 the Vitek class I recall, TMJ will finally learn how safe  
16 and effective TMJ Concepts and TMJ Implants, Inc., devices  
17 are.

18           The panel meeting is monumental in another aspect.  
19 It is the first time that a TMJ patient will voice the  
20 concerns of all of us. In 1993, the Human Development  
21 Report of the United Nations stated, "People today have an  
22 urge, an impatient urge, to participate in the events and  
23 processes that shape their lives. Properly harnessed, this  
24 resource can become a source of tremendous vitality and  
25 innovation."

1 We thank the FDA for recognizing the importance of  
2 letting someone speak for the many who can't. The TMJ  
3 patients issue a challenge to this panel and, ultimately, to  
4 the FDA. The challenge is to simply critically evaluate the  
5 scientific information that these two manufacturers have  
6 submitted to you.

7 We ask nothing more from you than to evaluate  
8 submitted studies and determine whether these products are  
9 so safe that you would have them put into your child, your  
10 spouse, or even yourself.

11 Thank you very much.

12 DR. JANOSKY: Thank you, Mr. Clark.

13 The next speaker is Dr. Diana Zuckerman from the  
14 National Women's Health Network.

15 DR. ZUCKERMAN: I am Dr. Diana Zuckerman. I am on  
16 the board of the National Women's Health Network which is a  
17 private, non-profit, consumer organization that has no  
18 financial ties to the TMJ issue. The Network is dedicated  
19 to improving healthcare for women and is especially  
20 interested in making sure that medical products are  
21 appropriately regulated and that women have accurate  
22 information about medical products and procedures.

23 I am here to urge you to carefully consider  
24 whether the studies submitted for the PMA today and tomorrow  
25 prove that these products are safe and effective for long-

1 term use. As you all know, TMJ implants are intended for  
2 long-term use and the history of jaw implants is that some  
3 implants have provided temporary relief in the short term  
4 and tragic consequences in the long term, as you have heard  
5 earlier today.

6 I have no experience with TMJ implants as a  
7 patient, but I have personally had a great deal of  
8 experience regarding FDA's role in the regulation of TMJ  
9 implants. For eight years, I worked as a Congressional  
10 investigator for the House subcommittee that has  
11 jurisdiction over all of the federal health programs.

12 In 1992, I urged the Chairman of that  
13 subcommittee, the late Representative Ted Weiss, to hold  
14 hearings on the inadequacy of FDA oversight of TMJ implants  
15 and I conducted the investigation for the subcommittee.

16 During our investigation, we were shocked that the  
17 FDA had allowed TMJ implants to be sold and continued to  
18 allow them to be sold despite very clear evidence of very  
19 serious, irreversible damage in many patients. At our  
20 hearing, which was held in June of 1992, James Benson, who  
21 was Head of the Center for Devices at FDA, promised--  
22 promised--the Congress that FDA would require the  
23 manufacturers to submit safety data through the premarket-  
24 approval process, "As swiftly as we can."

25 It was not long after that hearing that Mr. Benson

1 left the FDA and went on to a leadership position at HIMA,  
2 which is the Association for Medical Device Manufacturers.  
3 HIMA, of course, works very hard to keep devices on the  
4 market. Congressman Ted Weiss died a few months after the  
5 hearing on the TMJ implants and, as a result of his death, I  
6 also left the subcommittee.

7           It has taken seven years now, seven years, for FDA  
8 to finally hold these hearings on TMJ implants. I would  
9 have to say the system, so far, has failed that patients.  
10 These hearings are long overdue and it is now up to you to  
11 make sure that FDA finally gives these devices the scrutiny  
12 that they deserve.

13           I am a researcher by training and I realize it is  
14 very difficult, very, very difficult, to evaluate the  
15 effectiveness of these kinds of devices, particularly for  
16 long-term use. One particular problem is that so many of  
17 the patients have had other devices previously put in that  
18 have failed and yet you are supposed to evaluate these  
19 devices which are maybe different from the devices that  
20 these patients have had before.

21           But that is the real world. Those are the  
22 patients that are using these implants. That is the  
23 population that really does need to be carefully studied.  
24 The damage caused by unsafe TMJ implants, as you have heard,  
25 can be serious, debilitating and irreversible.

1 I have spoken to patients whose lives have truly  
2 been ruined by the pain and serious health problems cause by  
3 their implants. As you have heard, these are patients who  
4 cannot eat regular food. They cannot speak or kiss without  
5 pain and there are those who can barely think or function  
6 because of the pain and the debilitating effects of pain  
7 medication.

8 It is unfortunate that, because of that very  
9 serious damage, that there are not more people who were able  
10 to come and speak to you today. They are not in a position  
11 to do that and so those of us who can come, it is our  
12 responsibility to tell you what it is all about.

13 When FDA determines that a medical device is safe  
14 and effective, patients are, of course, much more likely to  
15 use it. Since these TMJ implants have already been  
16 available for many years due to grandfathering and due to  
17 the lax regulation, the standard for approval should be even  
18 higher than is usually the case in a PMA.

19 If FDA gives approval to implants that are not  
20 really proven safe or effective, obviously, it undermines  
21 FDA as an agency and the trust that Americans have in FDA,  
22 in particular, and in their government more generally. So,  
23 in reviewing these PMA applications, the National Women's  
24 Health Network asks you to consider the following three  
25 issues.

1           Number one; is there clear evidence that the  
2 product is safe for long-term use, by which we mean more  
3 than five to ten years, for patients who have not previously  
4 had any implants? How does the implant patients fare  
5 compared to patients who have not had any implants?

6           Number two; is there clear evidence that the  
7 product is safe for long-term use, again more than five to  
8 ten years, for patients who previously have had other kinds  
9 of implants? What is going to happen to those patients and  
10 how do those implant patients fare compared to other  
11 important patients who have previously had those kinds of  
12 implants but those implants were removed?

13           Three; if a patient has problems with one of these  
14 implants, do the problems persist after the implant is  
15 removed? What happens if an implant has to be removed?  
16 What happens to that patient? Can the implant cause  
17 irreversible damage even after the implant is removed?

18           Of course, I haven't seen the studies that you are  
19 going to be looking at this morning and reviewing. That is  
20 not what I am used to. I am used to having seen them before  
21 anybody else. But I can't, therefore, comment on the study  
22 design or the quality of the research. Based on my previous  
23 experience, I am concerned that they may not include a large  
24 random sample of patients who were followed for a  
25 substantial period of time, that they may not be evaluated

1 as objectively as possible by individuals who do not have a  
2 financial interest in the outcome of the study.

3           Studies of selected patients or patients who have  
4 been studied for short periods of time, or samples where a  
5 large percentage of the patients have dropped out, will not  
6 provide the kind of information that you need to determine  
7 whether these implants are safe and effective.

8           So, based on the experience of many TMJ implants,  
9 it appears that, to paraphrase an old advertisement,  
10 "Implants are forever." Unlike most drugs, the detrimental  
11 effect of unsafe implants may be and can be and has  
12 sometimes been irreversible. So, any short-term safety data  
13 doesn't tell us what we need to know.

14           In order for you to do your job to make sure that  
15 TMJ patients are protected, it is essential that a  
16 substantial number of patients be studied for a long period  
17 of time and that patients not disappear during follow up.  
18 Please keep that in mind as you review these studies. The  
19 lives and the quality of lives of many thousands of patients  
20 depend on it.

21           Thank you.

22           DR. JANOSKY: Thank you.

23           The two letters that I had alluded to earlier are  
24 concerning the Christensen device so we will hear those  
25 letters tomorrow during the open public forum.

1 Any questions or comments from panel members?

2 DR PATTERS: I would like to ask spokespersons  
3 from TMJ Association as well as Dr. Zuckerman that,  
4 hypothetically, if this panel found that, indeed, clear  
5 evidence of long-term safety and efficacy did not exist,  
6 what do you believe this panel should recommend to FDA?

7 DR. JANOSKY: Would one of the three presenters  
8 like to comment, Ms. Brown, Mr. Clark or Dr. Zuckerman?

9 DR. ZUCKERMAN: Given the history of TMJ implants,  
10 I would have to say that if there are no long-term safety  
11 data, that it doesn't prove that they are safe long-term,  
12 they shouldn't be approved for sale.

13 DR. JANOSKY: Additional comments or questions?

14 If not, then, at this time we would like to move  
15 into the presentation by industry. The presentation will be  
16 done by TMJ Concepts. You have one hour for the  
17 presentation.

18 **Industry Presentation**

19 **TMJ Concepts Patient-Fitted TMJ Reconstruction Prosthesis**

20 MR. ROSE: Good morning. My name is Greg Rose. I  
21 am the Director of Regulatory Affairs and Quality Assurance  
22 at TMJ Concepts. I am a mechanical engineer with twelve  
23 years of experience in the design and development of medical  
24 products with an emphasis on orthopedic implants and  
25 instrumentation.

1           This morning I will be presenting a description of  
2 our device and a summary of the preclinical studies that  
3 were performed. Following my presentation, Dr. Louis  
4 Mercuri will be discussing the clinical aspects of this  
5 implant and the summaries of the clinical studies.

6           This patient-fitted TMJ reconstruction prosthesis  
7 is comprised of a mandibular and a glenoid-fossa component  
8 that have been manufactured specifically for a particular  
9 patient. An anatomical bone model is produced from a CT  
10 scan of the patient's mandible and maxilla. This model is  
11 used to design and manufacture these implants to accommodate  
12 the patient's unique anatomy and the implanting surgeon's  
13 preoperative plans.

14           I have several slides to show, and I also have  
15 some samples that you are welcome to look at during the  
16 break.

