

Summary of Safety and Effectiveness

TMJ Implants, Inc. Partial Temporomandibular Joint Replacement System

I. GENERAL INFORMATION

Device Generic Names: Partial Temporomandibular Joint Prosthesis

Device Trade Names: TMJ Fossa-Eminence Prosthesis System
TMJ Patient Specific Fossa-Eminence
Prosthesis System

Applicant's Name and Address: TMJ Implants, Inc.
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Premarket Approval (PMA) Number: P000035

Date of Panel Recommendation: October 6, 2000

Date of Notice of Approval to the Applicant: February 27, 2001

II. DEVICE DESCRIPTION

TMJ Fossa-Eminence Prosthesis

The TMJ Fossa-Eminence Prosthesis is designed to provide a thin, rigid, well-fitting prosthetic covering for the articulating surface of the temporomandibular joint comprised of the glenoid fossa and articular eminence of the temporal bone. The articular surface of the prosthetic glenoid fossa and articular eminence is highly polished to minimize friction in joint movement.

The prosthesis, and the screws with which it is to be secured to the skull, are manufactured from surgical Co-Cr-Mo alloy (ASTM F75/ASTM F799). These devices are intended for permanent implantation and are for single use only.

All components in this Fossa kit, including individual prosthesis, drills and screws are sterilized by gamma-irradiation or e-beam radiation (2.5 Mrads), and are packaged in individual double-peel PETG and Tyvek containers.

Two additional NON-STERILE Fossa kits accompany this TMJ Fossa-Eminence Prosthesis System and are essential for its use. The Fossa-Eminence Trial Sizing System contains trial sizer components for each size of implant. The Instrument Kit contains screwdrivers and Fossa-Eminence holders.

These two accompanying kits must be steam sterilized prior to use in accordance with procedures outlined in Section 9 of the instructions for use.

III. INDICATIONS FOR USE

The TMJ Fossa-Eminence Prosthesis System is intended for use in treatment of severe temporomandibular joint disease due to:

- Inflammatory arthritis involving the temporomandibular joint not responsive to other modalities of treatment;
- Recurrent fibrosis and/or bony ankylosis not responsive to other modalities of treatment;
- Failed tissue graft;
- Failed alloplastic joint reconstruction ; or
- Internal Derangement confirmed to be pathological in origin by both clinical observation and radiographic findings, where the patient has moderate to severe pain and/or disabling dysfunction and has not responded to less invasive, conventional therapy.

IV. CONTRAINDICATIONS

The TMJ Fossa-Eminence Prosthesis System should not be used for patients with one or more of the following conditions:

- Infection or malignancy in the head or neck region;
- Known allergy to any of the components of the system; or
- Ability to exert significant post-operative masticatory muscle hyperfunction (clenching or grinding) which may lead to overload and fracture of the device or loosening of the screws.

V. WARNINGS

USE OF THE FOSSA-EMINENCE ALONE FOR INTERNAL DERANGEMENT

The medical literature reports:

- that many cases of Internal Derangement, resolve after non-surgical treatment, or, in some cases, with no treatment at all.
- that the complexity of contributing factors in this patient population must be considered in the diagnosis and decision to surgically treat patients.

- that replacement surgery, therefore, should be utilized only as a last resort after other treatment options are exhausted or determined not to be warranted in the medical judgment of the physician/dentist in consultation with the patient.
- that the Wilkes classification is a guide in determining the severity of the disease. This classification should not be relied on as a sole criterion for surgical treatment.

Wilkes Classifications for Internal Derangement¹

- Class I:** **Painless clicking. No restricted motion.** Slight forward displacement of disk.
- Class II:** **Occasional painful clicking, intermittent locking, headaches.** Slight forward displacement of disk, beginning deformity and slight thickening of posterior edge.
- Class III:** **Frequent pain, joint tenderness, headaches, locking, restricted motion, and painful chewing.** Anterior disk displacement with significant deformity/prolapse of disk.
- Class IV:** **Chronic pain, headaches, and restricted motion.** Increase in severity from III with early to moderate degenerative changes, flattening of eminence, deformed condylar head, sclerosis.
- Class V:** **Variable pain, joint crepitus, and painful function.** Disk perforation, filling defects, gross anatomic deformity of disk and hard tissues with degenerative arthritic changes.

The long-term effects of the TMJ Fossa-Eminence Prosthesis System on the natural mandibular condyle are unknown. Remodeling of the natural mandibular condyle has been observed. Other degenerative changes may be attributable to the TMJ Fossa-Eminence prosthesis. Therefore, the physician/dentist should periodically monitor the condition of the natural mandibular condyle.

PERFECT THE TECHNIQUE FOR IMPLANTATION

It is strongly recommended that the surgeon perfect the technique for implantation of this prosthesis through attendance at surgical demonstration courses, use of an instructional video, and manipulation of replica models. Instructional videos and literature are available from TMJ Implants, Inc. TMJ Implants Inc. can provide names of individuals, with extensive experience, independent from the company, for consultation prior to surgery.

READ ALL ACCOMPANYING LABELING

Prior to use, the surgeon must read the entire Instructions for Use and device labeling.

Dynamic fatigue tests were conducted on the TMJ Implants Inc. Metal-on-Metal Total Joint Replacement System with a force applied vertically to the Fossa-

¹ Quinn, P. "Color Atlas of Temporomandibular Joint Surgery" ; Chapter 4: *Surgery for Internal Derangements*, Table 4.1,p56. Mosby 1998.

Eminence prosthesis. No failures occurred at 130 lbs. Physicians/Dentists should carefully consider the results of these fatigue tests when patients present with particular anatomical considerations or unusual masticatory forces.

