

## Summary of Safety and Effectiveness Data

### I. General Information

Device Generic Name: Finger joint, semi-constrained, uncemented, prosthesis  
Device Trade Name: Ascension<sup>®</sup> MCP  
Applicant Name and Address: Ascension Orthopedics, Inc.  
8200 Cameron Road, C-140  
Austin, TX 78754  
Premarket Approval (PMA) Number: P000057  
Date of Panel Recommendation: August 9, 2001  
Date of Good Manufacturing Practice Inspection: April 16 – 18, 2001  
Date of Notice of Approval to the Applicant: NOV 19 2001

### II. Indications for Use

The Ascension MCP is indicated for use as a total joint replacement of index, long, ring, and small finger metacarpophalangeal (MCP) joints that exhibit symptoms of pain, limited motion, or inadequate bony alignment (i.e., subluxation/dislocation) secondary to articular destruction or degenerative disease related to rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis, or post-traumatic arthritis where soft tissue reconstruction can provide adequate stabilization.

### III. Contraindications

- inadequate bone stock at the implantation site
- active infection in the MCP joint
- nonfunctioning and irreparable MCP musculotendinous system
- physical interference with or by other prostheses during implantation or use
- procedures requiring modification of the prosthesis
- skin, bone, circulatory and/or neurological deficiency at the implantation site

### IV. Warnings and Precautions

#### WARNINGS

- Do not modify the Ascension MCP implant in any manner. Reshaping the implant using cutters, grinders, burrs, or other means will damage the structural integrity of the device and could result in implant fracture and/or particulate debris.
- Do not mismatch proximal and distal component sizes. For example, a Size 10 proximal component should be matched with only a Size 10 distal component. The wear behavior of mismatched proximal and distal component size combinations has not been evaluated, and is unknown.

- Do not grasp the Ascension MCP implant with metal instruments, or instruments with teeth, serrations, or sharp edges. Implants should be handled only with instrumentation provided by Ascension Orthopedics. Ascension MCP implants are made of pyrocarbon, which is a ceramic-like material. Mishandling implants could cause surface damage and reduce their strength, and could result in implant fracture and/or particulate debris.
- Do not use Ascension MCP components in combination with proximal and distal components from other products. The wear behavior of Ascension MCP components against proximal and distal component from other products has not been evaluated, and could damage the structural integrity of the device and result in implant fracture and/or particulate debris.

## PRECAUTIONS

- Do not use the Ascension MCP in a joint where soft tissue reconstruction cannot provide adequate stabilization. Similar to the natural joint, the Ascension MCP attains stabilization from the surrounding capsuloligamentous structures. Because soft tissue reconstruction may be unable to maintain joint stability, the Ascension MCP is not recommended for use in joints:
  - where it is not possible to reconstruct the radial-collateral ligament, or
  - in joints that exhibit extension lag greater than 45 degrees,
  - ulnar deviation greater than 30 degrees, or
  - severe subluxation and/or shortening greater than 1 centimeter.
- Special attention should be given to soft tissue reconstruction and joint stability in the ring and small fingers.
- Corrective wrist surgery may be required prior to use of the Ascension MCP. In patients with severe intercarpal supination and radial deviation of the wrist, ulnar deviation of the digits may not be correctable with MCP joint soft tissue reconstruction alone. In these instances, it is recommended that corrective wrist surgery be performed first at a separate setting.
- Obtain proper training prior to use. Surgeons should obtain training from a qualified instructor prior to implanting the Ascension MCP to ensure thorough understanding of the indications, implantation and removal techniques, instrumentation, and post-operative rehabilitation protocol.
- Inspect the articulating surfaces of the Ascension MCP to insure they are clean and free of all debris prior to use. Foreign debris could result in excessive wear.
- Do not resterilize this device. Resterilization could lead to mishandling and surface damage that could result in implant fracture and/or particulate debris.
- Do not reuse this device. Any implant that has been damaged, mishandled, or removed from the sterile field may have surface damage that could result in implant fracture and/or particulate and should be discarded.

## V. Device Description

The Ascension MCP is a two component, semi-constrained, uncemented, finger joint prosthesis intended to replace the metacarpophalangeal (MCP) joint of the hand. The proximal component has a “ball-shaped” articular surface and stem and the distal component has a “cup-shaped” articular surface and stem. The proximal component is intended to replace the articular surface at the head of the metacarpal bone, and the distal component is intended to replace the articular surface at the base of the proximal phalanx. The stem of each component is designed to be a press-fit into the shaft of the finger bone without bone cement. The Ascension MCP is a semi-constrained device, which limits dorsal-volar and medial-lateral component translation due to the geometric design of the articulating surfaces. The Ascension® MCP should only be used when reconstruction of surrounding soft tissues (e.g., muscles, tendons, and ligaments) is able to provide adequate joint stabilization.

Each component of the Ascension MCP device is comprised of a thick pyrocarbon layer encasing a high strength graphite substrate. Pyrocarbon has a modulus of elasticity similar to cortical bone making it biomechanically compatible with bone<sup>1,2,3</sup>. Numerous laboratory animal studies<sup>4,5,6,7,8,9,10</sup> and human clinical use<sup>11</sup> have confirmed the biocompatibility of pyrocarbon with bone and demonstrated that pyrocarbon implants support biological (i.e., bone and /or soft tissue) fixation.

The graphite substrate material in the Ascension MCP is impregnated with a small amount (10 weight percent) of tungsten. Due to the density difference between carbon and tungsten, 10 weight percent tungsten is approximately 1 atomic percent. This small amount of tungsten renders the graphite substrate radiopaque so that Ascension MCP components are clearly visible on radiographs.

Planar sub-articular collars on both components of the Ascension MCP provide for simple, one-cut, planar bone resections. Furthermore, collars are inclined so that minimal bone stock removal is required allowing for preservation of the anatomic insertion sites of the surrounding ligamentous structures. Relief planes on the radial and ulnar aspects of the proximal component allow clearance for collateral ligament motion during joint flexion/extension. Anatomic shaped component stems are designed to fill the medullary canal and promote component fixation.

The Ascension MCP implant is available in a range of five sizes. An alpha-numeric coding system in parallel with a two level color coding system is used to distinguish both implant sizes, and proximal and distal components. A full set of surgical instrumentation including x-ray overlay sizing templates, alignment guides, cutting guides, broaches, and sizing trial devices is available.