17           This demonstrates the unique nature of each set of  
18 implants.

19           The mandibular component is composed of a condylar  
20 head fabricated from raw cobalt-chromium-molybdenum alloy in  
21 a mandibular body that is fabricated from titanium alloy.

22           The glenoid-fossa component is comprised of a  
23 fossa bearing fabricated from ultra-high-molecular-weight  
24 polyethylene in a mesh backing which is fabricated from  
25 unalloyed titanium, as shown in this slide.

1           The implant fixation of both the mandibular and  
2 glenoid-fossa components is achieved using small bone  
3 screws, 2.0 millimeter diameter. 2.3 millimeter diameter  
4 screws are also provided as a safety screw.

5           The materials that are used to make these implants  
6 comply with various ASTM standards which are currently  
7 accepted by the Dental and Orthopedic Branches within ODE.  
8 They are also state-of-the-art materials that are used for  
9 orthopedic implants such as hips and knees.

10           We also provide an instrument set that is used to  
11 replace the implant for anchoring the bone screws.

12           Both the fatigue and the static-strength testing  
13 that were performed were done using a similar setup.  
14 Implants were held in an anatomic position. They were  
15 angled at 23 degrees in the anterior-posterior plane and 10  
16 degrees in the medial-lateral plane.

17           This shows the setup that was used to perform the  
18 static-strength testing.

19           The fatigue testing was done on six specimens that  
20 were manufactured to the worst-case conditions being the  
21 narrowest and thinnest implants. The loading was  
22 sinusoidal. It was done from 150 pounds maximum to 7 pounds  
23 minimum at 12 Hertz. Testing was performed over 10 million  
24 cycles. The failure criteria was for looking for gross  
25 fracture of the part or a crack present under zygopenetrant

1 inspection. No failures were observed.

2           The static-strength testing that was performed was  
3 on six specimens, also. The specimens were loaded until  
4 yielding a fracture and the peak load was recorded. The  
5 average failure was identified as 790 pounds.

6           Bond testing was performed to ascertain if the  
7 implant could withstand possible separation forces on the  
8 fossa component. Failure criteria was established at 75  
9 pounds force and shear. The normal implant loading is in  
10 compression and doesn't actually create any separation  
11 forces. This was established as a proposed impact load that  
12 the device may receive.

13           The results of this test was that there is no  
14 specimen failure and the average shear strengths were  
15 reported below. Low and high parameters were evaluated in  
16 the bonding process. Average shear strength at the low  
17 process parameters was 368 pounds and 322 pounds at the high  
18 parameters.

19           The wear testing that was performed was done on a  
20 special mechanism which was developed that articulated the  
21 device over 25 degrees of rotation. This provided about  
22 8.3 millimeters of translation and it was done under a  
23 9 kilogram constant load through the entire cycle. This was  
24 considered worst-case as, during the normal chewing cycle,  
25 the joint is actually only loaded temporarily.

1           There were six specimens tested over 5 million  
2 cycles under this constant load. The frequency rate was  
3 approximately 54 cycles per minute. The environment used  
4 was bovine serum at room temperature. The setup is shown  
5 here in this slide.

6           The depth of the wear track that was created in  
7 the fossa component was then directly measured. This was  
8 plotted against the number of cycles that implant had been  
9 exposed to.

10           A linear regression was then performed to estimate  
11 the wear rate that was occurring on each of the implants  
12 tested. You can see here the linear regressions and the  
13 slopes of the lines were determined.

14           The wear test results were then evaluated and we  
15 established a penetrative wear rate for the implant. We  
16 have a 3 millimeter minimum polyethylene thickness. The  
17 average penetrative wear rate was 0.0097 millimeters per  
18 million cycles shown in the bottom right-hand corner.

19           The worst case of all of these wears that were  
20 seen was looking at the worst one of these specimens. The  
21 wear life was estimated at 173 million cycles, looking at  
22 the worst case of these specimens. There are different  
23 models for the number of cycles a patient may see, but a  
24 commonly accepted one in the literature has been a million  
25 cycles per year and, with this testing, the device should

1 withstand more than a lifetime for any given patient.

2 That concludes the preclinical testing that was  
3 done. Thank you.

4 DR. MERCURI: Thank you to the panel for allowing  
5 us to present this material today. My name is Louis  
6 Mercuri. I am a professor of surgery at the Loyola  
7 University School of Medicine, Department of Oral and  
8 Maxillofacial Surgery.

9 I have been involved with temporomandibular-joint  
10 problems for over thirty years in my clinical career and I  
11 have been involved with the temporomandibular-joint concepts  
12 in Techmedica prosthesis since its inception. I have no  
13 financial involvement with the company as of the present  
14 date. I have received some computer support and a minimal  
15 consultant's fee for the work that I have done over these  
16 ten years.

17 Since we have such a diverse and varied group  
18 here, I don't want to be pedantic, but I think we should all  
19 be sure that we understand the problem that we are dealing  
20 with. I would like to start out by saying that we are  
21 dealing with temporomandibular-joint disorders here and it  
22 is a spectrum of problems that we deal with.

23 Today we are going to basically focus on the  
24 problems that affect the temporomandibular joint, itself.

25 Not only is there a spectrum of this disorder but

1 there is also a spectrum of the management for this  
2 disorder. This is my own classification of the modalities  
3 that have been used in the past. It is certainly not all-  
4 inclusive, but, for today's discussion, I would like to  
5 focus, again, down on the invasive modalities. We are  
6 specifically going to be talking about total  
7 temporomandibular-joint reconstruction.

8 I bring this slide to your attention because I  
9 would like you all to understand that my own philosophy is  
10 that the vast majority of patients with temporomandibular-  
11 joint dysfunction can be treated in a non-invasive manner,  
12 so I do not like the panel to feel that my thoughts on the  
13 clinical aspects of temporomandibular-joint management are  
14 only focussed on total joint replacement.

15 I firmly believe that the vast majority of  
16 patients, as we stand here today, can be treated in a  
17 noninvasive manner for generalized temporomandibular-joint  
18 dysfunction. But, for the sake of today's discussion, we  
19 will focus only on total joint reconstruction.

20 The reason I got involved in this was this is the  
21 profile of patients that I was starting to see in 1989. As  
22 I said, I have had ten years of involvement with this. They  
23 presented me with a significant problem. The patients that  
24 were discussed in the patient advocacy part of this  
25 presentation were basically these types of patients.

1 I was presented with the clinical dilemma of how  
2 to deal with the functional problems that these patients  
3 had. In 1989, the available prostheses, the stock  
4 prostheses, that were available, the TMJ implants that were  
5 available, could not handle the mutilated joints that we  
6 were seeing in these patients.

7 Therefore, we started looking at what should be  
8 the goal in treating this type of patient. We are now  
9 focussing in a very specific type of patient that I think  
10 you have gotten the flavor for. What should be the goal in  
11 reconstructing these types of patients?

12 I went back into the orthopedic literature and Dr.  
13 Petty's book talks about what the orthopedic surgeon would  
14 do to manage this type of problem because I firmly believe  
15 that this problem is an orthopedic problem.

16 These are the goals that have been developed for  
17 the management of this particular focussed group of  
18 patients. We would like to improve their function and form.  
19 We would like to reduce their suffering. We would like to  
20 contain excessive treatment--in other words, stop any  
21 further treatment that they would have to have, contain  
22 further costs to the system, and prevent further morbidity.

23 When I looked into the goals for  
24 temporomandibular-joint reconstruction that were proposed by  
25 the American Association of Oral and Maxillofacial Surgeons,

1 those goals do not address the problems of this particular  
2 type of patient. Expecting pain relief that is 100 percent  
3 is not possible in this particular type of patient.

4 So the criteria that was established by AAOMS and  
5 was published by AAOMS is really not applicable to this  
6 particular group of patients.

7 I then realized that I could not deal with  
8 treating these patients, or managing these patients, with  
9 autogenous tissue. Autogenous tissue failed routinely. In  
10 other words, we are talking now about rib grafts, bone  
11 grafts, these kinds of things, because these patients were  
12 so multiply operated that the vascular bed that is required  
13 for a free bone graft to exist and to head was not there.

14 So, again, borrowing from my experience in the  
15 orthopedic literature, this is basically a quote borrowed  
16 from Dr. Harris at Harvard, that, we saw an alloplastic  
17 temporomandibular-joint reconstruction--in other words, a  
18 temporomandibular-joint implant--as the only possible way to  
19 deal with these particular focussed groups of patients.

20 We must understand that an alloplastic  
21 temporomandibular-joint reconstruction is a biomechanical  
22 solution to severe debilitating anatomical joint disease.  
23 It is not a primary device. These devices are used to  
24 salvage patients who have an end-stage disease because they  
25 have pathologically mutilated joints.

1           We then looked at what types of materials have  
2 orthopedic surgeons used successfully over the years. If we  
3 can again go back to the work of Sir John Charnley, back in  
4 the 1960s, he found that having a stable part or a non-  
5 moveable part, being a metal-backed, ultra-high-molecular-  
6 weight-polyethylene fossa operating against a moveable metal  
7 condyle had the best potential for wear.

8           It also had the best potential for the device  
9 having long-term success. So, orthopedic surgery, the  
10 benchmark for devices was an ultra-high-molecular-weight  
11 metal-backed fossa with a chrome-cobalt-molybdenum mobile  
12 element or condyle. Therefore, the decision was made to  
13 develop a device that mimicked the success that was seen in  
14 orthopedic surgery with these benchmark materials.

