SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name: Total temporomandibular joint implant

Device Trade Name: Total Temporomandibular Joint (TMJ) Replacement System

Applicant's Name: Walter Lorenz Surgical Incorporated
1520 Tradeport Drive
Jacksonville, Florida 32218-2480

Premarket Approval Application (PMA) Number: P020016

Date of Panel Recommendation: August 22, 2002

Date of Notice of Approval to the Applicant: September 21, 2005

II. Indications for Use

The Total Temporomandibular Joint(TMJ) Replacement System is indicated for reconstruction of the temporomandibular joint. The reconstruction is necessary due to one of the following diagnoses:

1. arthritic conditions: osteoarthritis,
   traumatic arthritis
   rheumatoid arthritis
2. ankylosis including but not limited to recurrent ankylosis with excessive heterotopic bone formation,
3. revision procedures where other treatments have failed (e.g. alloplastic reconstruction, autogenous grafts)
4. avascular necrosis
5. multiply operated joints
6. fracture
7. functional deformity
8. benign neoplasms
9. malignancy (e.g. post-tumor excision)
10. degenerated or resorbed joints with severe anatomic discrepancies
11. developmental abnormality

III. Device Description

The Total TMJ Replacement System is a two component system comprised of mandibular condyle and glenoid fossa components. Both components are available in multiple sizes as right and left side specific designs and are attached to bone by screws. The individual components are not for use in partial joint reconstruction. The Total Temporomandibular Joint (TMJ) Replacement System is implanted in the jaw to functionally reconstruct a diseased and/or damaged temporomandibular joint. Included in the system are trials, instruments and instrument cases.

Materials:

Mandibular Component – Cobalt-Chromium-Molybdenum (Co-Cr-Mo) alloy per ASTM F 1537 with titanium alloy (Ti-6Al-4V) powder per ASTM F 1580) plasma spray coating or Titanium (Ti-6Al-4V) alloy per ASTM F 136 with titanium alloy (Ti-6Al-4V) powder per ASTM F 1580) plasma spray coating

Fossa Component – ArCom® ultra-high-molecular-weight (UHMWPE) per ASTM F 648

Screws – Titanium alloy (Ti-6Al-4V per ASTM F 136)

Trials – mandibular- aluminum fossa- Radel® plastic

Instruments – TMJ flat diamond rasp, TMJ diamond burs, TMJ double ended drill guide, retractors - stainless steel

Instrument Case – stainless steel, silicone, Radel® plastic

IV. Contraindications

1. Active or chronic infection.
2. Patient conditions where there is insufficient quantity or quality of bone to support the components.
3. Systemic disease with increased susceptibility to infection.
4. Patients with extensive perforations in the mandibular fossa and/or bony deficiencies in the articular eminence or zygomatic arch that would severely compromise support for the artificial fossa component.
5. Partial TMJ joint reconstruction.
6. Known allergic reaction to any materials used in the components.
   NOTE: Patients with known or suspected nickel sensitivity should not have Co-Cr-Mo devices implanted since this material contains nickel.
7. Patients with mental or neurological conditions who are unwilling or unable to follow postoperative care instructions.
8. Skeletally immature patients.
9. Patients with severe hyper-functional habits (e.g. clenching, grinding etc.)
10. Patients with a foreign body reaction due to previous implants.

V. Warnings and Precautions

The warnings and precautions can be found in the Total TMJ Replacement System labeling.

VI. Alternative Practices and Procedures

Alternative practices and procedures include autogenenous or allogeneic bone grafting and implantation of other marketed devices for total TMJ reconstruction.

VIII. Potential Adverse Effects

Adverse events that may occur following placement of the Total TMJ Replacement System are listed below. See Tables 7 and 8 for more detailed information on adverse events from the clinical trial.

- Removal of components(s) including, but not limited to the following:
  - implant changes caused by loading and/or wear
  - degenerative changes within the joint surfaces from disease or previous implants
  - implant materials producing particles or corroding
- Loosening or displacement with or without removal of the implant
- Infection (systemic or superficial)
- Foreign body or allergic reaction to implant components
- Fossa wear through
- Facial swelling and/or pain
- Facial nerve dysfunction
- Excision of tissue
- Heterotopic bone formation
- Neuroma formation
- Ear problems
- Dislocation

IX. Marketing History

Approval for marketing has been granted by Europe (EC-Certificate issued November 23, 2000). The system has been marketed in South Africa since January 2000. The medical device license for marketing from Canada was issued on January 14, 2004. The device has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

X. Summary of Preclinical Studies

Shelf Life and Package Tests

All packages were gamma irradiated twice (2 X) for the purpose of package validation.