Accurate placement of the proximal and distal components of the Ascension MCP results in a total joint arthroplasty that serves to reestablish functional joint mechanics. The range of motion allowed by all sizes of the prosthesis is 20 degrees of hyperextension to 90 degrees of flexion, and  $\pm 15$  degrees of abduction-adduction motion.

## VI. Alternative Practices and Procedures

Non-surgical early stage treatments include joint injections, anti-inflammatory drug therapy (e.g. aspirin, non-steroidal anti-inflammatory drugs), avoiding heavy stress through the joints or heavy

use of the fingers and hand, and physical therapy exercises to maintain joint range of motion and splints to correct finger deformity. Resting splints worn at night may slow the rate of disease progression.

Surgical intervention may restore some range of motion and is typically used when non-surgical measures no longer give relief. Surgical treatment may include fusion of the bones, interposition arthroplasty with tendon, or resection arthroplasty with a silicone rubber spacer. Individuals who are very active and use their hands for heavy labor may not be good candidates for resection arthroplasty with a silicone rubber spacer.

## VII. Marketing History

Ascension Orthopedics, Inc., has received approval to market the Ascension MCP in the following countries and regions: European Community (CE Mark), Canada, Australia, New Zealand, South Africa, Hong Kong, Malaysia, Pakistan, India, Singapore, China, Estonia.

The Ascension MCP has not been withdrawn from any market for any reason related to safety or effectiveness of the device.

## VIII. Potential Adverse Effects of the Device on Health

The sponsor used an earlier version of the Ascension MCP device clinically. Therefore, the reported adverse effects identified in this section are those observed while using the earlier device design. For clarity, the earlier device design is designated as the "Pyrocarbon MCP."

### REPORTED ADVERSE EFFECTS

The most commonly reported patient adverse events were:

- recurrent deformity
- subluxation / dislocation
- re-operation for soft tissue reconstruction
- implant removal
- implanted joint pain, and
- synovitis

A detailed discussion and complete list of the frequency and rate of complications and adverse events identified in the case history review is provided below in section X (Summary of Clinical Studies) and Table 6, Table 7, and Table 8.

### POTENTIAL ADVERSE EFFECTS

Potential adverse effects associated with total joint prostheses and surgery in general include, but are not limited to:

- pain
- bleeding
- infection

- swelling
- damage to surrounding blood vessels, nerves, or soft tissue
- implant migration within the bones
- implant loosening
- excessive implant wear and particulate debris
- allergic or foreign body reaction
- implant fracture
- bone fracture
- implant subluxation or dislocation
- finger deformity (radial or ulnar deviation, supination or pronation)
- reduction or loss of joint motion
- loss of finger or hand function
- lengthening or shortening of the finger

These adverse effects may lead to additional surgery and could result in:

- implant removal
- joint fusion
- amputation
- death

## IX. Summary of Pre-Clinical Studies

The Ascension MCP device described in section V is a modification to an earlier version of the device that was used in the baboon study (summarized below) and the clinical case series (summarized in section X). For clarity, the earlier device design is designated as the “Pyrocarbon MCP.” The following pre-clinical information was provided to support the safety and effectiveness of the Ascension MCP:

- a comparison of device designs and materials for the Pyrocarbon MCP and the Ascension MCP;
- a comparison of contact area, contact stress, and strength for the Pyrocarbon MCP and Ascension MCP,
- a summary of the baboon study performed using the Pyrocarbon MCP; and
- a summary of additional pre-clinical testing performed on the Ascension MCP including wear testing, fracture strength, cyclic endurance (fatigue resistance), coronal load fracture strength, and biocompatibility.

### COMPARISON OF DEVICE DESIGNS AND MATERIALS FOR THE PYROCARBON MCP AND THE ASCENSION MCP

#### Comparison of Device Designs

Both the Pyrocarbon MCP and the Ascension MCP are two component, semi-constrained, uncemented, finger joint prostheses intended to replace the metacarpophalangeal (MCP) joint of the hand. The proximal components for both device designs have a “ball-shaped” articular surface and stem and the distal components for both device designs have a “cup-shaped” articular surface and stem.

The Pyrocarbon MCP implant design has bisecting sub-articular collar planes requiring the surgeon to create bisecting osteotomies on the head of the metacarpal bone in order to mate with the component. The Ascension MCP has inclined, planar subarticulating collars on both the proximal and distal components that simplify the osteotomy technique, minimize bone resection, and preserve soft tissue structures by maintaining the anatomic insertion sites for the collateral and accessory ligaments.

Other “soft tissue” design refinements for the Ascension MCP are the relief planes on both the dorsal-ulnar and dorsal-radial aspects of the articular surface of the metacarpal component. These relief planes are meant to provide a free, non-interfering pathway for the collateral ligaments during joint flexion-extension. The Pyrocarbon MCP design does not have these relief planes.

The anatomic shaped stems of the Ascension MCP are intended to conform to the anatomic length and shape of the medullary canal of the metacarpal in order to more efficiently fill the canal and promote biological fixation. The stems of the Pyrocarbon MCP design are less contoured, having sharper edges than the Ascension MCP stem design.

Finally, the Pyrocarbon MCP is only provided in 3 sizes as compared to the 5 sizes available for the Ascension MCP. Therefore, minor modifications of stem lengths, proximal head diameters, and distal cup diameters were necessary. Microscopy techniques were used to quantify minor differences in stem lengths, proximal head diameters, and distal cup diameters. The additional sizes allow the Ascension MCP to accommodate a greater range of anatomical size variation and increase implant size selection options.

There were additional minor design differences between the Ascension MCP and the Pyrocarbon MCP including differences in pyrocarbon thickness, radial clearance, and articular surface sphericity. A toolmaker’s microscope, profile projector, and a 3-D coordinate measuring machine were used to quantify minor differences in pyrocarbon thickness, radial clearance, and articular surface sphericity. Mechanical testing and Finite Element Analyses (FEA) were performed on the Ascension MCP. The results are summarized below and demonstrate that the Ascension MCP has sufficient strength, wear resistance, and fatigue resistance to support functional joint motion and performance in the hand.

To summarize, the Pyrocarbon MCP device design was modified in order to:

- require minimal bone resection;
- allow preservation of soft tissue structures;
- create more anatomically shaped stems for the proximal and distal components; and
- increase surgical options with respect to implant size selection.

Each of these refinements is intended to simplify the surgical implantation technique. Other design differences between the Pyrocarbon MCP and Ascension MCP were minor.