15           As you have read in the PMA, these are the  
16 indications that have been proposed in the PMA for the use  
17 of the TMJ Concepts device.

18           What I would like to do now is go through some  
19 clinical slides to give you the flavor of the types of  
20 patients that we are dealing with.

21           The indications I want to talk about is, number  
22 one, ankylosis. For the non-clinicians in the group, this  
23 is a CT scan in a sagittal view. The temporomandibular  
24 joints are these areas right here, so we are looking at the  
25 right and the left temporomandibular joint. Normally, the

1 joint should look like a drumstick, the end of a drumstick,  
2 like a chicken leg.

3           You can see, obviously, that these joints are  
4 mutilated by the disease process and there is, to my  
5 estimation, and the estimation of many of my colleagues,  
6 there is no way that a stock device can be made stable to  
7 fit this situation.

8           As Mr. Rose has shown you, this is a model made  
9 from the CT scan of that particular patient's problem.  
10 There is no joint anatomy in this situation. Failed  
11 otogenous bone or soft-tissue grafts. These are rib grafts  
12 that were placed in a patient who had had Proplast/Teflon  
13 implants. You can see the penetration into the medial  
14 cranial fossa here.

15           Once again, these joints should look like  
16 drumsticks on a chicken leg and you can see you have a very  
17 mottled appearance here. These are failed rib grafts. The  
18 work of Wolford and his colleague have shown that the  
19 placement of autogenous tissue into a joint that has  
20 previously experienced Proplast/Teflon is doomed to failure.

21           This is a typical patient who has had a rib graft  
22 that has failed after Proplast/Teflon. Once again, you can  
23 see that there is no anatomy here. This is the fossa.  
24 There is no way a non-patient-fitted device or a stock  
25 device would be able to fit in this particular situation.

1 Destruction of autogenous graft due to pathology.  
2 This is an auricular cartilage graft that has failed in a  
3 patient who had Proplast/Teflon in place prior to that. You  
4 can see again, in a sagittal view, that the joint, the  
5 fossa, has been completely destroyed as well as condyle.  
6 The patient has lost vertical dimension because of that.

7 Here is the model that demonstrates the mutilated  
8 anatomy associated with this particular problem.

9 Failed Proplast/Teflon interpositional implants;  
10 here, again, is a sagittal view of the patient. This is  
11 posterior-anterior. This is left of the condyle. You can  
12 see the implant in place and the destruction that it has  
13 caused not only to the fossa but the to articular eminence  
14 as well.

15 Here is a model of that particular patient with  
16 the mutilated anatomy.

17 This is another patient who had Silastic in place  
18 for about seven years and the destruction that that had  
19 created, again creating a mutilated anatomy which is very  
20 difficult to deal with with a stock prosthesis. I must  
21 remind you that the principle in the alloplastic management  
22 of joint replacement is that the device must be stable in  
23 situ in order for it to have any sort of lifespan.

24 Failed total-joint prostheses, not only the Vitek.  
25 This happened to be a Vitek that is eroded into the

1 articular eminence. But we have also seen failure of other  
2 alloplastic implants. This is a device that fractured after  
3 one year because the stem was too narrow.

4 Here is another device that was used to  
5 reconstruct the temporomandibular joint that failed.  
6 Interestingly enough, we see, from the literature again, in  
7 Fontino's work, that typically temporomandibular-joint  
8 implants have a tendency to show failure within the first  
9 three or four years, if they are going to fail.

10 Most of these patients have these failures in that  
11 period of time. Here is another one, a fracture in the  
12 implant. Here is another implant; the screws are fractured  
13 as a result of the fact that it is much too thin.

14 This is a fossa that was grouted in place using  
15 polymethylmethacrylate. Someone determined that since  
16 orthopedic surgeons use polymethylmethacrylate, maybe we can  
17 grout these things into place. The problem with this in the  
18 temporomandibular joint is that we see fractures of the  
19 mantle of polymethylmethacrylate. This creates a foreign-  
20 body giant-cell reaction and causes these implants to fail.  
21 So grouting implants in is not a reasonable approach.

22 Here is another failed implant, fracture of the  
23 implant, also loss of the polymethylmethacrylate, the head.  
24 When we look at the tissue, we can see particulation of the  
25 polymethylmethacrylate, not a tremendous reaction.

1 Certainly nothing like we saw with Proplast/Teflon, but  
2 there is still particulation in the tissue.

3           Something we are seeing now are failures of the  
4 metallic fossa where the fossa is fracturing and creating  
5 particulation with the process of metallosis and a little  
6 bit more of a reaction to this type. So we are now seeing  
7 patients where we are removing these prostheses and, again,  
8 developing this mutilated anatomy that can only be dealt  
9 with with a--

10           Here is another one. This will give you the  
11 flavor for this. This is a patient with rheumatoid on the  
12 model. You can see there are no condyles in this patient,  
13 so it is a significant deformity for these folks.

14           If I could go to the overheads.

15           I just want to have one more--this is some data  
16 that we looked at in patients with failed devices. I am  
17 sorry that this doesn't project well but maybe you can see  
18 it. It was 162 patients with failed devices or failed  
19 grafts. This sort of gives you the distribution of the  
20 failed grafts. 33 percent of the patients had failed  
21 previous grafts; reported with failed devices, 48 percent  
22 with failed devices.

23           Obviously, the vast majority of those,  
24 22.8 percent of those, were Vitek devices but there are  
25 other devices associated with failure in here as well. So I

1 just want to give you a flavor for the devices that we have  
2 seen in the patient cohort that I am going to present to you  
3 now.

4 I am going to go into the clinical studies now.  
5 This data was collected from eight different surgeons in  
6 five different states using established inclusion and  
7 exclusion criteria with a protocol that was published in the  
8 1995 Journal of Oral Maxillofacial Surgery article that I  
9 authored along with three other surgeons and a  
10 biostatistician which formed that basis for the 510(k)  
11 application that was made and approved.

12 I am going to present three studies today. The  
13 first one is a review of this study, but all of these  
14 studies were based on the use, for subjective criteria, of  
15 the visual-analogue scale. Again, not to be pedantic but so  
16 that, again, we are all on the same wavelength, I would like  
17 to discuss the visual-analogue scale that was used in these  
18 studies.

19 The visual-analogue scale is a way for the patient  
20 to be able to objectify a subjective response. I think all  
21 of us will agree that pain, jaw function and a patient's  
22 ability to eat is a subjective response. In order to  
23 quantify that response, we have asked patients to make a  
24 mark along this 55-millimeter line as to where they consider  
25 their pain level to be, their jaw function to be and their

1 diet to be.

2           The left-hand anchor is the lowest possible  
3 response so the mark is 0. The right-hand anchor is the  
4 severest response or the worst-case scenario and that would  
5 be the highest level of pain. So a patient that would mark  
6 at this level would be a 55 and a patient who would mark at  
7 this level would be a zero.

8           This is from that article. It is a table that  
9 shows the changes in subjective and objective measures.  
10 When we address the subjective measures, what we are talking  
11 about here are the time elements, the time scale. We looked  
12 at the preoperative level of 215 patients with the mean  
13 score and their subjective responses for pain at 42.

14           Their mean, on a subjective response for function,  
15 was 39.5 and their mean diet score was 37.3. As we follow  
16 these patients along with an average of a 13-month follow  
17 up, we can see that these numbers drop significantly in the  
18 area of pain. 42.2 became 19.5.

19           Obviously, the higher score in these measurements  
20 reflects more dysfunction and all three measurements improve  
21 significantly over time. Paired T-tests showed that all  
22 improvements were significant at the p less than 0.0001  
23 level. Therefore, the improvements created by the  
24 prosthesis in this particular study appeared in the second  
25 month postoperatively and continued throughout the four-year

1 follow-up period.

2           We did the same thing with the objective scores.  
3 Objectively, we measured the interincisal opening of the  
4 patients using a bolley gauge. These measurements are  
5 recorded as shown here, that the mean preoperative opening  
6 was 24.2 and that increased as the study progressed over  
7 four years.

8           We also measured left and right lateral  
9 excursions, again because these could be measured  
10 objectively, easily. If we look at the statistics behind  
11 this again, it showed, using the paired-T-test that the  
12 improvement found in the objective results were  
13 statistically significant at the  $p$  equals 0.0001 level.

14           When we go to lateral excursions, we find that  
15 there is no significant change. In fact, the patients  
16 actually look like they got worse. The reason for that is  
17 that lateral excursions are controlled by the lateral  
18 pterygoid muscle which is attached to the condyle and, in  
19 the process of placing any reconstructive prosthesis, the  
20 lateral pterygoid is sacrificed and, therefore, lateral  
21 excursions do not change. In fact, they almost are  
22 completely eliminated.

23           In order to look at the closest follow-up patients  
24 in the study, we looked at 111 patients. These were  
25 basically my patients and Dr. Wolford's patients since they

1 seemed to have the closest follow up. We then did the same  
2 analyses using the subjective variables that I mentioned  
3 before using the visual-analogue scale. Then I will show  
4 you the objective variables in a moment.

5           This 111 patients were subjected--these were the  
6 111 patients that came out of the 215 that were mentioned in  
7 the 1995 study. You can see, again, a statistically  
8 significant decrease over the first six months in pain,  
9 function and diet scores which, as you follow these all the  
10 way through, seem to be consistent.

11           If you look at the raw data for this, you will see  
12 that, as we get down to here, there are small numbers of  
13 patients who have entered the study period. I will address  
14 that issue when I get to the life-table analysis towards the  
15 end of my presentation. But just to give you a flavor for  
16 that, there are about three patients here at 96 months.  
17 There are 13 patients at 84 months, 21 patients at 72  
18 months. And there are 41 patients at 60 months and then the  
19 number drops up into about 60--some patients at 48 months.