A. Bubble Emission Testing was performed: packages inflated to ~4 psi and packages were submerged for 2 minutes and observed for bubble leaks.

B. Burst Testing was performed: packages were slowly pressurized with air to the equivalent of submersion under 22.8 inches of water and held for 10 seconds, and then filled to burst.

C. Distribution Simulation: in accordance with ASTM D 4169, Distribution Cycle 13 (an appropriate cycle), Assurance Level I (the most rigorous level). Repeated 3 times, with real or mock devices.

D. Accelerated Aging was performed: at 55°C. At this temperature 37 days is equivalent to 1 year of real-time aging, and their 76 days exceeds the 2 year equivalent of 74 days by 2 additional days.

E. Real-time Aging was performed: on a significant number of fossa and mandibular packages. This was followed by Bubble and Burst testing, but no simulated shipping and handling was included.

F. Microbial Challenge test: performed on 47 Fossa and 47 Mandibular packages as baseline. Only 60 Fossa packages were tested after both accelerated aging and 3X Distribution Simulation

Four packages failed the Bubble Emission test after exposure to both 2 years of accelerated aging and 3X Distribution Simulation. All other test packages met the established acceptance criteria, including visual inspection. Package seals were strong and consistently met the acceptance criteria. A shelf life of one year was established for the Total TMJ Replacement System.

Biomechanical Tests

The following biomechanical tests were conducted on the Total TMJ Replacement System. Test results were all determined to be sufficient for the intended use of the construct/component.

A. Fatigue Testing of Fossa and Mandibular Component Construct
B. Static Testing of the Mandibular Component
C. Fossa Screw Head Pull-Through Test
D. Compression Strength of Fossa Component Flange
E. 2.7mm Self-Tapping Screw Pull-Out Strength

A. Fatigue Testing of Fossa and Mandibular Component Construct

Initial fatigue testing was performed on five joints with mandibular components minus the titanium plasma spray coating. No failures were seen after 10 million cycles at a maximum load of 145 lbs. at frequencies between 10 and 30 hertz. The same testing was repeated on four joints with mandibular components coated with titanium plasma spray. There were no failures after 10 million

cycles and no porous coating delamination was observed as expected from previous testing on orthopedic devices.

B. Static Strength Testing of the Mandibular Component

A mandibular component was fixed to porcine bone using four 2.7mm diameter screws and a load was applied to ultimate failure. At 575.9 lbs. the component's neck portion bent with neither fracture/pull-out of the bone screws or fracture of the component.

C. Fossa Screw (2.0mm) Head Pull -Through Test

Twelve specimens were tested to determine the force required to pull the fossa screw head through the UHMWPE zygomatic arch flange of the fossa component. A standard static tensile test was performed using a cross-head travel rate of 0.05"/minute and the ultimate tensile loads were recorded. The mean tensile strength was 79.8 ± 2.5 lbs.

D. Compression Strength of Fossa Component Flange

A fossa component was tested to establish the load required to collapse an unsupported fossa body and assure that failure in this fashion does not cause tearing or cracking of the UHMWPE junction between the body and flange of the fossa component. The fossa body collapsed against the flange at 83 lbs. without material failure at the body/flange junction.

E. 2.7mm Self-Tapping Screw Pull-Out Strength

Five 2.7mm screws used to fixate mandibular components were tested for pull-out strength in fresh frozen bovine cortical bone. This substrate was chosen to mimic the clinical application. The mean pull-out strength was 373.2 ± 68.8 lbs.

XI. Summary of the Clinical Studies

A. Objective

The study was designed to obtain clinical data to support the safety and effectiveness of this device.

B. Inclusion / Exclusion Criteria

Inclusion Criteria:

1. Patients requiring total joint reconstruction due to:
   - arthritis (osteo-, rheumatoid, traumatic)
   - ankylosis
   - avascular necrosis
   - benign neoplasms
   - multiple operated joints
   - malignancy
   - functional deformity
   - revisions
   - fracture
2. Patients who are skeletally mature.

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3. Patients must have at least one of the following criteria for surgical TMJ treatment.
    a. presence of considerable pain and/or limited function in the joint area.
    b. clinical and imaging evidence consistent with anatomic joint pathology.
    c. previous failure of non-surgical treatment/therapy or a failed implant.
    d. high probability of patient improvement by surgical treatment.
4. Patients must be able to return for follow-up examinations.
5. Patients without serious compromising general medical conditions.

