SUMMARY OF SAFETY AND EFFECTIVENESS

I. General Information

Device Generic Name: Total temporomandibular joint implant

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

Applicant's Name: Biomet , Inc.
56 East Bell Drive
P.O. Box 587
Warsaw, Indiana 46582 U.S.A.

Premarket Approval Application (PMA) Number:

Date of Panel Recommendation:

Date of Notice of Approval to the Applicant:

II. Indications for Use

The Total TMJ Replacement System is indicated for use in cases of:

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

III. Device Description

The Total Temporomandibular Joint (TMJ) Replacement System is implanted in the jaw to functionally reconstruct a diseased and/or damaged temporomandibular joint. 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.

Materials:

Mandibular Component – Cobalt-Chromium-Molydenum (Co-Cr-Mo) alloy per ASTM F 1537 with titanium alloy (Ti-6Al-4V per ASTM F 136) plasma spray porous coating

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

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

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 perforations in the mandibular fossa and/or bony deficiencies in the articular eminence or zygomatic arch comprising 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.)

V. Warnings

The following risks are associated with the use of a total TMJ system.

1. Implant loosening or displacement can occur.
2. The screws used to anchor the implant may loosen causing changes in bite, difficulty in chewing, limited joint function and/or unpredictable wear on implant components.
3. Implant breakdown may result in erosion or resorption of the glenoid fossa, which may result in intense pain.
4. A foreign body reaction may occur resulting in implant deterioration and migration of materials.
5. If the implant is not properly sterilized, infection may result.
6. If the implant materials are unable to withstand the forces or pressure placed on the implant, the implant can be torn, worn, perforated, fragmented, fatigued, or fractured resulting in failure of the device to function properly.
7. Degenerative changes within the joint surfaces and components of the TMJ due to implant breakdown may result in chronic pain.
8. Degenerative changes in the joint cartilage and/or bone from disease or previous implants may lead to failure of this device.
9. If the implant materials are subject to the production of particles or corrosion,

toxic elements may migrate to various parts of the body.

10. Placement of the implant in one joint only may result in harmful effects to the joint on the opposite side.
11. Placement of the implant may produce an improper relationship between the teeth surfaces that should contact during biting.
12. Implant breakdown may cause bony erosion, heterotopic bone formation, or reactive bone within the joint.
13. Use of implants may result in tinnitus or other ear problems.
14. Limited range of motion and chronic pain may continue after total TMJ surgery.
15. Infection can occur which may result in implant removal.
16. Damage to the facial and/or trigeminal nerve with temporary or permanent paralysis of the facial muscle and/or loss of feeling in the chin, teeth, tongue, or lower jaw may occur.

The surgeon must be thoroughly knowledgeable with the components, instruments and surgical procedure. In all cases sound medical practice is to be followed and the surgeon must select the type of device appropriate for treatment. Existing mandibular and/or zygomatic arch screw holes may compromise fixation. The Total TMJ Replacement System is designed for total joint reconstruction and components are to be used as a system. Do not use the individual components for partial joint reconstruction.

The patient is to be warned that the system does not replace normal healthy bone in their TMJ and they may continue to have chronic pain and limited range of motion. The system can break or loosen as a result of stress, activity, or trauma. Patients with severe hyper-functional habits may have an undesirable outcome. The patient is to be made aware of surgical risks and possible adverse effects prior to surgery and warned that failure to follow postoperative care instructions can cause failure of the implant and the treatment.

VI. Precautions

1. DO NOT USE if there is loss of sterility of the devices.
2. Discard and DO NOT USE opened or damaged implants and only use implants that are packaged in unopened or damaged containers.
3. DO NOT USE the individual components of this total system (e.g. mandibular components, fossa components, or screws) for partial joint reconstruction.
4. Infection can lead to failure and subsequent removal of the devices.
5. Damage to the implant can occur as a result of traumatic injury or excessive activity.
6. Neurovascular injuries can occur due to surgical trauma.
7. Metal sensitivity or foreign body reaction can occur due to the device materials or materials from previously implanted devices.
8. Implant breakdown and/or degenerative changes in the TMJ may cause pain, which may lead to re-operation.