TEST FOR ANY SUSPECTED SENSITIVITY TO MATERIALS

If the patient's history suggests allergy to costume jewelry or other metals, such as Nickel, the patient should undergo appropriate testing for sensitivity to Co-Cr-Mo alloy. Upon request, TMJ Implants, Inc. will supply a sample of this alloy and/or the chemical composition for pre-operative allergy testing. Should patch testing be positive then some alternate surgical plan should be considered.

IF LONGER SCREWS ARE NECESSARY

Occasionally, longer screws will be necessary to engage bone. It is important that the surgeon exercise great care to prevent injury to deeper vital structures. Care must be exercised not to penetrate or impinge any auditory structure, the middle cranial fossa, or any neuro/vascular structures.

IF EXCISING BONE

When performing an excision of bone in the area of the normal glenoid fossa and condyle, especially in cases of bony ankylosis, the surgeon must exercise great care to avoid penetration into the middle cranial fossa, the auditory canal, or other vital structures.

VI. PRECAUTIONS

Prior to Surgery

- All TMJ Fossa-Eminence Prostheses, screws, and drills, are provided sterile. Inspect sealed sterile package before opening. If seal is broken, do not use. Do not resterilize.
- Prior to use, the Fossa-Eminence Sizer kit and the Instrument Kit containing screwdrivers and Fossa-Eminence holders must be sterilized as outlined in Sections 8 and 9 of the device labeling.
- The surface of the device must remain clean and free of debris prior to implantation.
- The implant must be handled only with talc-free gloves to avoid introduction of talc into the implantation site.
- The prostheses must be protected from scratching or bending prior to and during surgical implantation, as such damage may cause weakening or fatigue of the metal or fracture of the part.

During Surgery

- The TMJ Fossa-Eminence Prosthesis System must be secured only through the use of the drills and screws supplied by TMJ Implants, Inc. The screws and drills

used with the TMJ Fossa-Eminence Prosthesis System have been specifically selected by size to ensure correct fixation of each prosthesis when used as directed. Any use of substitute drill bits or screws not supplied by TMJ Implants, Inc. in the TMJ Fossa-Eminence Prosthesis System may result in less than optimal long-term results and may adversely affect the performance of the prosthetic device.

- It is strongly recommended that at least four (4) Fossa-Eminence screws be used where practical to achieve firm fixation of the TMJ Fossa-Eminence Prosthesis.
- It is recommended that the head of the natural condyle be placed into the prosthetic glenoid fossa portion of the TMJ Fossa-Eminence Prosthesis with all interposing soft tissue removed. The condyle articulating surface should preferably be centered in the Fossa and should not contact the screws of the Fossa-Eminence Prosthesis.

VII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Types of adverse events observed in the clinical use of the TMJ Fossa-Eminence Prosthesis System include:

- Postoperative pain, swelling, jaw muscle spasm
- Facial nerve and muscle weakness or paralysis
- Ankylosis and Fibrosis
- Trauma
- Nausea
- Condylar dislocation
- Malocclusion
- Blurry vision
- Suspected allergic reaction
- Heterotopic bone formation
- Decreased interincisal opening
- Joint locking
- Hearing loss/problems
- Degenerative joint changes
- Poor fit of custom prosthesis
- Increased pain

In addition to the adverse events identified above, potential adverse events and complications associated with temporomandibular joint surgery and reconstruction may require further treatment and include but are not limited to:

- Hematoma formation
- Hemorrhage

- Foreign body or allergic reactions to the device materials
- Rejection of the device
- Wear, displacement of the device or implant loosening
- Fracture of the device / Surgical damage to anatomical structures adjacent to the TMJ
- Patient discomfort
- Speech problems
- Facial deformity

VIII. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for reconstruction may include reconstruction of the temporomandibular joint using autogenous or allogenic tissue grafts of bone, soft tissue, or cartilage or using another viable alloplastic implant. (See warnings)

IX. MARKETING HISTORY

The TMJ Implants Inc. temporomandibular joint prosthesis devices were previously on the market as Preamendments Class III devices. The applicant submitted their initial PMA application in response to the final rule published in the Federal Register of December 30, 1998, requiring the submission of PMA applications for temporomandibular joint prostheses by March 30, 1999. The PMA for the TMJ Metal-on-Metal Total Joint Replacement Prosthesis System was approved on January 5, 2001.

X. SUMMARY OF PRECLINICAL STUDIES

Biocompatibility

Tests were conducted to assess the biocompatibility of the cobalt chrome used in these devices. The tests conducted included: in-vitro Cytotoxicity, Genotoxicity, Mutagenicity, Irritation/Intracutaneous reactivity, Systemic Toxicity, and Contact Sensitization. All test results demonstrated the biocompatibility of the implant material. Results of a literature search also supports the suitability of this material for the chosen application.

A one-year assessment of the effects of wear particulates of cobalt-chrome on the temporomandibular joint space of 12 New Zealand white rabbits was conducted. This study indicated that after an early mild to moderate reaction to the particles, the joint spaces showed no lasting inflammatory response. No foreign body reaction was seen, and no giant cells were noted at any time. All other organ pathologies were normal, as were the results of all blood studies.

Material Characterization

Material Characterization confirmed the chemical composition and material properties of the implant materials. Potentiodynamic testing conducted on the cobalt-chrome alloys confirmed the low corrosion potential of these materials. Dimethylglyoxime testing

determined the amount of nickel released from the cobalt-chrome alloy was below the detectable limits of the test. Even with undetected nickel release, nickel sensitive patients should continue to be warned about the presence of nickel in this device.