Exclusion Criteria:

1. Patients with active infection.
2. Patient conditions where there is insufficient quantity or quality of bone to support the device.
3. Patients with perforations in the mandibular fossa and/or bony deficiencies in the articular eminence compromising support for the artificial fossa component.
4. Patients with mandibular and/or zygomatic arch screw holes compromising component fixation.
5. Patients requiring partial joint reconstruction or other TMJ procedures not listed as an indication.
6. Patients who are not skeletally mature.
7. Patients who are incapable or unwilling to follow postoperative care instructions.
8. Patients who are unable to return for follow-up examinations.
9. Patients with severe hyper-functional habits.
10. Patients on chronic steroid therapy.

C. Patient Population and Demographics

A total of 224 cases (329 joints) with a mean patient age of 40 years (range 13-82 years) were enrolled into the study. There were 198 females (88%) and 26 males (12%) comprised of 105 (47%) bilateral cases and 119 (53%) unilateral cases. Of the 119 unilateral cases, 53 (45%) are the right side and 66 (55%) are left sides only. Demographic data are summarized in **Table 1**. Most cases had multiple diagnoses with osteoarthritis and ankylosis being the most common. See **Table 2** for a complete listing of diagnoses.

The mean duration of symptoms prior to implantation with this device was 11 years (range 0.1- 40 years) with the mean number of 4.8 (range 0-29) prior surgeries.

Patients were categorized according to the Wilkes Classification. There were 3 (1%) cases in Class I, 1 (1%) in Class II, 8 (4%) in Class III, 90 (40%) cases in Class IV, and 122 (54%) cases in Class V.

TABLE 1
Demographic Characteristics

	Total Cases n=224
Age (years)	
Mean	40.3
Standard Deviation	±10.6
Range	13-82
Gender	
Female	198 (88.3%)
Male	26 (11.7%)
Side	
Unilateral	
Right	53 (23.7%)
Left	66 (29.5%)
Bilateral	105 (46.9%)

TABLE 2
Diagnosis

	Total Cases Right Side n=158		Total Cases Left Side n=171	
	n	%	n	%
1. Osteoarthritis	93	28%	107	30%
2. Rheumatoid Arthritis	9	3%	12	3%
3. Traumatic Arthritis	60	18%	64	18%
4. Malignancy	0	0%	0	0%
5. Benign Neoplasm	1	0%	1	0%
6. Functional Deformity	9	3%	9	2%
7. Revision: partial implant	8	2%	11	3%
8. Revision: total implant	45	14%	49	14%
9. Avascular Necrosis	42	13%	42	12%
10. Ankylosis	46	14%	50	14%
11. Fracture	16	5%	16	4%

D. Evaluation Schedule

Patients were evaluated preoperatively and postoperatively at 1 month, 3 months, 6 months, 1 year, 1.5 years, and 3 years. All data collected past the 3 years follow-up are included. The assessments carried out at each visit

labeled as Visit 1-Visit 11 are summarized in **Table 3**.

TABLE 3
Study Visits Schedule

	Vs 1: Screen Base-line	Vs 2: Surgery	Vs 3: 1 month follow-up	Vs 4: 3 month follow-up	Vs 5: 6 month follow-up	Vs 6: 1 year follow-up	Vs 7: 1.5 years follow-up	Vs 8: 3 years follow-up	Vs 9: 4 years follow-up	Vs 10: 5 years follow-up	Vs 11: 6 years follow-up
Inclusion/ Exclusion criteria met	X										
Informed Consent	X	Or X									
Preoperative Record: Medical history clinical examination	X										
Radiographic Assessment	X	*	X	X	X	X	X	X	X	X	X
Jaw pain & function: Jaw pain intensity, Interference with eating, Maximal incisal opening, Occlusion, Anterior open bite, cross bite	X		X	X	X	X	X	X	X	X	X
Operative Record		X									
Patient satisfaction with surgery			X	X	X	X	X	X	X	X	X
Wound healing			X	X	X	X	X	X	X	X	X

* immediate postoperative x-ray used for comparison only.

E. Study Design

The study was a prospective, multi-center, single treatment study. It was designed to compare baseline clinical and radiographic assessments to assessments made postoperatively.

F. Patient Accountability

Table 4 shows the number and percentage of cases with follow-up data at each of the visits. Compliance ranged from 91.0 % at the 1 month follow-up visit to 72.4 % at 3 years follow-up.