20           There has been a question raised about the gaps or  
21 the dropout rate that has been seen. There are a couple of  
22 issues here and I will address the statistical issue first.

23           This is the objective results which pretty much  
24 follows the other--we can see that the patients started at  
25 about 24.something and gradually increased their opening.

1 Again, remember, we are talking about three patients here so  
2 these numbers, as we come out here, may not be quite as  
3 significant.

4 I would like to address this dropout issue. Based  
5 on the 111-patient study which we are calling study 2, the  
6 gaps in the follow-up measurements appear to be random and  
7 unrelated to the values of the measurements. These patients  
8 with a one-year follow up are similar to those without, in  
9 fact. None of the baseline variables are different between  
10 the two groups.

11 This is an analysis that was done by the  
12 biostatistician and submitted on page 0900 of the PMA.  
13 Comparable analysis between the baseline variables of those  
14 patients with and without two-year follow up show that the  
15 two sets of patients are statistically similar.

16 So we are dealing with a subgroup of the large  
17 group. And when we look at them, they are statistically  
18 similar based on the statistical study that the groups were  
19 subjected to. You must understand that I am not a  
20 statistician. I am a clinician. I am presenting the data  
21 from that standpoint.

22 I would also like to read a quote from the review,  
23 Dr. Runner's report in the review, which you have in your  
24 presence. She states that, "Patients with one-year follow  
25 up are very similar to those patients without follow up with

1 no statistically different variables between the two  
2 groups." So this has been subjected to statistical analysis  
3 as well as the FDA's analysis as well.

4 The question also was raised as to, "Can we be  
5 sure that this is a sustained change?" So a  
6 biostatistician, Ms. Hurder, did a Wilcoxon Signed Rank Test  
7 which was performed on the dataset of this 111 patients for  
8 which she was able to subset out 69 patients to see if there  
9 were any significant changes between the baseline and twelve  
10 months.

11 She found, again, if we look at the p-values here,  
12 highly significant p-values which indicate that change in  
13 pain level between baseline and one year was there. For the  
14 mean change data, it appears that the pain levels declined  
15 significantly during the one-year post-operative period.

16 The average change data shown showed significant  
17 decreases in function and diet scores during the first year  
18 of follow up. The maximum incisal-opening scores increased  
19 significantly during the same time interval. In other  
20 words, if we look at the means here, a negative mean will  
21 mean improvement towards the positive side.

22 A positive down here in maximum incisal opening  
23 means that the patient has opened wider. Over the first  
24 year, using the Wilcoxon Signed Rank Test, it showed, at a  
25 very significant level, that there were changes.

1           What we also, then, wanted to look at is this  
2 change sustained over the 12, 24 and 36-month interval. And  
3 so a repeated measure ANOVA-F test was done to prove  
4 statistically that there were changes that occurred.

5           Stabilization is interpreted to mean that the  
6 slope over the interval is zero. In other words, it doesn't  
7 change. The slope of the regression line doesn't change and  
8 if we come up with a p-value of less than 5.0, then we have  
9 no change there.

10           The accompany table shows--I am looking at this  
11 table, now--the estimated coefficient of regression of the  
12 slope, standard error of the estimate of the coefficient,  
13 the degrees of freedom for the test and the f-value  
14 statistic and the p-value for each of the measurements.

15           Nonsignificant p-values for both pain and function  
16 would indicate that the slope of the regression line is not  
17 statistically different from zero; in other words, that  
18 there is a sustained change. Both of these measurements  
19 appear to show stability between 12 and 36 months. So, for  
20 pain and function, we have a significant change that is  
21 stable from 12 to 36 months.

22           The slope of the regression line for diet was  
23 significantly different from zero; therefore, there was a  
24 change. But when we look at the change that occurred, the  
25 change was 1.8 millimeters on the visual analogue scale per

1 year over the study period.

2           Also, the rate of change from the maximal incisal  
3 opening showed an improvement of 0.8 millimeters per year.  
4 Again, it wouldn't be reflected in the p-value because it is  
5 not a statistically significant number.

6           I would also like to comment from Dr. Runner's  
7 review. "A preliminary evaluation of the prospected  
8 postmarket surveillance study was also presented," which is  
9 what I am going to present at this time. "The results are  
10 consistent in the trends for decreased pain, increased  
11 function and increased interincisal opening."

12           What you have before you now is the initial data  
13 from the postmarket surveillance study that has been done on  
14 the patients that have been implanted since 1998. So we  
15 have basically a one-year follow up on these patients. I  
16 realize that one-year follow up is not something that we can  
17 actually base our presentation on but what I would like to  
18 be able to show you is that we can now reproduce the data  
19 that was shown in study 1 which was the report in the  
20 Journal of Oral and Maxillofacial Surgery and study 2 which  
21 was the subset, which, by the way, that study has been  
22 accepted for publication in the peer-reviewed Journal of  
23 Oral and Maxillofacial Surgery.

24           So we are now talking about 128 patients that have  
25 been implanted and ten of those patients have come to one

1 year at this point. So this slope of this line is in  
2 agreement with the slope of the lines of the other two  
3 presentations showing reproducibility of the data.

4 This is, again, the objective results of that same  
5 group of 128 patients. Again, to give you a flavor of the  
6 numbers of patients we are dealing with, this is 128  
7 patients at time 0. At two months, there were 80 patients.  
8 At six months, there were 52 patients and at one year, there  
9 were ten patients.

10 Again, I want to stress the reproducibility of  
11 this data.

12 I think it is important that we talk about adverse  
13 events that have been reported. These adverse events with  
14 the TMJ Concepts device only involved the removal of nine  
15 devices--I'm sorry; thirteen devices in nine patients. If  
16 you look closely at the categories, device removal due to  
17 failure or complication, there are five. These occurred  
18 early in the use of the device and were basically design  
19 issues.

20 The design, as Mr. Rose showed you and that I  
21 showed you, has changed to the point where we use more  
22 screws than were used before. Interestingly enough, even  
23 though we have gone to more screws, these all occurred early  
24 on. As I mentioned before, Fontino's report showed that  
25 alloplastic devices typically will show failure in the first

1 three to four years.

2 We also had devices removed not due to failure or  
3 complication. These were eight devices that were removed in  
4 four patients because the patients wanted them removed. I  
5 don't like to give you anecdotal data but one of the  
6 patients decided that she was receiving radio signals  
7 through it and decided she wanted it removed for that  
8 purpose.

9 Another patient had hers removed because she  
10 decided she didn't want to have metallic devices in place.  
11 We were able to retrieve the histology from the surgeons who  
12 removes these devices--I did not remove these devices--and  
13 found no clinical evidence of any failure of either bone or  
14 soft tissue associated with these devices.

15 So these devices were removed because the patients  
16 wanted them removed not because of a clinical reason to have  
17 them removed. So we only have thirteen devices that were  
18 removed. There was improper fit and dislocation involved  
19 early on. Again, we are talking about the patient-fitted  
20 device that involves a CT scan and it involves a new  
21 technology.

22 As with any new technology, the initial placement  
23 of these can result in learning-curve failures. The  
24 dislocation led to a change in the fossa, putting a lip on  
25 the anterior and a larger lip on the posterior. Since that

1 has been done, there has not been another dislocation that  
2 has been reported.

3           Postoperative infection was only seen in three  
4 devices and three patients all of which resolved easily.  
5 The largest adverse effect, again which didn't result in  
6 removal of the device, was the development of hypertrophic  
7 bone. When we did an analysis of these patients, we found  
8 out that all of these patients, the hypertrophic bone  
9 developed within the first thirteen months.

10           All of these patients had had ten or more prior  
11 procedures, so we feel that there is an important issue  
12 there that should be addressed. And there were others.

13           I would like to take you through the life-table  
14 analysis now. The feeling of a life-table analysis is that,  
15 since patients are not all entering the same interval at the  
16 same time, there should be a statistical way to find out how  
17 long a device that was implanted at time zero will last,  
18 what is the likelihood of that device lasting all the way  
19 through the period.

20           The life-table analysis was developed in two ways.  
21 The first one that you have before you is the life-table  
22 analysis, patients having devices explanted with or without  
23 indication. So that is both groups that I talked about in  
24 the previous slide; the patients who had an indication for  
25 removal of the device and those patients who did not have an

1 indication for the removal of the device.

2           This is in our dataset with the closest follow up  
3 of 11 patients. The key to this is if you look at the  
4 seventh column over, these are the patients that have not  
5 yet entered the period. We can see that there are a large  
6 number of patients who have not entered certain periods.  
7 One of the reasons that it appears that the data has a lot  
8 of holes in it is the fact that we have a large number of  
9 patients who have not even entered the period in order to  
10 collect the data.

11           The other one I would like you to look at is the  
12 fifth column across, this column right here, the total  
13 patients having patients having devices explanted. If we go  
14 down here and we find the fourth and fifth year, all of the  
15 explantations have occurred up in here which basically  
16 agrees with Fontino's study that I mentioned twice already.

17           But now, if we go back down to the fifth year all  
18 the way through the tenth year, granted that the numbers are  
19 small, we still should be seeing some devices that are  
20 failing if this is a bad device. We have no devices that  
21 have failed requiring explantation from the fifth year to  
22 the tenth year.

23           So this life table includes both implants that are  
24 explanted with or without indication and we can see that the  
25 95 percent confidence for the cumulative probability that

1 these devices will last to the ten-year mark, which is the  
2 orthopedic standard is about 85 percent.