#### **Comparison of Device Materials**

Both the Pyrocarbon MCP and Ascension MCP devices are comprised of a pyrocarbon layer encasing a machined graphite substrate.

The pyrocarbon layer for the Pyrocarbon MCP is Pyrolite® carbon (a registered trade name of pyrocarbon material produced by Carbomedics, Inc). The pyrocarbon layer for the Ascension

MCP is On-X® Carbon, produced by Medical Carbon Research Institute (MCRI). The following material properties were provided for the pyrocarbon coating: flexural strength, density, strain-to-failure, Young's modulus, hardness, fracture toughness (Ascension MCP only) and crystallite size (Pyrocarbon MCP only).

The graphite substrate material for the Pyrocarbon MCP is made of both AXF-5Q10W Grade Graphite (impregnated with 10-wt% of tungsten for radio-opacity) and AXF-5Q Grade Graphite without tungsten. Both graphite substrate compositions are produced by Poco Graphite, Inc. The composition of the graphite substrate material for the Pyrocarbon MCP was determined through energy dispersive x-ray (EDX) and microstructural analysis of implants retrieved after clinical use. The graphite substrate material for the Ascension MCP is AXF-5Q10W Grade Graphite, also produced by Poco Graphite, Inc. The following material properties were provided for the graphite substrate: flexural strength, density, Young's modulus (Ascension MCP only), hardness (Pyrocarbon MCP only) and compressive strength.

There were only minor differences in pyrocarbon coating and graphite substrate material properties for the Pyrocarbon MCP and Ascension MCP devices. Mechanical testing and Finite Element Analyses (FEA) were performed on the Ascension MCP. The results are summarized below and demonstrate that the Ascension MCP has sufficient strength, wear resistance, and fatigue resistance to support functional joint motion and performance in the hand.

## **COMPARISON OF CONTACT AREA, CONTACT STRESS, AND STRENGTH FOR THE PYROCARBON MCP AND ASCENSION MCP**

### **Finite Element Analysis - Contact Area and Contact Stress**

The Ascension MCP and the Pyrocarbon MCP were analyzed by FEA to determine the contact area and contact stress over a range of flexion/extension angles. FEA models were validated by comparing contact area diameter measurements with FEA solutions. Size 10, 30, and 50 Ascension MCP devices, and small and standard size Pyrocarbon MCP devices were analyzed. The affect of radial clearance and pyrocarbon layer thickness on contact area and contact stress was also examined.

Both devices exhibited similar behavior. Contact area analysis was insensitive to variations in flexion/extension angle and pyrocarbon thickness. However, smaller size devices and larger radial clearance results in smaller contact area and higher contact stress. For the Ascension MCP, the maximum contact stress occurs in the size 10 (smallest) and was approximately 5822 psi. For the Pyrocarbon MCP, the maximum contact stress in the standard size device was approximately 2300 psi. Although the contact stress for the Ascension MCP is higher than for the Pyrocarbon MCP, these stress values are an order of magnitude less than Ascension MCP component fracture stress, which is estimated to range from 32,500 to 36,200 psi.

### **Finite Element Analysis – Strength Comparison**

Strain gage testing and finite element analysis (FEA) studies were conducted in order to demonstrate that the fracture strength of the Ascension MCP is greater than or equal to that of the Pyrocarbon MCP. Standard size Pyrocarbon MCP components were evaluated because it was the middle size of three sizes implanted in the clinical case series, whereas for the Ascension MCP, the smallest size 10 and middle size 30 components were evaluated.

FEA models were validated by comparing strain results with strain measured on components equipped with strain gages that were subjected to the same constraint and loading conditions used in the strength and cyclic endurance studies. A fracture stress failure criterion was established using the FEA stress results in conjunction with component strength test results. The strength of the Pyrocarbon MCP was then estimated and compared to the strength of the Ascension MCP.

FEA results are summarized in Table 1. As shown, even the smallest size 10 Ascension MCP components have greater fracture strength than estimated for the middle, standard size Pyrocarbon MCP implants.

**Table 1. Summary of FEA Results.**

Device	Size	Component	Fracture Strength (lb.)
Pyrocarbon MCP	Standard	Proximal	122*
Ascension MCP	10	Proximal	279 <sup>+</sup>
Ascension MCP	30	Proximal	351 <sup>+</sup>
Pyrocarbon MCP	Standard	Distal	132*
Ascension MCP	10	Distal	186 <sup>+</sup>
Ascension MCP	30	Distal	234 <sup>+</sup>

\*Estimated fracture strength based on FEA.

<sup>+</sup>Fracture strength measured in component strength test.

### **PYROCARBON MCP BABOON STUDY**

The objectives of the baboon study were to demonstrate the potential for biological fixation of Pyrocarbon MCP components in bone and/or soft tissue, and to evaluate the clinical suitability of the uncemented, semi-constrained, two-component design concept.

Five Pyrocarbon MCP prostheses were implanted into the long finger metacarpophalangeal joints of baboons. Four of the Pyrocarbon MCP implants were inserted without bone cement; the fifth Pyrocarbon MCP implant was inserted using bone cement. Nine months after insertion, the implants and surrounding tissues were removed *en bloc* and evaluated radiographically and histologically.

Histologic evidence of direct appositional bone fixation along the medullary stem was observed in one of the uncemented Pyrocarbon MCP specimens, and a combination of bone fixation with an interposing fibrous tissue membrane was observed in the others. There was no evidence of bone resorption around the stems of the uncemented Pyrocarbon MCP implants, and functional fixation was obtained with all of the uncemented Pyrocarbon MCP implants. No foreign body reaction was observed in the soft tissues, and no evidence of intracellular particles was present with the uncemented Pyrocarbon MCP implants.

The cemented Pyrocarbon MCP implant showed evidence of bone resorption at the cement-bone interface around one component, and intermittent lucent lines along the cement-bone interface on the other component.

In conclusion, the results of this animal study demonstrate the potential for biological fixation of Pyrocarbon MCP implants in bone and/or soft tissue, and confirm the clinical suitability of the uncemented, semi-constrained, two-component Ascension MCP implant design concept.

## **ADDITIONAL PRECLINICAL TESTING PERFORMED ON THE ASCENSION MCP**

The sponsor performed the following additional pre-clinical testing on the Ascension MCP:

- Mechanical Testing, including:
  - wear resistance;
  - fracture strength;
  - cyclic endurance (fatigue resistance);
  - coronal load fracture strength; and
  - articulating surface contact assessment; and
- Biocompatibility Testing.