TABLE 4
Patient Accountability

	Follow-Up Time Periods								
	1mo	3mos	6mos	1yr	1.5yr	3yrs	4yrs	5yrs	6yrs
Theoretically Due (all cases)	213	204	199	179	164	123	81	47	35
Deaths	1	1	1	1	1	2	2	3	3
Permanent Removal of Total Joint	0	0	1	2	2	2	2	1	0
Have Follow-Up (all cases)	193	181	177	150	129	85	48	20	14
Percent Follow-Up	**91.0**	**89.2**	**89.8**	**85.5**	**80.1**	**72.4**	**64.2**	**51.1**	**48.6**
Have Follow-Up (all joints)									
right side only	44	46	45	42	39	26	15	4	4
left side only	56	50	52	42	29	25	14	7	5
bilateral	93	85	80	66	61	34	19	9	5
Total # of joints	286	266	257	216	190	119	67	29	19

G. Efficacy and Safety Parameters

1. Primary efficacy endpoints include:
   - Jaw pain intensity as measured on a 10 cm visual analogue scale (VAS) from preoperative assessment to assessment 3 years postoperative, adjusted for baseline at preoperative assessment,
   - Interference with eating as measured on a 10 cm VAS from preoperative assessment to assessment 3 years postoperative, adjusted for baseline at preoperative assessment,
   - Maximal incisal opening (MIO) measurement (in mm) from preoperative assessment to assessment 3 years postoperative, adjusted for baseline at preoperative assessment

Patient and Study Sucess

a. Patient Success

A patient was determined to be a success if:

1. patient has not had a permanent total joint removal, and
2. patient meets two of the following three criteria:
   - reduction of pain by 1 cm (VAS) from baseline to 3 years follow-up
   - reduction of interference with eating by 1 cm (VAS) from baseline to 3 years follow-up
   - increase in MIO of 10% from baseline to 3 years follow-up

b. Study Success

The study was deemed to be a success with 60% or more of the patients receiving the device having met the above Patient Success at 3 years follow-up.

In the cohort unimputed group, 84 of 85 (98.8%) cases are patient successes. In the cohort imputed group, 116 of 119 (97.5%) cases are patient successes. These patient success rates surpass the criteria for study success.

Analysis was performed on cases with 3 years follow-up postoperatively. These cases were defined as two groups. One is the cohort unimputed group comprised of 85 cases and the second group, cohort imputed, is comprised of 119 cases. The cohort imputed group used data points obtained at the follow-up visit closest to but not after the 3 years visit for analysis of the 34 cases missing data at the 3 years visit. The primary endpoints are summarized on the following table.

Table 5
Analysis of cases with 3 year follow-up

Primary Efficacy Endpoints	Cohort Imputed Cases n=119	Cohort Unimputed Cases n=85
	Difference between Vs 1 & Vs 8 ± SD	Difference between Vs 1 & Vs 8 ± SD
Jaw pain	5.69 ± 2.33 cm	6.03 ± 2.12 cm
Interference with eating	5.42 ± 2.58 cm	5.60 ± 2.32 cm
MIO	10.69 ± 8.22 mm	10.16 ± 8.72 mm

These primary efficacy endpoints showed a significant improvement from baseline to 3 years postoperative. Multiple analyses (t-test and repeated measures) demonstrate that significant improvement is evidenced after implantation of the Total TMJ Replacement System, same patterned effect for the cohort imputed and unimputed groups.

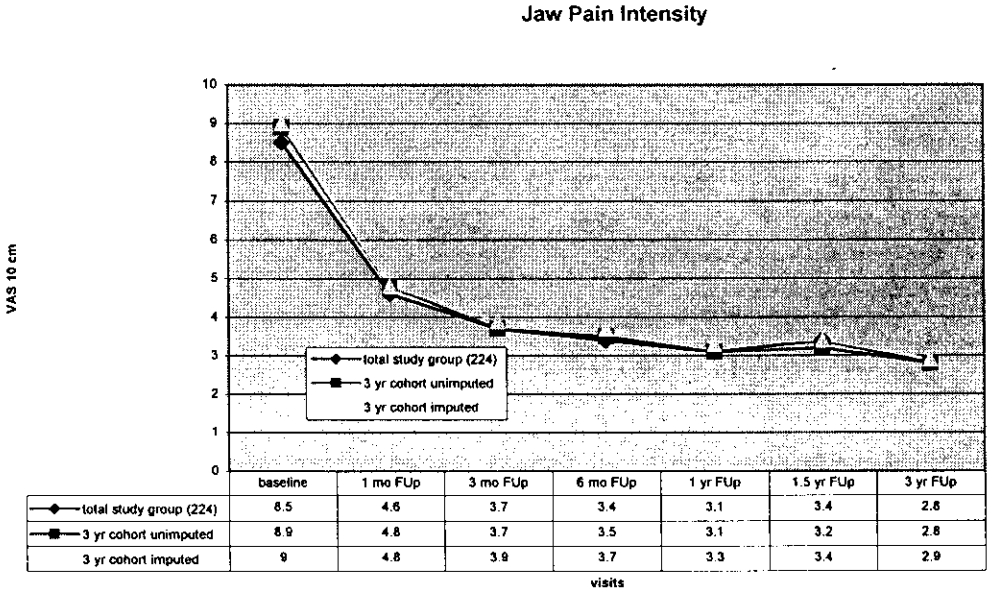
Further t-test analysis shows that in both the total group (n = 224) and the cohort imputed group (n = 119), there was a statistical difference ($p<.0001$) in all three primary endpoints between baseline (Vs 1) and assessments at all time points from 1 month follow-up to 3 years follow-up.