3           The next slide is the same life-table analysis  
4 that was done only with those devices removed for an  
5 indication. In other words, we have now eliminated the  
6 patients who requested the device with no clinical reason to  
7 have them removed from the study.

8           We can see, again, basically, that this column  
9 stays the same. There are none here. We have these  
10 patients entered at the interval here. Now, with the  
11 95 percent confidence interval for cumulative probability,  
12 the likelihood of an implant placed in day 1 surviving ten  
13 years is 90 percent.

14           So I think it is important that the panel and the  
15 audience understand that aspect.

16           I have a few more minutes. I would like to show  
17 the next series of slides. I think it is important for the  
18 panel and the audience to maybe see what a case looks like  
19 from the beginning to the end. I don't want to give you all  
20 the details on this case, but this is obviously a patient  
21 who has had multiple temporomandibular-joint procedures with  
22 a mutilated anatomy of the joint here.

23           She has an open-bite deformity. Her mandible is  
24 deviated to the right. She is in significant discomfort,  
25 not only from the fact that she can't open and close her

1 mouth but the fact that she has tremendous muscle spasms not  
2 only on this side but also on the opposite side because of  
3 the shift of the mandible.

4 This is the model of that particular patient and I  
5 think it is pretty evident, the shift in her jaw. You see  
6 her teeth don't come together on this side.

7 This shows the normal anatomy on the patient's  
8 left side and this is the mutilated anatomy on the right  
9 side. This patient had five prior temporomandibular-joint  
10 operations.

11 The model can then be adjusted to the patient's  
12 occlusion so that their bite can be placed appropriately. A  
13 wax-up of the device is done. Because there is a wax-up  
14 here and, for the people with dental training in the  
15 audience, does not mean that the device is cast. This is  
16 just merely a design. The device is actually milled so that  
17 there is no casting involved in this.

18 Casting can instill crystalline defects so milling  
19 the device is an appropriate way to deal with this. This  
20 just merely shows what the device would look like.

21 The device is placed through two incisions here.  
22 This was the lower device and, again, you can see, from Mr.  
23 Rose's presentation and my presentation, that all of these  
24 devices are completely different. They don't look the same  
25 at all.

1           This is the device in place before the screws have  
2 been placed in the fossa component as it is attached to the  
3 zygomatic arch. You can see that the ball which has a  
4 geometry which is perfectly mated to the geometry of the  
5 ultra-high molecular-weight polyethylene, again stressing  
6 the fact that this is the benchmark materials that have been  
7 used in orthopedic surgery for over thirty years. This  
8 shows that relationship.

9  
10           This is the patient's panoramic radiograph that  
11 shows the device in place. The fossa liner of the titanium  
12 mesh shows up on the radiograph. Obviously, the ultra-high  
13 molecular-weight polyethylene, since it is not radiodense,  
14 does not show up.

15           And then, in an anterior-posterior view, we can  
16 see how nicely the titanium mesh conforms to the remnant of  
17 the fossa, how centered the condyle is in the fossa and the  
18 bicortical nature of the screws as they pass through the  
19 implant and through the remnant of the ramus.

20           It also shows now that the patient's jaw is  
21 symmetrical and this patient has gone on to do very well.

22           That is the end of the slides.

23           I would like to close with a statement read  
24 directly from the report of the FDA, that "The TMJ Concepts  
25 Inc. documentation answers most of the essential questions

1 that should be asked in relation to total temporomandibular-  
2 joint reconstruction. They have presented evidence that the  
3 characteristics of the patients that did complete the  
4 extended period of follow up are very similar to those who  
5 were lost. The company has also started a postmarket study  
6 to prospectively follow additional patients.

7 "In addition, the engineering review of this  
8 implant has demonstrated that its principles of action are  
9 very similar to other, more fully characterized, joint  
10 reconstruction--i.e., total hips--in terms of the materials  
11 and the mechanical characteristics."

12 Thank you very much and I look forward to any  
13 questions that you may have.

14 DR. JANOSKY: At this time, we can have a few  
15 questions from the panel members for TMJ Concepts.

16 DR. PATTERS: Dr. Mercuri, can you estimate the  
17 percentage of adverse reactions?

18 DR. MERCURI: It is about 8 percent.

19 DR. PATTERS: And the percentage of implants  
20 removed was 13 percent in study 2?

21 DR. MERCURI: It was not 13 percent. It was 13.

22 DR. PATTERS: Out of 113 patients?

23 DR. MERCURI: Right; 113 patients.

24 DR. PATTERS: And 13 patients had them removed?

25 DR. MERCURI: Right.

1 DR. PATTERS: 12 percent?

2 DR. MERCURI: Right.

3 DR. PATTERS: What percentage of patients were not  
4 improved or their symptomatology was not improved, or was  
5 made worse?

6 DR. MERCURI: I didn't include that in my  
7 presentation. That depends on the number of prior  
8 operations that the patient had. We had that data in the  
9 PMA. It shows you that if a patient has had zero to four  
10 prior surgeries that the likelihood of them not improving is  
11 very low whereas if a patient has had five to nine, or nine  
12 or more, prior operations, that their improvement is much  
13 less.

14 So I would direct you to that data as a response  
15 to that particular question. That has also been reproduced  
16 in other studies that have been done in the literature. The  
17 more surgery that is done, the less likely the parameters  
18 that we looked at would improve other than for function.

19 DR. PATTERS: Lastly, then, if I understand your  
20 dataset, you show that the preoperative conditions of the  
21 patients that return for follow up did not significantly  
22 differ from the preoperative conditions of those who did not  
23 return. How can we be sure that the result of treatment  
24 wasn't different between those two groups?

25 DR. MERCURI: I think the reproducibility of the

1 data in basically three different studies which shows  
2 statistically significant improvement over the time period  
3 of the studies is a significant response to the device.

4 DR. PATTERS: Could it be argued that those  
5 patients who did not feel they were helped did not come  
6 back?

7 DR. MERCURI: That could be argued. It could also  
8 be argued that we are dealing with eight different surgeons  
9 over five different states and even in study 2, when it was  
10 just Dr. Wolford and my patients that we were looking at,  
11 because this was a limited clinical trial and there were a  
12 limited number of people doing these procedures, patients  
13 traveled a significant distance in order to receive  
14 treatment.

15 In many cases, the evaluation of these patients  
16 was left to the referring surgeon. In many cases, despite  
17 repeated attempts to have the referring surgeon or the  
18 patient respond to the data questions, it was impossible to  
19 receive that data.

20 DR. PATTERS: Thank you.

21 DR. BERTRAND: Peter Bertrand for Dr. Mercuri. On  
22 this gap of patients follow-up-wise, when you initially  
23 assessed the patients, was there any type of psychometric  
24 inventory to measure the impact of what has already happened  
25 to that patient in the past, or what kind of life challenges

1 they may have faced apart from the surgical procedures that  
2 had confronted them in order to more adequately characterize  
3 what kind of patient you were dealing with from the  
4 beginning?

5 DR. MERCURI: To answer your question quickly, in  
6 a majority of the cases, no. To expand upon that, the issue  
7 with these patients was, as I stated from the beginning, a  
8 functional issue and in hopes to try to allow them to regain  
9 some function and be able to eat, I think it was addressed  
10 in the patient advocacy group that these were patients whose  
11 lives had changed dramatically in terms of their ability to  
12 eat, their ability to gain weight because they were losing  
13 weight because they were not able to eat, it was important  
14 that they get their function back.

15 I also addressed, in one of the goals, the fact  
16 that these patients were suffering. When you are looking at  
17 the chronic-pain, the component of suffering increases  
18 rather dramatically in those patients. Part of the  
19 suffering that these patients have, as a clinician who sees  
20 these patients all the time, is the fact that, number one,  
21 they can't open and close their mouths and, number two, they  
22 don't look very good because their jaws are deviated from  
23 one side to the other.

24 I have found in my experience of over thirty years  
25 in dealing with these types of patients that as soon as we

1 send them off for psychometrics, and I understand that  
2 psychometrics is very important in dealing with these  
3 patients and I have a whole dataset on the psychometric  
4 component of this, but as soon as we start sending them off  
5 for psychiatric evaluation, or psychological evaluation, we  
6 immediately turn them off and they immediately leave.

7           The concern, at that point, is that they become,  
8 again as the patient-advocacy group spoke, "It is all in my  
9 head." That is a point that I, as a clinician and as a  
10 surgeon, have no expertise in that area.

11           We have referred some of the significant patients  
12 with significant psychometric problems to the clinical  
13 psychologist. But I cannot, as I sit here today, give you  
14 the exact number of those patients. It is a long answer to  
15 your question, but I think it is germane.

16           DR. BERTRAND: The literature on chronic-pain  
17 patients is showing that upwards of 50, 60 percent of them  
18 may have some type of history of abuse in their past. So,  
19 in this particular group of patients, we have no way of  
20 assessing whether that was ever an issue for these  
21 particular patients.

22           DR. MERCURI: That's correct. It is uncommon for  
23 a patient to volunteer that information even when asked  
24 directly. I read the same literature you have talked about  
25 and I have tried to address that issue as a clinician with

1 these patients, but, in most of the evaluations that I do of  
2 these patients clinically, the significant other, the  
3 spouse, is typically in the room and it is very difficult to  
4 get these patients to give that response.

5 But I agree with you.

6 DR. BERTRAND: Thank you.

7 DR. HEFFEZ: I have a question for the engineering  
8 department. I'm sorry; I didn't catch your name. My name  
9 is Leslie Hefez, by the way.