Modeling

Both Finite Element Analyses and Kinematic modeling of the implant components were conducted to determine the effects of stress and movement on the performance of the devices. These Finite Element and Kinematic models confirmed that the stock devices were mechanically a worse case scenario as compared to the patient specific devices. In the Kinematic model, the calculated joint forces in patients with total joint implants were lower than in patients with partial joint implants. Normal subjects (without implants) were found to generate the highest forces.

Mechanical Testing

Mechanical testing relating to the performance of the devices included Fatigue, Wear, Static Load, and Contact Stress Analysis. Because it is not possible to conduct these tests using natural bone against a metal fossa, these mechanical tests were performed with Metal-on-Metal total joint prosthesis configurations, using a metal-headed TMJ Condylar Prosthesis with a Fossa-Eminence Prosthesis.

Fatigue

Fatigue tests were performed on 14 metal-on-metal combinations for 10 million cycles or to failure, but the tests were done at three different times under 2 protocols. Loads ranged from 130 lbs. to 336 lbs. Five (5) samples achieved run-out condition (10 million cycles). All 14 points were plotted along a load/number of cycles curve. A statistical justification was provided to justify pooling the different test groups together on one curve. The fatigue limit is estimated to be 130 lbs.

Wear

Wear testing was conducted for 2 million cycles at a rate of 2 Hz, in bovine serum at 37° C. A cyclic load pattern varying from 10 to 35 lb was applied to the components, while a 30° arc of motion was applied by the condylar head over the fossa component. Wear patterns in the in-vitro test samples showed single wear zones with parallel surface scratches oriented in a uni-axial direction of motion. Surface profiling, both before and after the wear testing, indicated the average wear of the metal-on-metal TMJ implants was 0.197 mm³ per million cycles. Mass measurements showed an increase in mass after testing so the mass measurements were set aside as being erroneous.

The wear test results were compared with the results of an analysis of explanted devices. The in-vivo results showed evidence of randomly oriented scratches, indicating multi-axial motion. Also, the contact surfaces of the retrieved explanted devices were significantly smaller and were characterized as smoother and more polished than the in-vitro wear test samples. The in-vivo results are probably a better indicator of wear patterns.

Static Load

Static load tests indicated that the maximum loads the devices will withstand are greater than those seen in-vivo. The metal-on-metal devices were subjected to forces of at least 448 lb before failure. Failure was defined as implant fracture, extensive bending, or component dislodgment from the mounting.

Contact Stress Analysis

Contact area was measured and contact stress was analyzed for the metal-on-metal components. Contact areas ranged from 1.62 to 4.84 mm² for the metal-on-metal configuration. As expected, for increased loads, the contact areas also increased. The average contact pressure, assuming a uniform pressure distribution, ranged from 2592 psi to 7011 psi for the metal-on-metal configuration. All stress measurements were below the yield strength for ASTM F 75-98 cast Cobalt-Chrome alloy (65,000 psi).

Finished Product Analysis

In addition, Casting and Finishing, and Mating Tolerance analyses were performed. The Casting and Finishing report characterized the effect of the manufacturing process on the microstructure of the cast CoCr components. Random scratches and surface features were noted, believed due to the hand-polished nature of these devices. The etched metal surfaces revealed a dendritic microstructure. This microstructure is common for metallic materials. It is unclear what influence, if any, the microstructure has on the failure mode.

The mating tolerance analysis was conducted to determine the contact interference between the fossa and condylar TMJ components. The results indicate that the vertical distance between the fossa surface and the condylar head increases with increasing distance from the point of contact. The total angle of freedom in the mating tolerance is 70 degrees. Since this system is designed for point contact its mating tolerance is very large compared to other total joint systems.

Sterilization

Sterilization validation and bioburden studies confirm that the materials can withstand the sterilization process and sterility assurance levels of 10⁻⁶ are achieved. Sterilization validation was conducted per AAMI/ISO 11137, Method 1. Quarterly bioburden studies and dose audits are conducted to confirm the continuing validity of the sterilization process. The packaging materials used for the implantable products are PETG medical grade blister stock and DuPont Tyvek medical grade stock.

XI. SUMMARY OF CLINICAL STUDIES

There have been two studies conducted that support the safety and effectiveness of the TMJ Fossa-Eminence Prosthesis system. The first is the TMJ Implants, Inc. Registry; the second a prospective clinical study, TMJ-96-001.

The Registry is a collection of data on patients that receive a TMJ Implants device. The primary purpose of the Registry is for device tracking. Monitoring clinical progress is a secondary function. The operating surgeon is asked to voluntarily submit baseline

assessments of pain and interincisal opening and then is asked to submit clinical reports at 6 months, 1 year, 18 months, 2 years and yearly thereafter.

The prospective study, TMJ-96-001 was designed to evaluate the ability of the TMJ Fossa-Eminence Prosthesis, when used alone (partial joint replacement); to reduce TMJ pain and improve interincisal opening in appropriately selected patients. An additional objective of the prospective study included a review of device related adverse events occurring during the study

Pain measurements for both studies were recorded using a 10cm Visual Analog Scale (VAS). The left side of the scale represented no pain while the right side represented the most severe pain imaginable. The patients were instructed to mark a vertical line on the scale to indicate their perceived level of pain. At the point where this vertical line crossed the horizontal scale, a measure was recorded using a ruler graduated in millimeters. Interincisal opening was measured in millimeters using a Therabite™ Scale. The interincisal opening was measured at the point at which the patient cannot open his/her mouth any wider.

A. TMJ Implants, Inc. Registry

Demographics

The Registry included 1358 partial joint recipients representing 1909 devices. Nearly two-thirds (860) of the 1358 provided a Wilkes Staging Classification for Internal Derangement, of which 98 percent (839) were Wilkes Classifications III, IV, or V. The Registry data was described in two ways:

1. cross-sectional data where serial data on patients were not available, and
2. cohort data, where serial data on patients are available.