Figures 1, 2, and 3 graphically display the three primary endpoints for the total study group and the two cohort groups from baseline to the 3 years visit.

Comparison of Total Group (n=224) to 3 Year Cohort Unimputed and 3 Year Cohort Imputed

Comparison Means per Visit Groups on Jaw Pain Intensity

Figure 1



	baseline	1 mo FUp	3 mo FUp	6 mo FUp	1 yr FUp	1.5 yr FUp	3 yr FUp
total study group (224)	8.5	4.6	3.7	3.4	3.1	3.4	2.8
3 yr cohort unimputed	8.9	4.8	3.7	3.5	3.1	3.2	2.8
3 yr cohort imputed	9	4.8	3.9	3.7	3.3	3.4	2.9

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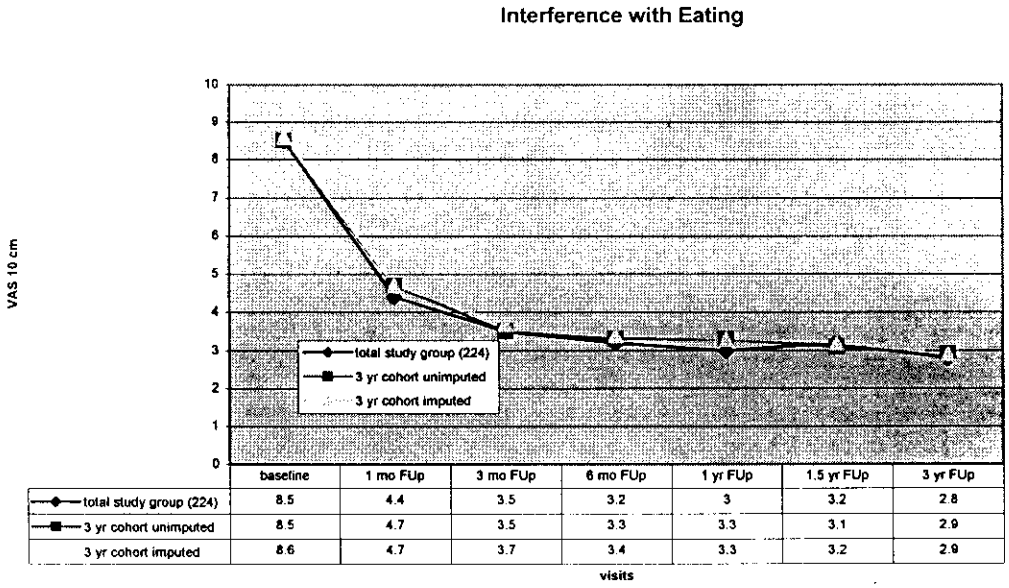
Comparison of Total Group (n=224) to 3 Year Cohort Unimputed and 3 Year Cohort Imputed