10 MR. ROSE: Greg Rose.

11 DR. HEFFEZ: And then I would like to ask Dr.  
12 Mercuri two questions.

13 You tested in vitro the mechanics of the joint in  
14 worst-case scenarios. You also tested it with translation  
15 of the components; is that correct?

16 MR. ROSE: That's correct.

17 DR. HEFFEZ: I would like to know, from an  
18 engineering point of view, do you feel that the worst-case  
19 scenario would be one in which there was no translation  
20 versus one that there is translation?

21 MR. ROSE: Are you referring specifically to the  
22 wear study?

23 DR. HEFFEZ: Wear study and--I don't have the  
24 names of the studies.

25 MR. ROSE: The fatigue strength and the static

1 strength were done without any translation to assess the  
2 likelihood of the mandibular component to withstand  
3 fracture. And that was done with compressive loads. There  
4 was no translation in that test.

5 In the wear study, we created translation and we  
6 loaded it throughout the cycle and that was considered  
7 worst-case since those loads would not normally be seen by  
8 the implant throughout the chewing cycle.

9 DR. HEFFEZ: Did you test it at all for pure  
10 rotation? Did you test the wear under pure rotation?

11 MR. ROSE: No; the wear was tested with  
12 translation.

13 DR. HEFFEZ: I have a question for Dr. Mercuri.  
14 Typically, these patients are a heterogeneous population  
15 with heterogenous symptoms. One of the problems is that you  
16 identify indications for doing the procedure but there are,  
17 within those indications, one particular subset which is  
18 particularly difficult to reconstruct, and that is the  
19 Proplast/Teflon patient, we will call it.

20 When you mix the data between the different types  
21 of populations, sometimes it is hard to interpret the data.  
22 Did you make any effort to identify simply that patients who  
23 have been implanted with Proplast/Teflon and their outcomes?

24 DR. MERCURI: That data was looked at. It was  
25 done a while ago. I don't believe there was any difference

1 in the ultimate end result. That has not been published and  
2 I don't think that is part of your report. Dr. Wolford  
3 presented a paper where he looked at the Proplast/Teflon  
4 patients and compared autogenous grafting to alloplastic  
5 reconstruction and found a statistically significant  
6 improvement using an alloplastic over autogenous tissue.

7 That is not the same study that you are talking  
8 about but it is an analogous study.

9 DR. HEFFEZ: One of the problems is that, as a  
10 clinician, one can see the results of treating patients with  
11 inflammatory disease and patients being treated for bony  
12 ankylosis. Those patients typically do better than the  
13 other type of patient which is one who has had a failed  
14 prosthesis.

15 It would be interesting to know how your data  
16 plays out simply looking at that data rather than those  
17 other patients which typically do better postoperatively, or  
18 medically.

19 DR. MERCURI: I would suspect that they would do  
20 better. I think we have the data that would show that. I  
21 just don't have it available.

22 DR. HEFFEZ: I have one last question. Is there  
23 any disadvantage to not having the ultra-molecular-weight  
24 material radiopaque and monitoring the device as far as  
25 fracturing of the material, or significant wear of that

1 material?

2 DR. MERCURI: I think from the wear data that Mr.  
3 Rose has presented, it is so minor and minimal that it would  
4 be not measurable on a radiograph. In my 1995 paper, I  
5 present two- and three-year histology taken from patients  
6 who have been implanted for two and three years of the soft  
7 tissue between the ultra-high molecular-weight polyethylene  
8 and the chrome-cobalt-molybdenum head.

9 In fact, I have those slides if anybody is  
10 interesting in seeing them. The histology shows no  
11 particulation. We are seeing just dense fibrous connective  
12 tissue. So, again, in two to three years, follow up on  
13 those patients, we don't see that.

14 DR. HEFFEZ: Early in the device fabrication,  
15 there was some separation of the ultra-molecular-weight from  
16 the backing.

17 DR. MERCURI: There was one case; yes.

18 DR. HEFFEZ: That has not occurred since?

19 DR. MERCURI: That has not.

20 DR. BURTON: Richard Burton for Dr. Mercuri. I  
21 have three short questions for Dr. Mercuri. The first one  
22 is have you made any kind of judgment--you said that the  
23 orthopedic standard is approximately ten years on what is  
24 the potential life span. Most of these people, looking at  
25 your demographic data, are still relatively young and

1 looking at life spans, whether or not this device should  
2 have at least some type of life span associated with it?

3 DR. MERCURI: We have given you the life-table  
4 analysis for ten years. I think that, since the device has  
5 only been used for ten years, we have to say that following  
6 the benchmark of orthopedics that we are talking about ten  
7 years. But I will amend that by saying that we know that  
8 patient-fitted devices--in other words, devices that are  
9 made specifically for the anatomical problem that is  
10 associated with these patients--since they fit so well and  
11 that the failure of devices is typically when these devices  
12 do not fit well and that they start to move, the analogy for  
13 the dental group here is dental implants, that if we place a  
14 dental implant that is not completely solid in bone and it  
15 rocks or it moves, it is going to fail, whereas if you have  
16 an implant that fits perfectly or fits as close to perfect  
17 as we can humanly make it, that the implant will stay for a  
18 long period of time.

19 So my feeling is that because these are patient-  
20 fitted devices, or fit so well to the patient, that they  
21 should last longer. But I have no data that will prove  
22 that.

23 DR. BURTON: This may be for either one of you,  
24 but why did you develop a subset of your original data and  
25 present it sort of as a secondary study when, really, my

1 reading of it is it is an extension of the one grouping of  
2 patients, in terms of just involving two surgeons by the  
3 total eight?

4 DR. MERCURI: As I stated in my presentation, we  
5 felt that we wanted to look at the patients that were the  
6 closest followed of that large group; in other words, where  
7 the data was the most complete and, for the reasons I  
8 mentioned before for Dr. Patters, the fact that we have  
9 eight different surgeons, five different states, in the  
10 original study.

11 The dropout rate, trying to get the data, was  
12 large so we wanted to narrow it down so that we were only  
13 looking at the patient that had the best follow up. Again,  
14 even with two surgeons, because we are dealing with patients  
15 coming from different parts of the country, different  
16 countries, we still were not able to get the data as closely  
17 as we would like to.

18 So that is the reason for the 111.

19 DR. BURTON: One last point. You mentioned, in  
20 your presentation--you showed, in fact, one set of  
21 radiographs in a rheumatoid arthritis patient. How many of  
22 these have been used in rheumatoid reconstruction as opposed  
23 to patients with other types of surgery. Dr. Heffez  
24 mentioned Proplast. Do you have any idea what that might  
25 be?

1 DR. MERCURI: It is a smaller number. Again, I  
2 have that data someplace. I just don't have it with me now,  
3 but I can tell you percentagewise, it is a smaller number  
4 than Proplast/Teflon patients. It is a smaller number than  
5 the multiply operated patients.

6 I can all tell you, as, again, I responded to Dr.  
7 Patters' question before, these are the patients that  
8 represent the zero prior operations. I will tell you that  
9 those patients do remarkably well compared to--if we broke  
10 out just those patients and showed you that particular data,  
11 it would be remarkably different.

12 DR. BURTON: Thank you.

13 DR. JANOSKY: Dr. Rekow, just one last question  
14 and then we will resume later.

15 DR. REKOW: Can I make it two short ones?

16 DR. JANOSKY: Okay; two short questions.

17 DR. REKOW: This is Diane Rekow. Dr. Mercuri, you  
18 had a few patients that you ended with failures from your  
19 device. I assume that they were explanted, at least a few  
20 of them. I don't remember the number.

21 DR. MERCURI: Yes.

22 DR. REKOW: What happened to those patients?

23 DR. MERCURI: I can only tell you about two of  
24 those patients. I received information from my colleagues  
25 in other cities where these patients had these devices

1 explanted--are you talking about the patients that had them  
2 explanted for no reason?

3 DR. REKOW: No, no, no. The ones--

4 DR. MERCURI: You are talking about the failures.

5 DR. REKOW: Yes.

6 DR. MERCURI: Those patients ended up with either  
7 rib grafts or the Christensen prosthesis. I don't know how  
8 those patients did. Of the patients that had them removed  
9 for no clinical reason, there were two patients that I was  
10 able to follow up on and do the histology from. As I  
11 mentioned in my talk, one of those patients ended up having  
12 nothing done.

13 The other patient ended up having a rib graft  
14 placed that failed and then she had a Christensen prosthesis  
15 placed that she then also had removed. And she is now left  
16 with nothing.

17 DR. REKOW: The other question I have is for Mr.  
18 Rose. Could you tell us a little bit more about what wear  
19 degree you did see when you were doing your tests, what size  
20 particles? You had some wear, so I assume that there was  
21 some debris of some sort. What size was it? How much of it  
22 was there and what shape and what were some of the  
23 mechanisms you suspect were the cause of the wear?

24 MR. ROSE: The wear that we saw was just caused by  
25 the translation. We approximated the volumetric wear by

1 calculating the area of the wear tract that we saw. We did  
2 not do any analysis of the particulates.

3 DR. REKOW: Did you collect any of them?

4 MR. ROSE: No; we did not collect any of them.

5 DR. JANOSKY: You will be available this afternoon  
6 for additional questions by panel members; is that correct?

7 MR. ROSE: Yes.

8 DR. JANOSKY: I am pretty sure panel members do  
9 have some questions. We will let those go until after lunch  
10 and after the FDA presentations.

11 MR. ROSE: Can I point out that we have some  
12 implants that we are going to leave on the table if people  
13 would like to look at them during the break.

14 DR. JANOSKY: Is it my understanding that they  
15 need to be described for the record, what those implants  
16 are? Is that true? Okay; that's fine.