Two cohorts were analyzed: one representing 157 patients with Wilkes Classifications, pre-op and 2 year pain and opening data, and one representing 84 patients with Wilkes Classifications, pre-op and 3 year data. The majority of the patients in each group received “stock” devices (i.e. FER, FEL models). The mean age of the cross-section group of patients was 40 ± 12 years and of each cohort was 41 ± 12 years and 42 ± 12 years respectively. There were 90% female in the cross-section and 94% and 91% in each cohort respectively.

Pain: Partial Joint Reconstruction

The cross-sectional data in Table 1 has different patient sets and decreasing observations at each successive time point. The samples at various time points are arbitrary and not drawn according to a sampling scheme. From the cross-sectional data set, there is a mean reduction in pain within the first month after surgery, as demonstrated by Figure 1. The cross-section of patients appear to reach their greatest mean pain relief within 6 months of surgery and continue to improve on average through 5 years implant duration. The cohort data with serial measures on one group of patients over two years and another group of patients over three years demonstrated a similar trend (see Tables 2 and 3).

Figure 1: Partial Joint Pain Scores

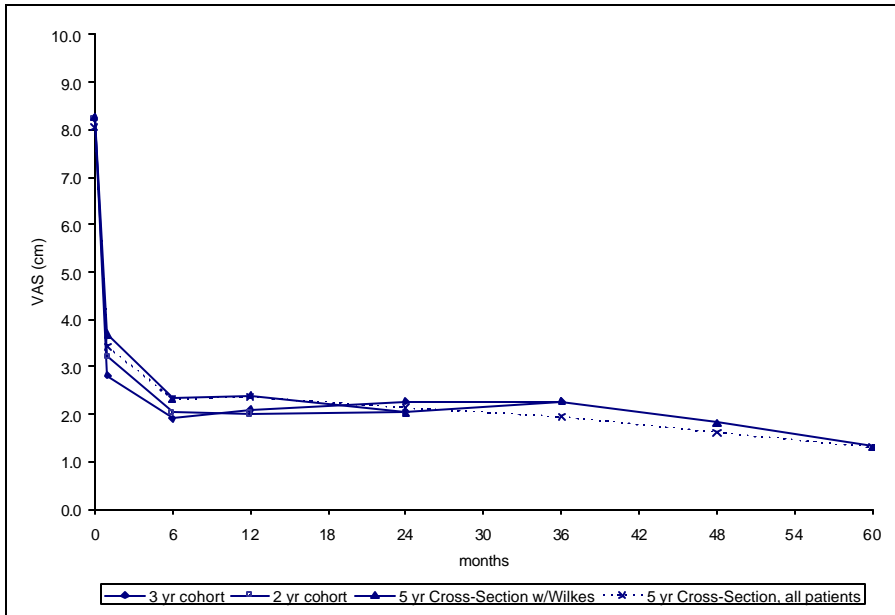


Table 1: Partial Joint, Pain Cross Section Data

| Months | 0 | 1 | 6 | 12 | 24 | 36 | 48 | 60 |
|--------|------|------|-----|-----|-----|-----|-----|-----|
| Mean | 8.0 | 3.4 | 2.3 | 2.4 | 2.1 | 1.9 | 1.6 | 1.3 |
| n | 1358 | 1295 | 807 | 555 | 286 | 166 | 80 | 32 |

Table 2: Pain 3 Yr. Cohort Data

| | 0 | 1 | 6 | 12 | 24 | 36 |
|------|-----|-----|-----|-----|-----|-----|
| Mean | 8.2 | 2.8 | 1.9 | 2.1 | 2.3 | 2.3 |
| n | 84 | 80 | 71 | 64 | 65 | 84 |

Table 3: Pain 2 Yr. Cohort Data

| | 0 | 1 | 6 | 12 | 24 |
|------|-----|-----|-----|-----|-----|
| Mean | 8.2 | 3.2 | 2.0 | 2.0 | 2.0 |
| n | 157 | 152 | 124 | 115 | 157 |

Interincisal Opening: Partial Joint Reconstruction

From the cross-section data in Table 4, there is a mean improvement in the interincisal opening at 6 months after surgery, as demonstrated by Figure 2. Patients appear to reach their greatest mean improvement at 6 months after surgery and maintain that level of improvement on average through 5 years implant duration. A similar trend of improvement in opening is demonstrated with a cohort of 75 patients and 136 patients with complete data at 3 years and 2 years implant duration respectively, Tables 5 and 6.