Comparison Means per Visit
Interference with Eating

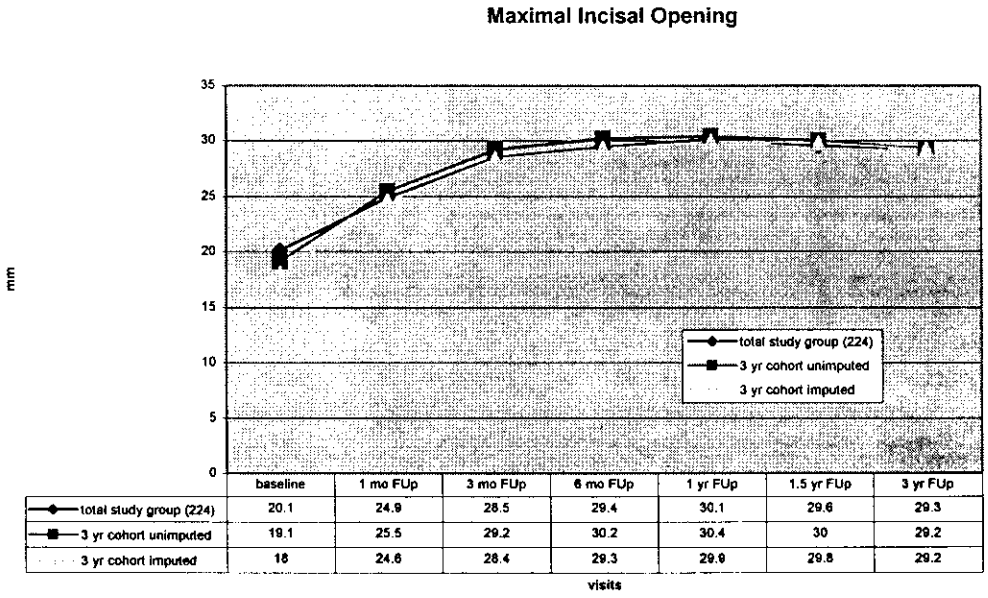
Figure 2



	baseline	1 mo FUp	3 mo FUp	6 mo FUp	1 yr FUp	1.5 yr FUp	3 yr FUp
total study group (224)	8.5	4.4	3.5	3.2	3	3.2	2.8
3 yr cohort unimputed	8.5	4.7	3.5	3.3	3.3	3.1	2.9
3 yr cohort imputed	8.6	4.7	3.7	3.4	3.3	3.2	2.9

Comparison of Total Group (n=224) to 3 Year Cohort Unimputed and 3 Year Cohort Imputed
Comparison Means per Visit
Maximal Incisal Opening

Figure 3



	baseline	1 mo FUp	3 mo FUp	6 mo FUp	1 yr FUp	1.5 yr FUp	3 yr FUp
total study group (224)	20.1	24.9	28.5	29.4	30.1	29.6	29.3
3 yr cohort unimputed	19.1	25.5	29.2	30.2	30.4	30	29.2
3 yr cohort imputed	18	24.6	28.4	29.3	29.9	29.8	29.2

2. Secondary efficacy endpoints include (Vs 1 comparison to Vs 3 – 8):
   - Jaw pain intensity, interference with eating, and maximal incisal opening
   - Patient satisfaction, with a focus on the comparison from postoperative baseline (Vs 5) to 3 years follow-up (Vs 8):
     - in hindsight, whether the patient would choose to have this surgery;
     - degree of satisfaction with surgery across time

The secondary efficacy endpoints demonstrated a gradual improvement over time in terms of jaw pain, interference with eating, and MIO. **Table 6** lists the means and standard deviation for the three endpoints at visits Vs 1 - Vs 11.

TABLE 6
Secondary Efficacy Endpoints
Visits 1 - 11

		Jaw Pain	Interference with Eating	MIO
Visit (interval)	N	Mean ± SD	Mean ± SD	Mean ± SD
Vs 1 (baseline)	224	8.5 ± 2.3	8.5 ± 1.6	20.1 ± 10.0
Vs 3 (1 mo)	193	4.6 ± 2.4	4.4 ± 2.3	24.9 ± 5.8
Vs 4 (3 mos)	181	3.7 ± 2.5	3.5 ± 2.4	28.5 ± 5.8
Vs 5 (6 mos)	177	3.4 ± 2.3	3.2 ± 2.4	29.4 ± 6.1
Vs 6 (1 year)	150	3.1 ± 2.4	3.0 ± 2.3	30.1 ± 5.8
Vs 7 (1.5 yr)	128	3.4 ± 2.3	3.2 ± 2.5	29.6 ± 6.1
Vs 8 (3 yrs)	85	2.8 ± 2.1	2.8 ± 2.0	29.3 ± 6.0
Vs 9 (4 yrs)	48	3.5 ± 2.4	3.4 ± 2.6	28.4 ± 6.6
Vs 10 (5 yrs)	20	4.0 ± 2.7	4.3 ± 2.3	28.9 ± 6.8
Vs 11 (6 yrs)	14	3.7 ± 2.1	3.2 ± 2.0	26.8 ± 5.9

Note: Visit 2 is the day of surgery.

Most patients were satisfied with their outcome as demonstrated with over 90 % of cases reporting at least satisfied or better at every follow-up visit. Furthermore, over 90 % of the cases in hindsight would choose to have this surgery at all time points. More specifically for Vs 3 – Vs 8, between 94 –99 % of the cases said yes to the question " In hindsight would you choose to have this surgery?"

3. Safety

   a. Radiographic assessment (position of components, heterotopic bone formation, osseous erosion, fossa resorption) was performed at each follow-up visit.

      The position of mandibular and fossa components and the mandibular and fossa screws were assessed by investigators in comparison to immediate postoperative radiographs. There were three mandibular components reported as having a change in position: one at Vs 4 and two at Vs 8. The case noted at Vs 4 also had a change of position of the mandibular screws and the joint was removed at 6 months postoperative. No change of position was reported for fossa screws.