17 At this time, let's break for lunch. My watch  
18 says that it is 12:50. We will return at 1:50 which is one  
19 hour. We will resume at 1:50.

20 [Whereupon, at 12:50 p.m., the proceedings were  
21 recessed to be resumed at 1:50 p.m.]



1 fossa prosthesis, the intraarticular-joint prosthesis. This  
2 occurred on December 20 of 1994.

3 . The panel believed that these devices presented a  
4 potential unreasonable risk to health and that insufficient  
5 data and information existed to determine that general  
6 controls were adequate to provide safety and effectiveness  
7 information for these devices. This classification, as you  
8 all know, came after several very well-known implant  
9 disasters related to TMJ implants.

10 The earliest day by which PMAs could be called for  
11 was June 30, 1997, thirty months after the original  
12 classification. The FDA subsequently issued a proposed and  
13 final rule to require the filing under Section 515(b) of  
14 premarket approval applications. The actual call for PMAs  
15 then occurred last December 30, 1998.

16 The FDA did receive a reclassification petition on  
17 April 30 of 1996. This requested that the agency reclassify  
18 from class III to class II the mandibular-condyle implant  
19 that is meant for temporary reconstruction in tumor-  
20 resection patients. Based on panel recommendations and  
21 data, the panel recommended that class II with special  
22 controls was reasonable for this type of device.

23 This reclassification does not encompass all of  
24 the indications for the mandibular-condyle implant. This is  
25 limited to the intended use for implantation in the human

1 jaw for temporary reconstruction of tumor-resection  
2 patients. The agency intends to grant this reclassification  
3 but it has not become finalized yet.

4 The term "temporomandibular-joint disorders," as  
5 you have heard a lot about today, is a collective term and  
6 it may include a variety of different diseases of the  
7 masticatory muscle system and the associated joint. The  
8 mechanics of this joint allow insight into its function and  
9 its dysfunction.

10 The temporomandibular joint, like other joints in  
11 the body, is subjected to intrinsic and extrinsic stresses  
12 and the normal process of aging. The TMJ, itself, is a very  
13 complex joint and it is intimately related to the muscles of  
14 mastication, the teeth, the nervous system and other  
15 cranial-facial musculature.

16 A fibrous disc divides the joint compartment into  
17 two cavities and provides a moveable articular surface. The  
18 nervous system provides joint and the associated muscles  
19 with important information on pain, touch and movement.

20 The terminology involved with temporomandibular  
21 joint has also had a complex history. We have heard it  
22 called TMJ, craniomandibular dysfunction, occlusal-  
23 mandibular dysfunction, temporomandibular-joint dysfunction,  
24 et cetera, et cetera.

25 The original symptoms and signs of the varying

1 disorders do include pain, joint sounds and limited  
2 mandibular movement and range of motion. Disorders of this  
3 joint are an extremely important source of oral-facial pain,  
4 especially in women. Treatment strategies range from  
5 reversible recommendations for reversible therapies such as  
6 mandibular splints and two more non-reversible therapies  
7 such as occlusal adjustments and invasive surgical  
8 procedures.

9           Most recent recommendations suggest that  
10 conservative approaches to therapy should be initiated  
11 before non-reversible therapies are tried. There is,  
12 however, a patient population for whom nonsurgical treatment  
13 is not an option. This subset of patients has had a variety  
14 of previous non-surgical treatments and has also had at  
15 least one previous surgical procedure.

16           These surgical procedures could include failed  
17 Proplast/Teflon implants or other types of alloplastic-joint  
18 reconstruction or failed autogenous grafts. Often, these  
19 patients have experienced numerous surgeries to one or both  
20 joints. The original presenting complaint is often clouded  
21 because numerous surgical procedures have complicated the  
22 diagnostic picture.

23           Inflammatory and/or immunologic responses in some  
24 of these patients may preclude further autogenous  
25 reconstruction. These patients present with severe pain, as

1 you have heard, and extremely limited function.

2           The population in need of surgical reconstruction  
3 may also include patients with severe trauma, neoplasms,  
4 arthritis to the joint, that render it dysfunctional. There  
5 is a significant need in the clinical community for devices  
6 to reconstruct this joint. Success of the surgical results  
7 from these reconstructions has to be tempered with the  
8 realization that the reduction in painful symptoms and the  
9 increase in function may be limited at best for many of the  
10 patients.

11           Total joint replacement in the temporomandibular  
12 joints have had a mixed history as well. Surgeries to  
13 address the lack of function and chronic pain have been  
14 overutilized. This overutilization of irreversible  
15 procedures was well-documented at the National Institutes of  
16 Health Technology Assessment Conference in 1996.

17           The overutilization of procedures has resulted in  
18 use of some materials that have been inadequately  
19 characterized prior to implantation. The result of this is  
20 a cohort of patients who have significant chronic pain and  
21 dysfunction with few alternatives except for total-joint  
22 reconstruction.

23           Adequate examination of the mechanical and  
24 structural characteristics as well as biocompatibility  
25 characteristics of the materials used in prosthesis joints

1 is essential to successful reconstruction.

2 Perfect biological substitutes, of course, have  
3 not been developed but we do know that the characteristics  
4 of successful reconstruction include biocompatibility of  
5 materials, devices that are designed to withstand applied  
6 loads, and stability. It is important, from the agency's  
7 point of view, that devices that are intended to reconstruct  
8 this joint have a complete characterization and include as  
9 much patient information and preclinical testing as is  
10 reasonable.

11 In addition, adequate follow up of the patients  
12 receiving reconstruction is essential to interrupt any  
13 potential problems that may occur. With this information in  
14 mind, I would like to present my clinical review of the PMA  
15 that we are considering today.

16 TMJ Concepts has presented clinical data to  
17 support their premarket approval application for their total  
18 joint. This study was initiated to evaluate the outcome on  
19 215 patients which included 363 joints. They were treated  
20 with the same protocol by eight different oral and  
21 maxillofacial surgeons, as you have heard before.

22 Endpoints in the study were pain, function and  
23 interincisal opening. All patients were fully informed as  
24 to the nature of their prosthesis and the nature of their  
25 diagnosed condition.

1           The CADCAM TMJ reconstruction device was placed.  
2 This dataset, on initial analysis, suffered from a  
3 significant loss-to-follow-up. Approximately 35 percent of  
4 the initial group was lost to follow up. A second analysis  
5 was performed that analyzed a subset of these patients which  
6 you heard before, another 11 patients, that were primarily  
7 seen by two surgeons, who were implanted with 195 joints.

8           Overall results, as you have also heard in terms  
9 of their statistical analysis, was remarkably similar to the  
10 characteristics of the total group.

11           At issue is are the characteristics of these  
12 patients any different from the patients in the larger group  
13 and are these characteristics different from patients that  
14 were lost to follow up. We have heard some of the  
15 explanations for these kinds of missing points of data.

16           In addition to the data from this previous study,  
17 the company, after receiving their 510(k) clearance, did  
18 initiate a required postmarket surveillance study. This  
19 study, as you have also heard in their very early  
20 preliminary data, also correlates well with the data from  
21 their previous studies. This study was prospectively  
22 designed and approved by the agency and, to date, over 100  
23 patients have been enrolled.

24           The TMJ Concepts documentation answers, as you  
25 have heard my words come back to me, most of the essential

1 preclinical questions that should be asked in relationship  
2 to the total temporomandibular-joint reconstruction. Follow  
3 up is not ideal. They had many patients that were lost to  
4 follow up.

5 The sponsor has provided some explanation for this  
6 loss to follow up but they also have provided preclinical  
7 data that indicates that the characteristics of this joint  
8 are similar to other successful joints that are  
9 reconstructed in other parts of the body; i.e., total hips.

10 We are going to go on with our evaluation here and  
11 Ms. Angela Blackwell will give her engineering review.

12 DR. HEFFEZ: Dr. Runner, can I ask you a question.

13 DR. RUNNER: Yes.

14 DR. HEFFEZ: The approval of the prospective  
15 study; what was, exactly, approved, the methodology or--

16 DR. RUNNER: The company, after they received  
17 their 510(k) clearance, because they received clearance to  
18 market the device before PMAs were called for, and because  
19 this was a device that has a required postmarket study, the  
20 company came to the agency with a prospective protocol which  
21 included numbers of patient, endpoints, follow up, all the  
22 forms that you would in a prospective study.

23 We went back and forth a few times and then it was  
24 cleared for them to begin this study.

25 DR. HEFFEZ: So this is essentially--it is not

1 similar to an IRB institutional review; is that right?

2 DR. RUNNER: It is more similar to an IDE-type of  
3 review, if you had to compare it, because we had to approve  
4 the protocol before they could begin the study.

5 DR. BERTRAND: This study is ongoing; correct?

6 DR. RUNNER: This study is ongoing.

7 DR. BERTRAND: For how long?

8 DR. RUNNER: It is a required three-year follow up  
9 of the patients that are enrolled. So, once they reach  
10 their--I don't remember how many patients. It is  
11 100 percent of all patients that received the joint for the  
12 first two years it is on the market. So that is the  
13 requirement. And they will be followed for three years.

14 DR. BERTRAND: Thank you.

15 MS. BLACKWELL: I am the lead reviewer for the PMA  
16 for TMJ Concepts. I also performed the engineering review  
17 of this PMA.

18 The sponsor has conducted appropriate fatigue and  
19 wear testing. In my presentation, I will outline the  
20 summary of the data that was presented.