Figure 2: Partial Joint, Opening Data

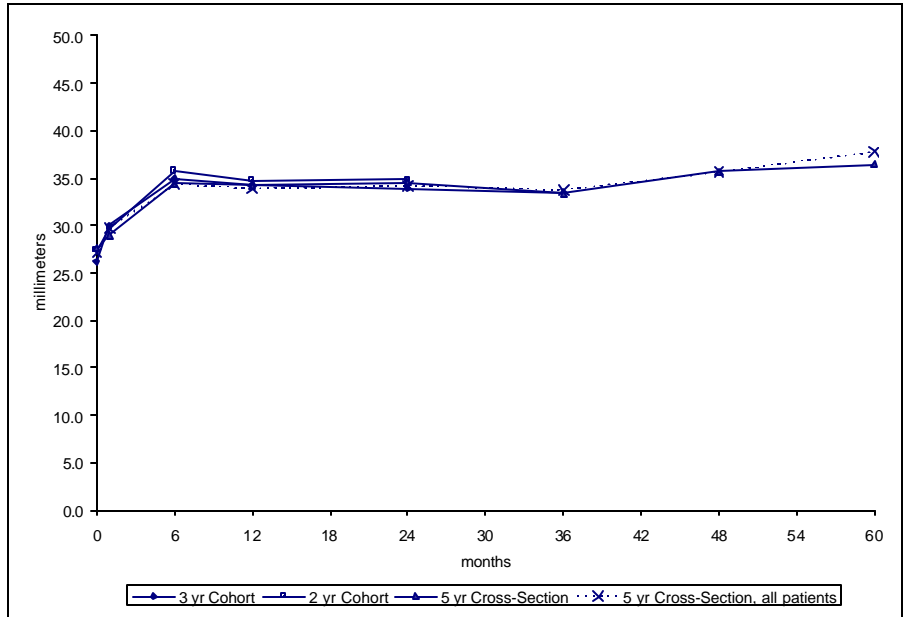


Table 4: Partial Joint, Opening Cross Section Data Table 5: Opening 3 Yr. Cohort Data Table 6: Opening 2 Yr. Cohort Data

| Months | 0 | 1 | 6 | 12 | 24 | 36 | 48 | 60 |
|--------|------|------|------|------|------|------|------|------|
| Mean | 27.1 | 29.7 | 34.4 | 33.9 | 34.2 | 33.8 | 35.7 | 37.8 |
| n | 1175 | 1123 | 714 | 491 | 261 | 152 | 76 | 29 |

| | 0 | 1 | 6 | 12 | 24 | 36 |
|------|------|------|------|------|------|------|
| Mean | 26.2 | 30.0 | 35.0 | 34.4 | 33.9 | 33.5 |
| n | 75 | 74 | 62 | 53 | 57 | 75 |

| | 0 | 1 | 6 | 12 | 24 |
|------|------|------|------|------|------|
| Mean | 27.4 | 29.7 | 35.7 | 34.8 | 34.9 |
| n | 136 | 133 | 111 | 97 | 136 |

B. Prospective Study – TMJ-96-001

Demographics and Indications

Of the 131 subjects enrolled in the study and implanted with a partial joint, there are 109 subjects for which data are currently available. Of this data set 90% of the 109 subjects are female and 90% are Caucasian. The mean age is 39±11 years.

Eighty seven subjects included in this protocol were treated with a diagnosis of internal derangement. The subjects that were available for evaluation with the diagnosis of internal derangement were then retrospectively categorized with a Wilkes classification. These patients had all or some of the criteria necessary for a classification of Wilkes class III, IV, or V.

The indications for surgery are as follows:

Table 7: Indications for Surgery

| Indication | n | Cum. % | Wilkes Correlation |
|-------------------------------------------------------|----|--------|--------------------|
| Internal Derangement without meniscal perforation | 48 | 44 | III,IV |
| Internal Derangement with meniscal perforation | 31 | 72 | V |
| Internal Derangement and meniscus status unidentified | 8 | 80 | III, IV, V |
| Inflammatory arthritis | 10 | 89 | V |
| Recurrent Fibrosis and/or bony ankylosis | 9 | 97 | N/A |
| Failed alloplastic joint reconstruction | 2 | 99 | N/A |
| Failed tissue graft | 1 | 100 | N/A |

The mean reduction in pain scores as measured using a VAS and the interincisal opening for all subjects receiving a partial joint replacement are represented in Figures 3 and 4.

Figure 3: Mean Pain levels, all subjects with partial joint replacement

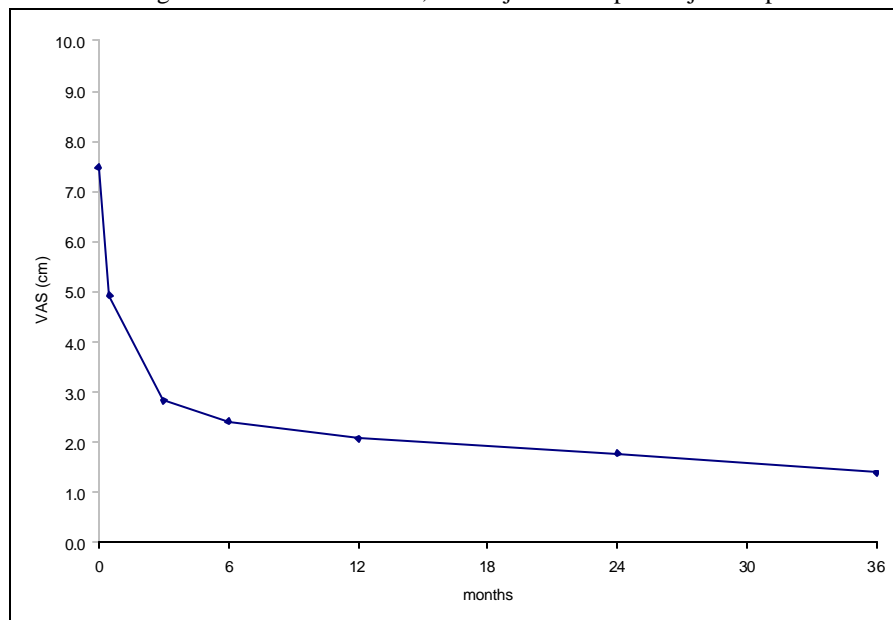
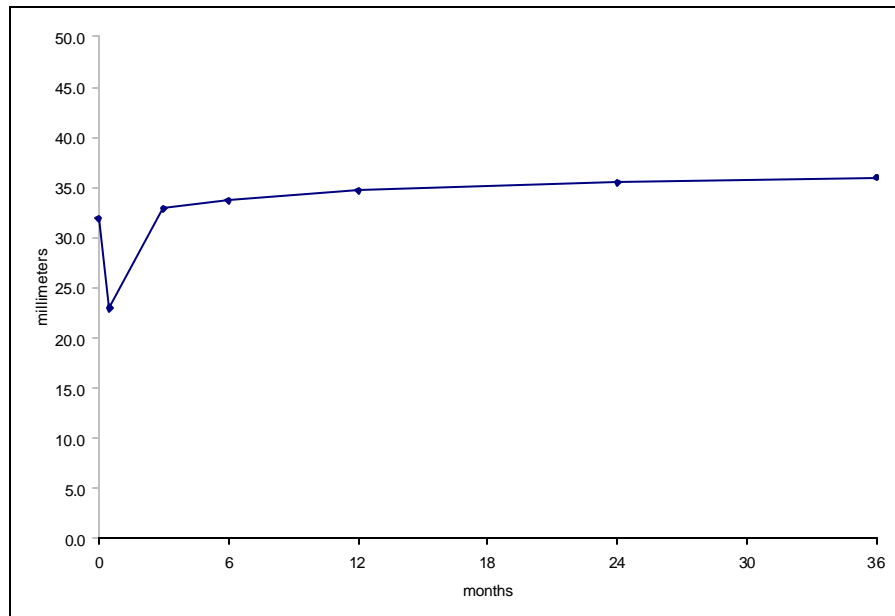