      Heterotopic bone formation was found in 15 joints, 8 rights and 7 left joints. There are no reports of osseous erosion or fossa resorption.

   b. Adverse events

      Adverse Events (AEs) were documented for all cases throughout the duration of the study. There have been no unanticipated device related

adverse events reported. Overall, 121 AEs were reported in 80 cases (35.7 %) of the 224 cases. Three cases (1.3 %) terminated the study due to their permanent total joint removal AEs. **Table 7** summarizes AEs requiring device removal. **Table 8** summarizes AEs not requiring device removal.

TABLE 7
Adverse Events Requiring Device Removal

Device Removals	Cases (n=224) #	Cases (n=224) %	Joints (n=329) #	Joints (n=329) %
1. Permanent removal of fossa component: a. One due to aseptic necrosis b. Two due to infection c. One due to swelling d. One due to heterotopic bone removal	5	2.2 %	6	1.8 %
2. Removal (non-permanent)[1] of mandibular component: a. Two bilateral removals of heterotopic bone b. One due to dislocation c. Two due to reposition for malocclusion	5	2.2 %	9	2.7 %
3. Permanent removal of mandibular component: a. Larger component causing a dislocation removed and replaced with smaller component	1	0.4%	1	0.3%
4. Permanent removal of total joint: a. One unilateral patient requested removal due to pain and swelling after 6 months b. Three removals due to infection	4	1.8 %	4	1.2 %
Permanent removal	10	4.5 %	11	3.3 %
Non-permanent removal	5	2.2 %	9	2.7 %
TOTAL	**15**	**6.7 %**	**20**	**6.1%**

[1] Mandibular components were taken out in the operating room for removal of heterotopic bone or re-positioning and then were placed back in the joint.

TABLE 8
Adverse Events Not Requiring Device Removal

Adverse Events	Cases (n=224) #	Cases (n=224) %	Joints (n=329) #	Joints (n=329) %
Reflex Sympathetic Dystrophy (RSD)	1	0.4	1	0.3
Excision of tissue (excluding neuroma and/or heterotopic bone)	4 (10)*	1.8 (4.5)	6	1.8
Heterotopic bone excision	4 (9)	1.8 (4.0)	6	1.8
Chronic severe masseter muscle spasms	2	0.9	3	0.9
Motor vehicle accident (MVA) - increased pain regardless of facial impact	14	6.3	22	6.7
Facial trauma (excluding MVA)	9	4.0	10	3.0
Head trauma with no jaw involvement	2	0.9	3	0.9
Neuroma excision	12 (13)	5.4 (5.8)	15	4.6
Death (all unrelated)	3	1.3	3	0.9
Coronoidectomy	16 (17)	7.1 (7.6)	25	7.6
Unrelated disease diagnosis (multiple sclerosis, Multiple myeloma, meningitis)	3	1.3	5	1.5
Abscess (stitch/facial/intraoral)	3	1.3	5	1.5
Skin infection (not in area of prosthesis)	1	0.4	2	0.6
Dislocation (mandible)	1	0.4	1	0.3
Ear infection (two with tympanic membrane perforation)	5	2.2	8	2.4
External ear canal problems: 1. Perforation 2. Granulation formation	2	0.9	2	0.6
Scalp alopecia from anesthesia tubing pressure	1	0.4	2	0.6
Muscle tenderness	1	0.4	2	0.6
Decreased range of motion	1	0.4	1	0.3
Allergy to resorbable sutures	1	0.4	2	0.6
Contralateral Subcondylar osteotomy for pre-existing disease	1	0.4	1	0.3
Patient reported episodic "floaters" in right eye	1	0.4	2	0.6
Dysesthesia of pre-auricular scar	1	0.4	1	0.3
Ankylosis	2	0.9	3	0.9
Facial numbness	1	0.4	2	0.6
Loose fossa screw	1	0.4	2	0.6
Fistula	1	0.4	1	0.3
Total Cases	**94**	**42.0%**	**136**	**41.3%**
Total Incidence	(107)	(47.8)		

* These numbers in parenthesis ( ) are the incidence.

H. Safety Analysis

1. Deaths

There have been three deaths reported in the study, none of which were device related.