### **Mechanical Testing**

The objectives of the mechanical studies performed were to characterize the mechanical properties and performance of the Ascension MCP.

All tests were conducted on final sterilized Ascension MCP components. Test specimens were mounted and loaded to simulate biologically demanding physiologic support and loading conditions. Specimen mounting and loading conditions were determined based on a review of the biomechanics literature.<sup>12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28</sup> A biomechanically demanding load was determined to be 80 lb.

### **Wear Resistance**

Wear testing in a joint motion simulator was conducted to evaluate the wear resistance of the Ascension MCP. Size 10 and size 50 Ascension MCP devices were tested. For comparison purposes, a legally marketed MCP device (CoCr on UHMWPE, 1 size “XL” and 1 size “SM”) was tested as a control.

Testing was conducted at 4 Hz in bovine serum at room temperature with an axial load of 14 pounds for 10 million cycles. Articular surfaces were dimensionally measured with a coordinate measuring machine (resolution  $\approx 0.0002$  inch), and examined with a laser based optical interferometer to obtain topographical information. Visual inspection and scanning electron microscopy (SEM) examination of all specimens was performed, and the mass of the UHMWPE specimens was measured to a resolution of 0.1 mg.

Test results revealed that Ascension MCP wear behavior was independent of device size. Wear was characterized by an absence of macroscopic material removal from the articulating surface, and by the occasional shallow scratch (0.3 – 0.5 micrometers) on the articulating surface. Measurable material removal (resolution  $\approx 0.0002$  inch) did not occur.

In contrast, the legally marketed MCP control exhibited wear. At 10 million cycles, the control size “SM” UHMWPE distal specimen had 0.0040” of wear. Also, at 10 million cycles, the control size “XL” UHMWPE distal specimen had 0.0018” of wear. There were visible changes in surface morphology and macroscopic material removal. There were grooves and scratches on the control CoCr specimens 1-5 micrometers deep. This was an order of magnitude deeper than the scratches on the Ascension MCP.

These results demonstrate the Ascension MCP exhibits an adequate degree of wear resistance

under the test conditions outlined above.

### **Fracture Strength**

Strength tests were conducted to evaluate the fracture strength and failure mode of the Ascension MCP. Size 10, 30, and 50 proximal and distal components were tested. Specimens were held with 1/3 of the stem proximal to the collar unsupported and the distal 2/3 of the stem rigidly supported. Specimens were oriented so that loading produced bending in the sagittal plane. The load angle was 40 degrees for proximal components and 20 degrees for distal components. Testing was conducted at room temperature in air.

For all specimens, the failure mode was catastrophic crack propagation, and the fracture location was on the axis of the stem where it protruded above the fixture. Size 10 components exhibited lower average fracture strength than larger size components, and for a given size, distal components exhibited lower average fracture strength than proximal components. Overall, the size 10 distal component exhibited the lowest average fracture strength of 186 lb. with a range from 150 to 219 lb. The observed fracture strength is much greater than a biomechanically demanding load of 80 lb.

These results demonstrate that Ascension MCP components are capable of supporting biomechanically demanding loads.

### **Cyclic Endurance (Fatigue Resistance)**

Cyclic endurance tests were conducted to evaluate the fatigue endurance behavior of the Ascension MCP. Size 10 proximal and distal components only were tested because they exhibited the lowest average fracture strength compared to larger sizes. As with the strength test, specimens were held with 1/3 of the stem proximal to the collar unsupported and the distal 2/3 of the stem rigidly supported. Specimens were oriented so that loading produced bending in the sagittal plane. The load angle was 40 degrees for proximal components and 20 degrees for distal components. Specimens were subjected to an 8 to 80 lb. sinusoidal load at 30 Hz for 10 million cycles at room temperature in air.

All test specimens survived the 8 to 80 lb. cyclic load for 10 millions cycles. Visual and dye penetrant inspection revealed that the applied cyclic load did not damage the test specimens. Furthermore, endurance testing did not reduce the average fracture strength of test specimens as compared to non-endurance tested components.

These results demonstrate that Ascension MCP components exhibit high fatigue resistance, and are capable of supporting biomechanically demanding loads in the long term.

### **Coronal Load Fracture Strength**

A coronal load strength test was conducted to simulate a fracture location on the head of the distal component. Size 10 distal components only were tested because they exhibited the lowest fracture strength compared to larger sizes. Specimens were held with 1/3 of the stem proximal to the collar unsupported and the distal 2/3 of the stem rigidly supported. Specimens were oriented so that loading produced bending in the coronal plane. The load angle was 20 degrees. Testing was conducted at room temperature in air.

Two different fracture locations were observed: a stem fracture similar to that observed in the

strength test, and a head fracture. There was no significant difference between the strength of stem fracture specimens as compared to head fracture specimens. The average fracture strength of all specimens was 172 lb. The observed fracture strength is much greater than a biomechanically demanding load of 80 lb.

These results demonstrate that Ascension MCP components are capable of supporting biomechanically demanding loads even when the loads are acting in the coronal plane.

#### **Articulating Surface Contact Assessment**

An articulating surface contact test was conducted to determine the extent of damage on the articulating surface due to a biomechanically demanding load. Size 10, 30, and 50 proximal and distal components were subjected to an 80 lb. load with a mating component. As with the strength test, specimens were held with 1/3 of the stem proximal to the collar unsupported and the distal 2/3 of the stem rigidly supported. Specimens were oriented so that loading produced bending in the sagittal plane. The load angle was 40 degrees for proximal components and 20 degrees for distal components. Testing was conducted at room temperature in air.

The articulating surface was inspected before and after the applied load. Visual inspection with a stereo microscope and with dye penetrant revealed that the applied load did not damage the articulating surface of the specimens.

These results demonstrate that the Ascension MCP is capable of supporting functional joint loads without sustaining damage to the articulating surface.

A brief summary of the mechanical test results discussed above is provided in Table 2.