Figure 4: Mean Interincisal Opening, all subjects with partial joint replacement



Tables A, and B describe the current status of the 97 patients diagnosed with internal derangement classified into Wilkes III-V, and/or inflammatory arthritis in the ongoing trial.

Table A: Pain

| months | 0 | 0.5 | 3 | 6 | 12 | 18 | 24 | 30 | 36 |
|---------------------------------------|------|-----|-----|-----|-----|-----|-----|-----|-----|
| mean pain | 7.5 | 5.0 | 2.9 | 2.3 | 1.9 | 2.5 | 1.8 | 0.8 | 1.4 |
| completed visits | 97 | 95 | 82 | 71 | 43 | 29 | 29 | 11 | 12 |
| SD of mean pain | 2.1 | 3.0 | 2.8 | 2.4 | 2.4 | 3.2 | 2.0 | 1.5 | 2.4 |
| Expected # of subjects | 97 | 97 | 95 | 91 | 83 | 70 | 59 | 52 | 40 |
| Actual or potential lost to follow-up | 0 | 2 | 13 | 20 | 40 | 41 | 30 | 41 | 28 |
| % completed visits | 100% | 98% | 86% | 78% | 52% | 41% | 49% | 21% | 30% |

Table B: Interincisal Opening

| months | 0 | 0.5 | 3 | 6 | 12 | 18 | 24 | 30 | 36 |
|---------------------------------------|------|-----|-----|-----|-----|-----|-----|-----|-----|
| Mean opening measurement | 33 | 23 | 33 | 34 | 35 | 34 | 36 | 36 | 36 |
| completed visits | 97 | 95 | 82 | 71 | 43 | 29 | 29 | 11 | 12 |
| SD of mean opening | 11.0 | 6.8 | 4.8 | 4.5 | 5.4 | 5.6 | 5.4 | 3.6 | 5.9 |
| Expected # of subjects | 97 | 97 | 95 | 91 | 83 | 70 | 59 | 52 | 40 |
| Actual or potential lost to follow-up | 0 | 2 | 13 | 20 | 40 | 41 | 30 | 41 | 28 |
| % completed visits | 100% | 98% | 86% | 78% | 52% | 41% | 49% | 21% | 30% |

Mean pain and interincisal opening for the group of subjects with internal derangement and/or inflammatory arthritis correlating to Wilkes class III-V are represented in Figures 5 and 6 respectively.

Figure 5: Mean Pain Reduction, subjects with Wilkes III-V

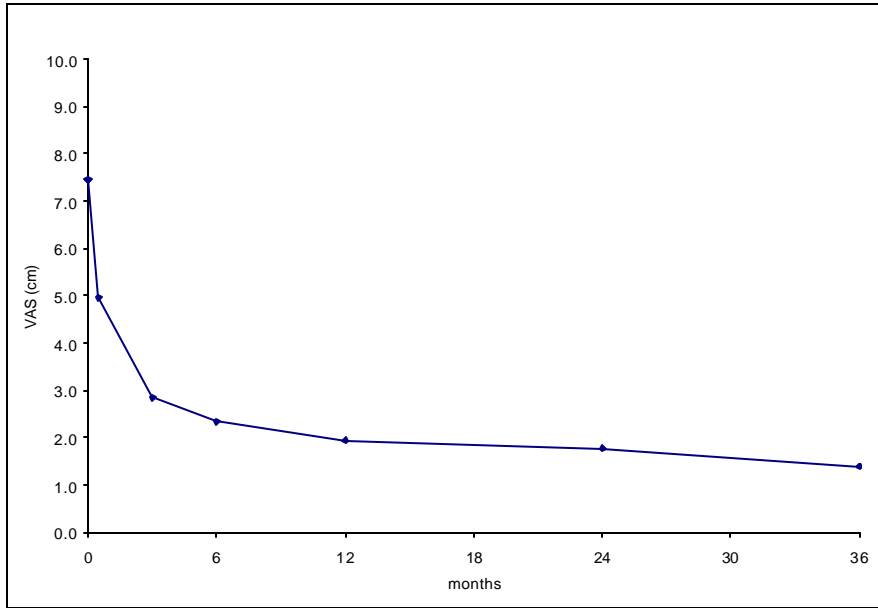
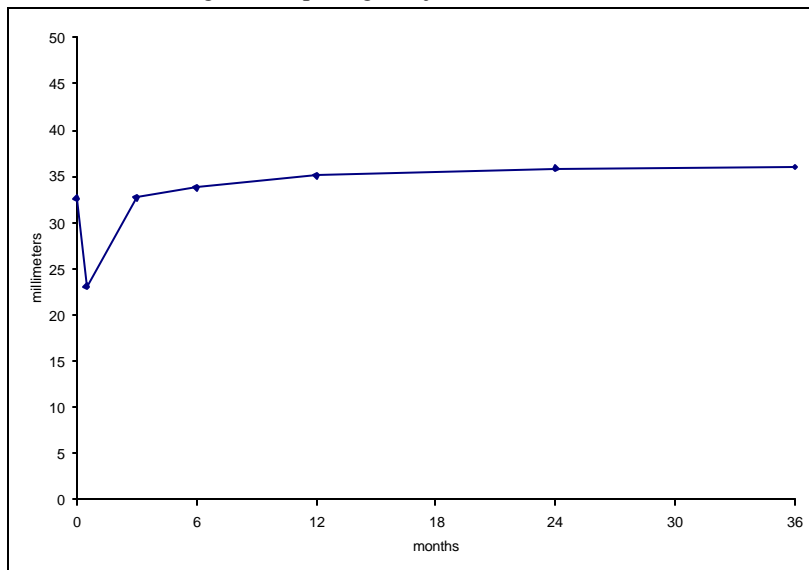