2. Revisions/Removals

   a. Total joint removed
      1. Case # 20
         Bilateral patient first had the right fossa component removed (10 months postoperative) due to infection. A year later the right mandibular component was removed also due to infection. The right side (case #103) was re-implanted 7 months later. Case # 20 is now a left side only.
      2. Case # 61
         Unilateral patient first had her fossa removed 10 months postoperative and subsequent mandibular removal 6 months later due to infection. This case is lost to follow-up.
      3. Case # 100
         Unilateral (right side) patient had removal of prosthesis at 6 months postoperative due to chronic swelling and pain. This case is lost to follow-up.
      4. Case#242
         Bilateral patient had left prosthesis removed 2 months post-op due to chronic infection. The left side prosthesis was re-implanted and is now case #250. Case #242 is now right side only.

   b. Fossa component only revised/removed
      1. Case # 1
         Bilateral patient had removal of left fossa component due to aseptic necrosis at almost 2 years postoperative and 3.5 years after the removal had it replaced.
      2. Case # 13
         Fossa component was removed secondary to infection in the ear canal at 2.5 years postoperative and was replaced a month later.
      3. Case # 19
         Fossa component removed 4 years postoperative due to a late infection of the ear.
      4. Case # 44
         Bilateral fossa components replaced because they were damaged during surgery to remove heterotopic bone.
      5. Case # 117
         At 11 months postoperative the fossa was removed to see if this would decrease swelling. There were no signs of infection but heavy encapsulation was noted.

   c. Mandibular component only revised
      1. Case # 183

This bilateral case was treated for an anterior dislocation by removing the right 50mm mandibular component and replacing it with a 45mm component.

3. Additional Safety Measurement

   a. Surgical Site (wound healing)

      Most surgical wounds healed by 3 months postoperative with 100 % (right side) and 98 % (left side) healed. Redness and drainage accompanied with infection are documented as adverse events.

XII. Conclusions Drawn from Studies

Preclinical
The results of the pre-clinical studies demonstrate the Total Temporomandibular Joint Replacement System has adequate strength and durability for its intended use. The shelf life and package testing resulted in a shelf life of 1 year.

Safety
The types of adverse events reported in the clinical study and the rate at which they occurred are not unexpected in this compromised patient population with many previous surgeries involving failed tissue grafts and/or failed implants which may leave behind material particulates.

Efficacy
The clinical study showed that for patients with complete data at the 3 year follow-up (85 patients) the Total Temporomandibular Joint Replacement System provided statistically significant levels of reduced jaw pain, reduced interference with eating and increased maximal incisal opening. Similar trends, although not statistically significant were observed in the entire patient population. The cohort patients are representative of the target patient population.

XIII. Panel Recommendation

At an advisory meeting held on August 22, 2002, the Dental Products Panel recommended that Walter Lorenz's PMA for the Total TMJ Replacement System be approved subject to the following conditions:

1. The labeling should provide a clearer description of hyperfunctional habits such as clenching or bruxing and this information should be addressed in a different location in the labeling (i.e., moved from the contraindication section to the warnings or precaution section).

2. The Indications for Use section should state the indications for which the device has been well tested. For indications that were not evaluated in the clinical study, the Indications for Use section should state that the device has not been adequately evaluated for these indications.

3. Information regarding the potential for foreign body reaction should be included in patient labeling and physician's information.

4. The sponsor should remove all references to the use of a cemented fossa and state that the device will be marketed as a non-cemented device.

5. All surgeons implanting these devices should be required to receive didactic and hands-on training before they are able to use the device.

6. The following additional in vitro and in vivo testing should be performed:

   a. The sponsor should perform wear testing that simulates the temporomandibular joint

   b. The sponsor should test the fossa components for possible changes in fixation stability due to creep.

   c. All explants should be retrieved and studied for wear, creep, and possible corrosion due to use of dissimilar metals.

   d. For explant cases, the sponsor should perform histologic examination for wear particles.

7. The sponsor should submit data from the fatigue testing of the fossa with the post removed and the fossa made without a post to FDA.

8. The sponsor will seek full or partial data on all 180 cases, including retrieving VAS scores from patients at long distances and collecting full or partial post-market data. All 180 cases presently included in the study should be followed for 3 years for safety and effectiveness.

XIV. FDA Decision

CDRH concurred with the panel recommendations except for the engineering recommendation of wear testing that simulates the temporomandibular joint. This recommendation is not feasible given the lack of an adequate model for the loading of the temporomandibular joint. The labeling, training and other engineering recommendations have been completed.

A postapproval study will be conducted in order to collect additional long-term safety and effectiveness data. Three year follow-up data will be obtained on all subjects enrolled in the clinical study. Reports will be submitted to the PMA

annually. The labeling will be updated via a supplement, when the study is complete.

The applicant's manufacturing faculties were inspected and found to be in compliance with the Quality System Regulations (21 CFR 820).

CDRH issued an approval order on September 21, 2005.

XV. Approval Specification

- 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 Restrictions: See approval order.