**Table 2. Summary of Mechanical Test Results for the Ascension MCP.**

Test	Device Type and Size	Results
Wear Test	Ascension MCP Size 10 Ascension MCP Size 50	Size 10 and Size 50 Ascension MCP implants exhibited identical wear behavior.  Measurable wear did not occur on Ascension MCP components (sensitivity = 0.0002 inch).
	For comparison, wear testing of a legally marketed MCP device (CoCr-on-UHMWPE) sizes "XL" and "SM" was performed.	Measurable wear did not occur on the CoCr proximal components (sensitivity = 0.0002 inch).  Wear on the UHMWPE distal components ranged from 0.0018 to 0.0040 inches.
Strength Test	Size 10 Proximal Size 30 Proximal Size 50 Proximal	279 ± 46 lb. (205 – 324) 351 ± 56 lb. (268 – 446) 454 ± 64 lb. (327 – 544)
	Size 10 Distal Size 30 Distal Size 50 Distal	186 ± 22 lb. (150 – 219) 234 ± 31 lb. (190 – 275) 353 ± 64 lb. (307 – 423)
Endurance Test	Size 10 Proximal Size 10 Distal	No failures occurred. All specimens survived 10 million cycles with 80 lb. maximum load.
Coronal Load Strength Test	Size 10 Distal	Stem fractures: 171 ± 31 lb. (121 – 213) Head fractures: 174 ± 28 lb. (148 – 204)
Articulating Surface Contact Test	Size 10, 30, 50 Proximal Size 10, 30, 50 Distal	No damage occurred on articulating surfaces subjected to 80 lb. load.

**Biocompatibility Testing**

Biocompatibility evaluations were conducted with test specimens manufactured under the exact same conditions as used in processing Ascension MCP components.

Biocompatibility studies on the pyrocarbon material used in the Ascension MCP were conducted in accordance with ISO 10993 and U.S. Pharmacopeia 23, 1995. Test specimens were manufactured under the exact same conditions as used in processing Ascension MCP components. All biocompatibility studies revealed that the pyrocarbon is non-mutagenic, non-cytotoxic, negligible irritant, non-pyrogenic, and having physiochemical properties exceeding the minimum U.S.P. levels set for plastics.

**Sterilization**

The Ascension MCP is sterilized by moist heat. The sterilization method was validated using the ANSI/AAMI/ISO 11134 "Overkill" method. The SAL was 10<sup>-6</sup>. If either the implant or the package appears damaged, or if sterility is questioned for any reason, the implant should not be used. Resterilization of this product is not recommended.

## X. Summary of Clinical Studies

The Ascension MCP device described in section V is a modification to an earlier version of the device that was used in the baboon study (summarized above in section IX) and the clinical case series (summarized below). For clarity, the earlier device design is designated as the “Pyrocarbon MCP.” Section IX contains a comparison of the Pyrocarbon MCP and Ascension MCP devices. The following clinical data for the Pyrocarbon MCP was provided to support a determination that the Ascension MCP is safe and effective.

### OBJECTIVE AND DESIGN

Between 1979 and 1987, a total of 151 Pyrocarbon MCP finger joint devices were implanted in 53 patients at the Mayo Clinic, Rochester Minnesota, USA by Drs. Beckenbaugh and Linscheid. Of these, 147 implants were primary ball-and-cup, uncemented, Pyrocarbon MCP implants; 2 were condylar pyrocarbon implants (implants with a conical shaped bump in the center of the articulating surface of the distal component that interfaced with a groove on the proximal component’s articulating surface); and 2 were revision ball-and-cup Pyrocarbon MCP implants (one uncemented and one cemented). The 53 patients who received the 147 primary ball-and-cup uncemented Pyrocarbon MCP implants represent the case series upon which the clinical data in this PMA is based.

A retrospective case series analysis of the 53 patients who received the 147 primary, ball-and-cup, uncemented, Pyrocarbon MCP total joint implants was reviewed to evaluate the safety and effectiveness of the Ascension MCP. In this retrospective case history review, 53 patients received 147 Pyrocarbon MCP prostheses and the last patient evaluation was at an average of 8.5 years (range 1.7 months – 17.2 years) after implantation. Case histories for the study population were reviewed and information used to evaluate device safety and effectiveness was gathered. An independent contract research organization (CRO) audited and validated the accuracy and completeness of the case history records. The CRO entered information into a computerized database, and analyzed the data to determine study population demographics, patient evaluations, and the frequency and severity of all adverse events.

To evaluate safety and effectiveness of the Ascension MCP, patients were stratified and evaluated based on two baseline medical conditions: 1) osteoarthritis/post traumatic (OA/Trauma), and 2) rheumatoid arthritis/systemic lupus erythematosus (RA/SLE). Success/failure criteria with respect to device effectiveness endpoints (including criteria for implanted joint pain, joint function, and radiographic data) and success/failure criteria with respect to device safety endpoints (including implant and bone fracture, infection, and adverse biological reactions) were established retrospectively.

Separate success/failure criteria were defined for the OA/Trauma and RA/SLE patient groups as summarized below. Each implant was determined to have an outcome of excellent, good, unsatisfactory, or indeterminate. Implants with an excellent or good outcome were considered a success while implants with an unsatisfactory outcome were considered a failure. Patients lacking information required as part of the success/failure definition were considered indeterminate.

### PATIENT POPULATION AND DEMOGRAPHICS

The study population consisted of 45 females and 8 males with a mean age of 57.5 years (range

21 – 78 years). Patients were diagnosed with one of four conditions: 43 (81%) patients had rheumatoid arthritis (RA), 2 (4%) had systemic lupus erythematosus (SLE), 5 (9%) had arthritis due to trauma (TA), and 3 (6%) had osteoarthritis (OA). For patients diagnosed with RA or SLE, the mean time from diagnosis until implantation of the first Pyrocarbon MCP was more than 16 years (range 3-36 years).

**Table 3. Patient Demographics and Baseline Clinical Characteristics.**

	All Diagnoses	OA/Trauma	RA/SLE
Age (years)			
N	53	8	45
Mean (sd)	57.5 (12.6)	54.9 (18.4)	58.0 (11.5)
Median	60	60	58
Min – Max	21 – 78	21 – 77	35 – 78
Gender			
Male	8 (15%)	7 (88%)	1 (2%)
Female	45 (85%)	1 (12%)	44 (98%)
Hand dominance			
Right	49 (92%)	7 (88%)	42 (93%)
Left	2 (4%)	1 (12%)	1 (2%)
Unknown	2 (4%)		2 (4%)
Diagnosis			
OA	3 (6%)	3 (38%)	-
Trauma	5 (9%)	5 (62%)	-
RA	43 (81%)	-	43 (96%)
SLE	2 (4%)	-	2 (4%)
Time from diagnosis to first pyrocarbon implant surgery (years) for RA/SLE patients			
N	-	-	40
Mean (sd)	-	-	16.3 (8.4)
Median	-	-	16.0
Min – Max	-	-	3.0 – 36.0

**PATIENT EVALUATIONS**

The mean last evaluation time point for all patients was 8.6 years (range 1.7 months – 17.2 years). Two years after receiving a Pyrocarbon MCP implant, 82% (41/50) of the patients were evaluated. At greater than ten years post implantation, 72.5% (29/40) of the patients were evaluated.