Figure 6: Opening, subjects with Wilkes III-V



Of the 97 subjects, 40 subjects have had the TMJ Fossa-Eminence Prostheses implanted for at least 3 years. Follow-up is continuing. The periods of follow-up have been divided into the following groups based on the currently available long-term follow-up data:

Group A: 12 subjects with follow-up data for 3 or more years

Group B: 16 subjects with follow-up data for 2 - 3 years

Group C: 4 subjects with follow-up data for 1 - 2 years

Group D: 9 subjects with follow-up data for less than 1 year

Results for the subjects in each group are presented below:

Pain (measured using a 10 cm Visual Analog Scale)

Group A. Of the 12 subjects in Group A, 7 had a baseline pain score ranging from 5.5 to 9.1. These 7 subjects had 3-year pain scores ranging from 0.0 to 0.3. Of the remaining 4 subjects, one had a baseline pain score of 10.0 and a 3-year pain score of 1.7, 2 subjects declined in pain scores at 3-years from 6.0 to 5.0 and 8.9 to 6.6 respectively, and one subject had a baseline pain score of 5.0 and reported "no pain" at 3-years. These 12 subjects represent 30% of the subjects expected at this time point. The remaining 70% are either lost to follow-up, withdrawn, or potentially lost to follow-up.

Group B. Of the 16 subjects in Group B, 6 subjects had baseline pain scores ranging from 5.0 to 9.8, and had a 2½-year pain score of 1.0 or less. Five subjects had baseline pain scores ranging from 5.0 to 9.3, and had a 2-year pain score of 1.1 or less. Four subjects had a change from baseline ranging from 5.9 to 9.9 and a 2-year pain score of 1.9 to 4.1. One subject had a baseline score of 4.9 and a 2-year pain score of 7.2.

Group C. Of the 4 subjects in Group C, one subject had a baseline pain score of 8.1 and a 1-year pain score of 4.4; the second had a decline in pain score 10.0 to 4.2 at 1-year; the third subject had a decline in pain score from 2.2 to 0.1 at 1-year; and the fourth had a decline in pain score from 9.0 to 5.3 at 18 months.

Group D. Of the 9 subjects in Group D, 4 subjects had baseline pain scores ranging from 5.5 to 8.2 and 6-month pain score ranging from 1.0 to 1.8. One subject declined in pain score from 8.0 to 6.0 at 6 months; another subject declined in pain score from 7.4 to 4.0 at 6 months. One subject had a baseline pain score of 3.1 and a 6 month score of 5.0. Two subjects with 3 month follow up data declined in pain from 8.6 to 2.8 and from 10.0 to 0.5, respectively.

Interincisal Opening (measured in millimeters)

The 40 forty subjects having had the TMJ Fossa-Eminence Prostheses implanted for at least 3 years were being treated primarily for significant TMJ pain. As can be expected with the placing of an alloplastic implant, there was a decrease in interincisal opening at 2 weeks post-surgery. However, at the 3-month follow-up visit, opening had increased from the 2-week measurement in all but 1 patient. The last available opening score for

36 subjects (follow-up ranging from 6 months to 3 years) was 30 mm or greater. Of the remaining four subjects one had an opening score of 26mm at 3 months, the other 3 subjects had opening scores of 27, 28, and 29mm, respectively at 2 years. On average patients interincisal opening decreased by 2 millimeters from the ir preoperative opening measurements.

Adverse Events, all subjects

Fifty adverse events were reported from 22 different patients in the prospective study. The adverse events that were reported may be associated with the implementation of the TMJ Implants, Inc. fossa-eminence prosthesis.

| Event Category | # of subjects/events | % of total subjects (109) |
|-----------------------------------------------------------------------|-----------------------------|----------------------------------|
| Facial nerve and muscle weakness, paralysis, hearing problems | 8/16 | 7% |
| Postoperative pain, swelling, jaw muscle spasm and hematoma formation | 11/15 | 10% |
| Degenerative joint changes, development of joint arthritis | 8/10 | 7% |
| Foreign body or allergic reactions, implant rejections | 1/1 | 1% |
| Jaw dysfunction | 1/1 | 1% |
| Limited range of motion | 1/1 | 1% |
| Other | 5/6 | 5% |

Two of the 109 subjects required additional surgery during their participation in the study. Note: these 2 subjects were not part of the 40 subjects with the device implanted for at least 3 years reported above. Both events occurred within 1½ years of the original surgery. One subject progressed from a unilateral Fossa-Eminence prosthesis to a bilateral prosthesis due to progressive internal derangement in the contralateral joint. The other subject progressed from a unilateral Fossa-Eminence prosthesis to a bilateral total joint replacement due to progressive, bilateral degenerative joint disease and heterotopic bone formation.