21 Testing was reviewed under the 510(k) K954224  
22 except for the bond-strength validation. So, in other  
23 words, all of the engineering testing that appeared on the  
24 PMA was present when we reviewed the 510(k) in 1995. The  
25 materials and designs for this implant are similar to

1 successful orthopedic implants.

2           One of the types of testing they performed was  
3 dynamic-fatigue testing. The parameters of the test, I  
4 believe most of these were stated earlier in the company's  
5 presentation, but it was 12 Hertz assessed in air for  
6 10 million cycles. They used six samples and their  
7 sinusoidal load was between 7 and 150 pounds.

8           They had no failures and there were no cracks  
9 detected when they used a dye-penetration test. No S/N  
10 curve was generated because there were no failures.  
11 Normally, an S/N curve is the type of data that you would  
12 generated from a fatigue test, but you have to have at least  
13 one failure to get your endpoint for the curve. So if you  
14 have no failures, it is not really useful.

15           Literature references show that the maximum bite  
16 force is in the range of 300 pounds. If you look back, we  
17 will see, on the testing parameters, there load went up to  
18 150 pounds. So that is why this is of importance.

19           The TMJ surgical patient would have a decreased  
20 bite force secondary to a loss of muscle attachment. So,  
21 the 150 pounds is reasonable for a maximum considering that  
22 your patient is going to have some of their muscles missing.

23           The average yield strength for the device was  
24 790 pounds. So that is much higher than the average bite  
25 force referenced in the literature.

1 Another type of testing performed was wear  
2 testing. This was for 5 million cycles in bovine serum. It  
3 was 55 cycles per minute with a load of 9 kilograms or  
4 19.8 pounds, approximately.

5 There were two types of wear data reported. One  
6 is penetrative wear which means that distance that condyle  
7 head wears into the fossa. That was given as  
8 0.01 millimeters per million cycles.

9 Volumetric wear, that is the volume of material  
10 worn away by the fossa. That was reported as 0.39 cubic  
11 millimeters per million cycles. Both of these numbers are  
12 very small compared to the volume or the size of the  
13 implants in question.

14 The company calculated that, for a 3-millimeter-  
15 thick fossa, the average wear life was 309 million cycles.  
16 That was a maximum. I think one of the other numbers they  
17 came up with was 173 million. The general assumption that  
18 we make when asking for testing, for TMJ implants and other  
19 types of dental implants as well, is that the average  
20 patient has 1 to 2 million cycles of chewing per year.

21 If you assume that that is, indeed, the case, then  
22 the data indicates the device should have sufficient wear  
23 characteristics over the life of the implant.

24 Thermal-bond testing was used to determine the  
25 mechanical bond between the titanium mesh backing and the

1 ultra-high molecular-weight polyethylene which is the fossa  
2 component. These two components are essentially compressed  
3 together while the ultra-high molecular-weight polyethylene  
4 is in a heated state. So there are no screws or anything  
5 else to disturb the articulating safety of the fossa.

6 Under mechanical compression, all the samples had  
7 a shear strength greater than 75 pounds.

8 The company used a literature model for loading on  
9 the TMJ to determine that the worst-case scenario would be a  
10 side-impact load of about 25 pounds and that would be right  
11 at the juncture of the polyethylene and the backing which,  
12 you would think, would be the most serious thing that could  
13 occur.

14 Probably, in a patient, it would be from trauma, a  
15 car accident or something, could cause it to separate. So,  
16 using that 25-pound load that they calculated with their  
17 model and using a three-times safety factor, they came up  
18 with the 75 pounds. So if their testing showed that  
19 everything had greater than 75 pounds shear strength, that  
20 should be sufficient.

21 Are there any questions?

22 DR. LI: Ms. Blackwell, did you see any retrieved  
23 devices that were submitted to you as examples of how a  
24 device would look after it was used for some period of time?

25 MS. BLACKWELL: I don't know that they have any

1 retrieved ones that are recent. The only failures are early  
2 in their study and that was six years ago.

3 DR. LI: So there is no way for you to compare  
4 whether or not the wear area or wear type of damage that  
5 occurs in their force simulator is similar to what they  
6 might find clinically.

7 MS. BLACKWELL: No. Unfortunately, that is not  
8 the case. But even in cases in orthopedics, I don't think  
9 the lab's correlation is very close. Even for well-  
10 characterized hips and knees, they don't have a real good  
11 way to generate the same type of particles in the lab. So  
12 that is not really expected for preclinical testing.

13 DR. HEFFEZ: The maximum bite force you indicated  
14 was 300 pounds but 150 pounds would be reasonable. Was  
15 there any study indicating that, in these types of patients  
16 or in different types of subsets of patients, that they do  
17 generated only maximally 150 pounds?

18 MS. BLACKWELL: There is a model that is in the  
19 literature that shows the different contributions of the  
20 different muscles for how much force for each muscle. So if  
21 you take the muscles out of the model that are missing in  
22 the TMJ device patient, then you get an estimate that is  
23 about 50 percent.

24 DR. HEFFEZ: Which muscles were eliminated to make  
25 that model?

1 DR. RUNNER: Lateral pterygoids.

2 DR. HEFFEZ: So the later pterygoid muscle  
3 contributes 150 percent of the biting force?

4 DR. RUNNER: And the temporalis.

5 MS. BLACKWELL: And the temporalis.

6 DR. HEFFEZ: So the temporalis plus the lateral  
7 pterygoid contributes 50 percent of the biting force. Is  
8 that the assumption?

9 DR. RUNNER: That was the estimation; yes.

10 DR. JANOSKY: Is there anyone from the sponsor  
11 that would like to respond to the question that was  
12 presented to Ms. Blackwell concerning retrieved devices? It  
13 is an invitation to respond. It is not a requirement.

14 Is it fair to assume there is no response from the  
15 sponsor?

16 MR. ROSE: The early failures that we saw were  
17 with loosening on the mandibular component. Many of those  
18 devices were replaced with well-fixed components of the new  
19 design.

20 DR. JANOSKY: Would you please state your name?

21 MR. ROSE: I'm sorry; Greg Rose. So there were no  
22 fossa components to examine that were removed from patients  
23 where we could examine wear patterns. It was due to the  
24 nature--those failures were not to remove the entire device.

25 DR. LI: May I follow up on that?

1 DR. JANOSKY: Yes.

2 DR. LI: Steve Li, just to follow up on that  
3 question. For those patients, for instance the ones that  
4 requested removal of their device, obviously the component  
5 was removed in those cases. Did no one look at the devices  
6 to get an idea of what those things would look like?

7 DR. MERCURI: Louis Mercuri responding to the  
8 question about the wear pattern. Yes, to answer question,  
9 Dr. Li, those devices were looked at and the wear pattern  
10 was what was to be expected in a patient who had this  
11 device. It was a short, transitory wear pattern with a  
12 rotational component to it.

13 DR. LI: How close was that wear pattern to the  
14 posterior flange?

15 DR. MERCURI: At but not beyond.

16 DR. LI: So, was there wear against the posterior  
17 flange I guess is my real concern.

18 DR. MERCURI: Not as much as would be seen in the  
19 fossa component. Not significant. And, as I stated before,  
20 in the 1995 paper, we have two-year and three-year histology  
21 of this device in patients with no evidence of  
22 particulation.

23 DR. LI: Could I follow up on that? Steve Li,  
24 again. Polyethylene, especially submicron particles, are  
25 notoriously hard to see in histological sections. Did you

1 use any staining techniques such as oil red O at high  
2 magnification because often submicron particles, for  
3 instance in your repetitive kind of reference back to  
4 orthopedics, total hips and total knees, the most  
5 biologically active particles are virtually invisible to the  
6 eye unless you stain them and use very high-power  
7 microscopy.

8           So typical histology often does not yield  
9 polyethylene particles where a closer examination might.

10           DR. MERCURI: Polarized light was used but not the  
11 stain that you alluded to.

12           DR. HEFFEZ: I would like to return to the  
13 question about maximal bite force. Was there any effort--I  
14 will direct this to the company. Was there any effort in  
15 studying the maximum bite force in those patients prior to  
16 placement of the implants?

17           DR. MERCURI: To directly answer the question, no.  
18 And one of the reasons for that is that many of these  
19 patients were not able to function at all and so it was felt  
20 that it was impossible to develop any kind of significant  
21 data, number one. Number two, we looked into the mechanism  
22 to do that. All the mechanisms that appeared to be  
23 available were too crude to measure the amount of  
24 preoperative bite force that these patients would be able to  
25 generate.

1 DR. HEFFEZ: How did they study it in the model in  
2 which they attributed certain percentages to different  
3 muscles?

4 DR. MERCURI: The 50 percent figure was generated  
5 from some literature. It was a citation to the literature.  
6 It talks about the percentage of force that is lost by  
7 muscle, by not having certain muscles. The other problem  
8 that has become quite evident, as I have proceeded through  
9 this, is that, unlike orthopedic surgery where anatomical,  
10 mechanical and mathematical models have been developed for  
11 force, unfortunately, due to the complex mechanism  
12 associated with the temporomandibular joint, no adequate  
13 anatomical, mathematical or mechanical model has been  
14 developed.

15 That is something that the NIH is well aware of  
16 and is presently looking for RFPs to look at a solid model  
17 for the temporomandibular joint, taking into consideration  
18 all of the muscular forces that are place on the mandible  
19 that vary, unlike the hip and the knee, with head posture.  
20 Through some research that I did as a resident, I found out  
21 that variations in head posture will change the forces that  
22 are placed upon the mandible by the muscles.

23 DR. HEFFEZ: If no mathematical model exists, are  
24 we relying on data that is generated from a model to  
25 indicate 300 pounds based on such a mathematical model?