9. Use of the system with filler material:
   The fossa component may be used with a filler material when it is desired to fill voids between the fossa prosthesis and the glenoid fossa bone. The filler should never be used for fixation of the device or in any load bearing application. If a filler is used in the fossa region, screws are placed after polymerization of the filling material, if applicable. Use of any legally marketed craniomaxillofacial filler material is recommended.

VII. Alternative Practices and Procedures

Alternative practices and procedures include autogenenous or allogeneic bone grafting, soft tissue grafts or implantation of other devices for partial or total TMJ reconstruction.

VIII. Potential Adverse Effects

Adverse events can occur following placement of TMJ implants and specific risks are associated with this type of surgery. See the package insert for adverse events reported with the use of this system during an approved Food and Drug Administration (FDA) clinical study. The occurrence of a complication may be related to or influenced by prior medical conditions or treatment and may require further treatment. These adverse events include but are not limited to the following:

- Infection
- Post-operative pain, swelling, bruising, jaw muscle spasm, or hematoma formation
- Chronic or recurring pain
- Heterotopic bone formation, neuroma formation, adhesions, resorption or bony erosion, and/or ankylosis
- Facial nerve dysfunction
- Dislocation
- Removal of components(s) and/or revision
- Harmful effects to the contralateral joint in unilateral cases
- Implant wear, loosening, damage, migration or displacement
- Changes in bite, difficulty in chewing, limited joint function
- A foreign body or allergic reaction to implant materials
- Ear problems
- Degenerative changes in the joint cartilage and/or bone

IX. Marketing History

[redacted]

X. Summary of Preclinical Studies

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

[redacted]

[redacted]

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.
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 180 cases (268 joints) with a mean patient age of 40 years (range 12-82 years) were enrolled into the study. There were 161 females (89%) and 19 males (11%) comprised of 88 (49%) bilateral cases and 92 (51%) unilateral cases. Of the 92 unilateral cases, 46 (50%) are the right side and 46 (50%) 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- 34 years) with the mean number of 5.2 (range 0-29) prior surgeries.

Patients were categorized according to the Wilkes Classification. There were 2 (1%) cases in Class I, none in Class II, 4 (2%) in Class III, 68 (38%) cases in Class IV, and 106 (59%) cases in Class V.

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**.

E. Study Design

The study was a prospective, multi-center, non-randomized controlled 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 95.0 % at the 1 month follow-up visit to 82.5 % at 3 years follow-up.

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

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 45 cases and the second group, cohort imputed, is comprised of 59 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 for the 14 cases missing data at the 3 years visit. The primary endpoints are summarized on the following chart.

Primary Efficacy Endpoints	Cohort Imputed Cases n=59	Cohort Unimputed Cases n=45
	Difference between Vs 1 & Vs 8 ? SD	Difference between Vs 1 & Vs 8 ? SD
Jaw pain	5.43 ? 2.73 cm	5.70 ? 2.40 cm
Interference with eating	5.59 ? 2.95 cm	5.80 ? 2.27 cm
MIO	10.61 ? 8.44 mm	10.27 ? 8.33 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 = 180) and the cohort imputed group (n = 59), 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.

2. Secondary efficacy endpoints include (at visits Vs 1, 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 5** lists the means and standard deviation for the three endpoints at visits Vs 1 - Vs 11.

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)

      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: two at Vs 4 and one at Vs 7. One of these cases 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 13 joints, 7 rights and 6 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, 90 AEs were reported in 55 cases (30.6 %) of the 180 cases. Four cases (2.2 %) terminated the study due to their permanent total joint removal AEs. **Table 6** summarizes AEs requiring device removal. **Table 7** summarizes AEs not requiring device removal.

4. Patient and Study Success

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, 44 of 45 (97.8%) cases are patient successes. In the cohort imputed group, 57 of 59 (96.6%) cases are patient successes. These patient success rates surpass the criteria for study success.

H. Safety Analysis

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2. [redacted]

3. Additional Safety Measurement

   a. Surgical Site (wound healing)

      Most surgical wounds healed by 3 months postoperative with 99 % (right side) and 98 % (left side) healed. Redness and drainage accompanied with infection are documented as adverse events.

XII. Conclusions Drawn from Studies

The pre-clinical and clinical data provide reasonable assurance of the safety and effectiveness of the Total TMJ Replacement System for the stated indications.