XII. CONCLUSIONS DRAWN FROM THE STUDIES

PRECLINICAL

Pre-clinical tests were undertaken on the total joint system which contains the Fossa-Eminence to demonstrate that the TMJ Implants, Inc. prosthetic devices have adequate strength and durability for their intended use. The total joint system has an estimated fatigue limit of 130 lbs. The fatigue limit of the partial joint is unknown, but due to the limitations of testing with a natural condyle the testing of the total joint is sufficient since the natural condyle will do less damage to the fossa-eminence than the metal condyle of the total joint system.

CLINICAL

The subject device is a Class III preamendments device which has been marketed since the 1960's . Temporomandibular Joint Disease (TMD) is thought to be a disease of

multifactorial origin with several recognized therapeutic alternatives, each with its own strong proponents and detractors.

Safety

A review of the types of adverse events reported within the Prospective Clinical Study TMJ-96-001 demonstrates an incidence rate of all events that is not unexpected of this patient population. FDA also considered a retrospective review of patient charts and radiographs by a clinical investigator in the prospective study. The study was intended to determine the effect of the partial joint implant (TMJ Fossa-Eminence Prosthesis) on the remaining natural condyles, as evidenced by the clinical outcomes of patients implanted with the TMJ Implants Inc. Fossa-Eminence Prosthesis. This review indicates that the selected patients who have had the Fossa-Eminence prosthesis for greater than 3 years in this investigator's practice do not have an unusually high incidence of bony changes to the natural condyle. This study did not find evidence of degradation of the natural condyle as a result of the use of the metal fossa liner.

Effectiveness

The TMJ Implants, Inc. Registry, though not a controlled clinical study, provided significant human experience with the fossa-eminence prostheses manufactured by TMJ Implants, Inc. The cohorts derived from the Registry data through 3 years duration demonstrated a reduction in perceived pain and improvement in interincisal opening. The data from the ongoing Prospective Clinical Study, TMJ-96-001, demonstrated a similar trend in pain scores and an average decrease of 2mm in interincisal opening from the preoperative opening data.

XIII. PANEL RECOMMENDATIONS

The device was considered by the Dental Products Advisory Panel on two separate occasions; once as part of a PMA submission which included both the partial joint (subject device) prosthesis, and a total TMJ replacement joint prosthesis. The Panel recommended approval of the "combined" PMA at the time of the first meeting and subsequently the total joint has been approved. The approval recommendation contained numerous conditions for additional clinical and preclinical data and a request that data be presented again to the panel. Recognizing that there may be significant differences in the target populations and, therefore, in the risk/benefit analysis for the partial, as opposed to the total joint, the agency elected to separate the partial joint as a separate PMA and present that subset of data to the Panel. This time a recommendation from the Panel was to "not approve" the partial joint. The Panel believed that the safety and effectiveness data for the device was inadequate. In addition, the Panel believed that the indications for use needed to be clarified. The Panel recommended the following steps in order to bring this application into an approvable form:

- Clarification of the indications for use
- Specific labeling that addresses the indications for this type of surgery
- Labeling that specifies that this is not a primary intervention

- Completion of additional patients in the prospective study
- Clarification and standardization of radiologic criteria for assessing and monitoring the natural mandibular condyle
- TMJ Implants Inc. should make every attempt to locate and evaluate patients that are listed as lost to follow-up.

XIV. FDA DECISION

FDA considered and concurred with the Panel's concerns about the prospective and retrospective studies. FDA continued to work with the sponsor to address these scientific concerns. The sponsor submitted an updated cohort analysis for the registry patients and for the prospective study patients. The updated data are incorporated into Tables 1 through 7 and Tables A and B above. The updated data on the registry patients included information on the temporomandibular joint classification of the patient prior to surgery and an additional break out of patients with complete data out to 2 years. The updated data from the prospective study included additional follow-up data and information on patient demographics, surgical history, and surgical findings. The addition of this updated data narrowed the internal derangement indication for use, offered additional follow-up data on patients in the prospective study, provided further supportive information on the condition of the natural condyle, and offered insight into the surgical protocols used by implanting surgeons. The labeling was revised to reflect this new information and to clearly indicate in warnings that this is not a primary intervention.

FDA balanced the scientific concerns related to the limited clinical data with the knowledge that there appears to be a group of patients for whom this device seems to provide a reasonable treatment option. FDA concluded that there is a reasonable benefit to risk ratio associated with the device under the conditions of use in the labeling. The patient and professional labeling adequately ensures that patients receiving the device are appropriately informed with respect to their disease, all treatment alternatives, and the information presently known and unknown about the subject device. To that extent, the labeling reflects the data available, and includes appropriate warnings and precautions to address the remaining issues.

In addition, the applicant must conduct a post-approval study in order to further evaluate the long-term safety and effectiveness of the device. Subjects enrolled in the applicant's prospective study will continue to be followed for 3 years and data collected will include 1) a quantitative analysis of the condition of the natural condyle; 2) an evaluation of all explants of the device; 3) an analysis of the subjects requiring implantation of an alloplastic condyle following partial joint implantation; and 4) documentation of efforts to locate and evaluate patients that are listed as lost to follow up.

FDA inspections completed January 4, 2001, determined the manufacturing facilities to be in compliance with the Quality System Regulations (QSR).

CDRH issued an approval order on February 27, 2001.

CDRH issued a tracking order on February 27, 2001

XV. APPROVAL SPECIFICATIONS

- Directions for use: See the labeling.
- Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.
- Postapproval requirements and restriction: See approval order.