**Table 4. Last Patient Evaluation Time Point.**

	All Diagnoses	OA/Trauma	RA/SLE
<b>Patients</b>			
N	53	8	45
Mean	8.6 y	9.0	8.5
Min – Max	1.7 m – 17.2 y	1.7 m – 16.0 y	8.1 m – 17.2 y
<b>Implants</b>			
N	147	9	138
Mean	7.8 y	9.4 y	7.7 y
Min – Max	0.9 m – 17.2 y	1.7 m – 16.0 y	0.9 m – 17.2 y

**Table 5. Proportion of Patients Evaluated Over Time.**

Evaluation (years)	Cumulative Deaths	Patients Left	Patients Evaluated	Proportion of Patients Evaluated (%)
0	--	53	53	100%
≥ 1	--	53	49	92%
≥ 2	3	50	41	82%
≥ 5	6	47	38	81%
≥ 10	13	40	29	73%

**COMPLICATIONS AND ADVERSE EVENTS**

The complications and adverse events identified during the case series analysis of the Pyrocarbon MCP are provided below. The most commonly reported patient adverse events were:

- recurrent deformity
- subluxation / dislocation
- re-operation for soft tissue reconstruction
- implant removal
- implanted joint pain, and
- synovitis

**Table 6. Complications and Adverse Events.**

Complication / Adverse Event	Implants (N = 147)	% Implants	Patients (N = 53)	% Patients
Recurrent Deformity	49	33%	20	38%
Subluxation/Dislocation	31	21%	17	32%
Soft-tissue Re-operation	22	15%	11	21%
Implant Removal	21	14%	11	21%
Implanted joint pain	13	9%	11	21%
Synovitis	24	16%	10	19%
Stiffness / Loss of Motion	12	8%	6	11%
Subsidence	9	6%	6	11%
Loosening	7	5%	5	9%
Black Tissue Stain	7	5%	4	8%
Implant modification	5	3%	3	6%
Radiographic changes:				
lucency	4	3%	3	6%
sclerosis	1	1%	1	2%
heterotopic bone	2	1%	2	4%
cyst	1	1%	1	2%
erosion	2	1%	1	2%
Superficial Wound Infection	--	--	2	4%
Sensory Abnormality	3	2%	2	4%
Excessive erythema	2	1%	2	4%
Implant Fracture:				
in vivo fracture	0	0%	0	0%
intra-op fracture:				
at implantation	4	3%	4	8%
at removal	6	4%	3	6%
Bone Fracture:				
in vivo fracture	0	0%	0	0%
intra-op fracture	3	2%	2	4%

**Implant Removals**

A total of 21 (14%) Pyrocarbon MCP implants were removed from 11 (21%) patients. No implants were removed for implant fracture or clinical complications such as bone fracture, infection, sensory abnormality, allergic or foreign body reaction, iatrogenic complications or wound complications. Three (2%) implants were removed for loosening while 18 implants (12%) were removed for deformity associated with disease progression related to RA/SLE (extensor lag, flexion contracture, ulnar deviation, subluxation or dislocation). All removed implants were successfully revised; fifteen were replaced with silicone spacers, four Pyrocarbon MCP implants were reinserted with bone cement, and two new Pyrocarbon MCP implants were used. Of the 21 implants that were removed, 6 implants were removed less than 1 year after implantation; 9 implants were removed between 1 and 5 years after implantation; and 6 implants were removed greater than 5 years after implantation (range 5-11 years).

**Table 7. Summary of Implant Removals.**

	All Diagnoses (N=53 patients)	OA/Trauma (N=8 patients)	RA/SLE (N=45 patients)
Number of Implants	147	9	138
Number of Removals	21 (14%)	1 (11%)	20 (14%)
Reason for Removal			
Fracture	0 (0%)	0 (0%)	0 (0%)
Loosening, Subsidence, Migration	3 (2%)	1 (11%)	2 (1%)
Clinical Complication	0 (0%)	0 (0%)	0 (0%)
Disease Progression	18 (12%)	0 (0%)	18 (13%)

**Soft Tissue Re-Operations**

Eleven (11) soft tissue re-operation procedures were performed on a 22 (15%) joints in 11 (21%) Pyrocarbon MCP patients. Procedures were performed to correct recurrent MCP joint deformities such as implant subluxation/dislocation, ulnar/radial deviation, extension lag or loss of motion, or extension contracture. All but one of the soft tissue re-operations was on RA/SLE patients. Three (3) of the 22 implants were eventually removed, all due to recurrent subluxation or dislocation. Sixteen (16) of the 22 joints were operated on less than 1 year post-implantation.

**Table 8. Summary of Soft Tissue Re-operations.**

	All Diagnoses (N=53 patients)	OA/Trauma (N=8 patients)	RA/SLE (N=45 patients)
Number of Implants	147	9	138
Number of Implants Re-operated	22 (15%)	1 (11%)	21 (15%)
Reason for Re-operation			
Subluxation / Dislocation	7 (5%)	0 (0%)	7 (5%)
Ulnar / Radial Deviation	7 (5%)	1 (11%)	6 (4%)
Extension Lag / Loss of Motion	5 (3%)	0 (0%)	5 (4%)
Extension Contracture	3 (2%)	0 (0%)	3 (2%)

**Intraoperative Implant Fractures**

There were a total of 10 intraoperative Pyrocarbon MCP implant fractures, i.e., fractures that occurred during either implantation or revision of the device. Four of the 10 intraoperative fractures occurred during the implantation of 295 components for a rate of 1.4% (4/295). In 3 of the 4 cases, the fractured component was easily removed and a new Pyrocarbon MCP component was inserted while in the fourth case, the fragment was left *in situ* and a silicone spacer was inserted. Six of the 10 fractures occurred during implant revision and removal of 42 components (21 devices) for a rate of 14% (6/42). Five of these fractured devices were replaced with a silicone spacer while the 6<sup>th</sup> fractured device was essentially intact and was reinserted with bone cement. All intraoperative fractures were uneventful and no *sequelae* resulted.

**Black Staining of Tissue and Synovitis**

Although the sponsor concluded that there was no adverse tissue reaction to the Pyrocarbon MCP joint implant, carbon particles, or “fine particle matter” in samples evaluated by the histopathologist, there were reports of black staining of tissue and synovitis.

### **Black Staining of Tissue**

A total of 7 implants caused black stained tissue in 4 of 53 patients for a rate of 7.5% (4/53). Four (4) events occurred during removal of implants from each finger on one patient's hand. All four fractured implants were removed by drilling them out of the bone. After the drilling process, black stained tissue was observed in each finger. No tissue samples were taken from this patient.

In addition, there were 3 events observed during operations to remove implants that were potentially loose in 3 patients. Tissue samples from these three patients were excised during removal for histopathologic examination. The histopathologist concluded that the tissue did not reveal any negative tissue reaction. All implants were revised. Two (2) implants were revised to silicone spacers and 1 Pyrocarbon MCP implant was reinserted with cement.

### **Synovitis**

A total of 24 synovitis events were reported for 10 patients for a rate of 19% (10/53). Tissue samples were available for examination from 5/24 joints including samples from 2 RA patients and one Trauma patient. The histopathologist's review concluded that there was no adverse tissue reaction to the implant, carbon particles, or "fine particle matter" in these samples.

## **SUCCESS/FAILURE ANALYSES**

To evaluate safety and effectiveness of the Ascension MCP, patients were stratified and evaluated based on two baseline medical conditions: 1) osteoarthritis/post traumatic (OA/Trauma), and 2) rheumatoid arthritis/systemic lupus erythematosus (RA/SLE). Success/failure criteria with respect to device effectiveness endpoints (including criteria for implanted joint pain, joint function, and radiographic data) and success/failure criteria with respect to device safety endpoints (including implant and bone fracture, infection, and adverse biological reactions) were established retrospectively.

Separate success/failure criteria were defined for the OA/Trauma and RA/SLE patient groups as summarized below. Each implant was determined to have an outcome of excellent, good, unsatisfactory, or indeterminate. Implants with an excellent or good outcome were considered a success while implants with an unsatisfactory outcome were considered a failure. Patients lacking information required as part of the success/failure criteria were considered indeterminate.

The OA/Trauma patients and the RA/SLE patients presented with distinct treatment objectives and associated physician expectations. Treatment objectives and physician expectations were derived retrospectively from the pre-operative notes and physical exam records. Safety and effectiveness criteria were defined retrospectively with the treatment objectives and physician expectations in mind.

## **RA/SLE PATIENTS**

### **Treatment Objectives (RA/SLE)**

The following 4 potential primary objectives for finger joint replacement in the RA/SLE group were defined:

- A. In cases with limited extension (that is 30 degrees or more of extension lag), the primary expectation was to increase extension.
- B. In cases with pain, the primary expectation was to relieve pain.
- C. In cases with a destroyed or eroded articular surface, the primary expectation was to replace the eroded surfaces and provide a reduced joint.
- D. In cases with a pre-operative dislocation, the primary expectation was to provide a reduced or subluxed joint.
- E. And, in cases presenting with a combination of these conditions, that is A, B, C, and/or D, the primary objective was to address each of the individual conditions.

Each patient's treatment objectives were derived retrospectively from pre-operative surgeon's notes and physical exam records.

### **Success/Failure Analysis (RA/SLE)**

For the RA/SLE group, effectiveness criteria were defined for a 1-5 year treatment outcome analysis, and for a longer-term treatment outcome analysis. Both sets of criteria acknowledge and accommodate the potential confounding influence on treatment outcomes of soft tissue attenuation related to progression of the RA/SLE baseline medical condition.

### **Effectiveness Analysis (RA/SLE 1-5 Year Evaluation)**

For the RA/SLE cohort, the following effectiveness criteria were applied on an implant basis to determine the treatment outcome category for each implant. An implant with an Excellent or Good outcome was considered a Success while an implant with an Unsatisfactory outcome was considered a Failure.

#### Excellent

1. Physical exam, ROM data, and radiographic data > 1 year\* indicating:
  - a. Improvement of all treatment objectives;
  - b. Pain free joint; and
  - c. Reduced implant position.
2. Subjective or objective information indicating a reduction in the improvement of treatment objectives after 5 years is acceptable.

#### Good

1. Physical exam, ROM data, and radiographic data < 1 year\* indicating:
  - a. Improvement of all treatment objectives;
  - b. Pain free joint; and
  - c. Reduced implant position; and
2. Subjective or objective information (a physical exam at another clinic (orthopedic, rheumatology, etc.), radiographic data, a questionnaire or telephone conversation with a physician) at > 1 year indicating:
  - a. maintenance of the improvements; or
  - b. implant survival.

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\* Note: Although a 1 year criteria was established for an implant to be considered a success (i.e., excellent or good outcome), as discussed in the following results section, 72% of the successful implants had an evaluation at > 2 years post implantation.

3. Subjective or objective information indicating a reduction in the improvement of treatment objectives after 5 years is acceptable

Unsatisfactory

1. Primary treatment objective(s) same or not improved by the surgery;
2. Implant related pain at last evaluation;
3. Implant loosening;
4. Implant removal < 5 years;
5. Implant dislocation < 5 years; or
6. Post-operative implant fracture

Indeterminate

1. No information > 1 year, or insufficient information > 1 year to indicate maintenance of the improvements at < 5 years

**Effectiveness Results (RA/SLE 1-5 Year Evaluation)**

In the RA/SLE cohort, the 1-5 year effectiveness analysis revealed the following:

**Table 9. RA/SLE 1-5 Year Effectiveness Results.**

	<b>Implants (N = 138)</b>	<b>Patients (N = 45)</b>
“Success”	82 (59%) (46 Excellent, 36 Good)	--
“Failure”	37 (27%)	--
“Indeterminate”	19 (14%)	--
Patients w/ All Implants “Success”	--	27 (60%)
Patients w/ All Implants “Failure”	--	8 (18%)
Patients w/ All Implants “Indeterminate”	--	3 (7%)
Patients w/ multiple Implant Outcomes (“Success” and/or “Failure”, and/or “Indeterminate”)	--	7 (15%)

Forty-six (46) implant outcomes were considered excellent with a final evaluation occurring at an average of 8.3 years (range 1.0-16.8 years) after implantation, and 37 of the 46 implants having a final evaluation > 2 years after implantation. Thirty-six (36) implant outcomes were considered good with a final evaluation occurring at an average of 5.9 years (range 1.2-13.6 years) after implantation, and 22 of the 36 implants having a final evaluation > 2 years after implantation. Thus, 59 of the 82 successful implants had a final evaluation at greater than 2 years after implantation, a rate of 72% (59/82).

Successful implants were in 33 of the 45 RA/SLE patients, a rate of 73% (33/45). Of the 33 patients who had at least one successful implant, 27 had all their implants considered successful, a rate of 82% (27/33). Therefore, 60% (27/45) of the patients in the RA/SLE cohort had all their implants considered successful.

For the group of implants demonstrating excellent and good outcomes, there were no reports of implanted joint pain at a final evaluation occurring at an average of 6.4 years (range 0.4 to 16.8 years) after implantation, with 1 patient reporting hand pain at 10.0 years. The average extension increase was 34.0 degrees (range -20 to 125 degrees) with a final evaluation occurring at an average of 2.0 years (range 0.1 to 11.7 years) after implantation. All patients with a primary treatment expectation of increasing extension showed an extension increase except for 2 implants

(1 each in 2 patients) that showed no increase, but had ROM > 40 degrees. Accordingly, these 2 implants had an outcome of Good. Five implants in 4 patients with a treatment expectation of joint reduction and/or surface replacement and/or pain relief showed an extension decrease, but had good to excellent post-operative ROM averaging 29.0 degrees (range 20 to 50 degrees). Of the 82 implants considered successful, 77 had a final radiographic evaluation that showed 61 implants reduced at an average of 3.9 years (range 0.1 to 12.9 years) after implantation, a rate of 79% (61/77). Eleven implants were subluxed (average final evaluation of 7.0 years, range 1.4 - 13.0 years), and 5 were dislocated. Of the 5 dislocated implants, 4 were in one patient with 2 dislocations noted at 10.0 years and 2 more noted at 11.5 years, and the 5<sup>th</sup> was in another patient and noted at 11.0 years after implantation. There were 6 implants removed from 2 patients in this group; 4 implants were removed from 1 patient at 5.5 years due to disease related flexion contracture and ulnar deviation deformity, and 2 implants were removed from the other patient at 11.0 years due to subluxation/dislocation related to soft tissue attenuation. All removed implants were successfully converted to a silicone spacer.

For the group of implants with an unsatisfactory outcome, 14 implants in 8 patients were removed. Two implants were removed due to loosening (1 at 1.5 years and 1 at 4.9 years). The 12 other implants removed were revised due to disease related soft tissue degradation that resulted in flexion contracture (4 implants: 2 each in 2 patients), ulnar deviation deformity and dislocation (3 implants in 1 patient), or subluxation/dislocation (5 implants: 1 in 1 patient, and 2 each in 2 other patients). All removed implants were successfully revised (9 were replaced with silicone spacers, 4 Pyrocarbon MCP implants were reinserted with bone cement, and 1 new Pyrocarbon MCP implant was inserted).

The other 23 implants with an unsatisfactory outcome were in 8 patients, and were unsuccessful due to extension contractures (4 implants: 3 in 1 patient and 1 in another patient), lack of extension improvement or extension deficit (12 implants: 4 each in 2 patients, and 2 each in 2 other patients), recurrent severe ulnar deformity (4 in 1 patient) and dislocation (3 implants: 2 in 1 patient and 1 in another patient). Thus, of the 37 implants with unsatisfactory outcome in 15 patients, only 2 were directly related to implant loosening. All other unsatisfactory outcomes were due to disease related soft tissue degradation leading to loss of extension or joint location, or recurrent ulnar deformity.

### **Effectiveness Analysis (RA/SLE Longer-Term Outcome Evaluation)**

To conduct the Longer-Term Outcome Evaluation, the Effectiveness Criteria for all outcome categories (Excellent, Good, Unsatisfactory, and Indeterminate) that were established for the 1-5 year evaluation were modified so that reductions in treatment improvements at evaluation times greater than five (5) years were considered during implant outcome evaluation. Thus, the following effectiveness criteria were applied on an implant basis to determine the treatment outcome category for each implant.

#### Excellent

1. Physical exam, ROM data, and radiographic data > 1 year\* indicating:
  - a. Improvement of all treatment objectives;

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\* Note: Although a 1 year criteria was established for an implant to be considered a success (i.e., excellent or good outcome), as discussed in the following results section, 67% of the successful implants had an evaluation at > 2 years after implantation.

- b. Pain free joint; and
- c. Reduced implant position.

Good

1. Physical exam, ROM data, and radiographic data < 1 year\* indicating:
  - a. Improvement of all treatment objectives;
  - b. Pain free joint; and
  - c. Reduced implant position; and
2. Subjective or objective information (a physical exam at another clinic (orthopedic, rheumatology, etc.), radiographic data, a questionnaire or telephone conversation with a physician) at > 1 year indicating:
  - a. maintenance of the improvements; and
  - b. implant survival.

Unsatisfactory

1. Primary treatment objective(s) same or not improved by the surgery;
2. Implant related pain at last evaluation;
3. Implant loosening;
4. Implant removal;
5. Implant dislocation; or
6. Post-operative implant fracture

Indeterminate

1. No information > 1 year, or insufficient information > 1 year to indicate maintenance of the improvements

**Effectiveness Results (RA/SLE Longer-Term Evaluation)**

In the RA/SLE cohort, the longer-term evaluation revealed the following:

**Table 10. RA/SLE Longer-Term Effectiveness Results.**

	Implants (N = 138)	Patients (N = 45)
“Success”	51 (37%) (30 Excellent, 21 Good)	--
“Failure”	73 (53%)	--
“Indeterminate”	14 (10%)	--
Patients w/ All Implants “Success”	--	17 (38%)
Patients w/ All Implants “Failure”	--	18(40%)
Patients w/ All Implants “Indeterminate”	--	3 (7%)
Patients w/ multiple Implant Outcomes (“Success” and/or “Failure”, and/or “Indeterminate”)	--	7 (15%)

Thirty (30) implant outcomes were considered excellent with a final evaluation occurring at an average of 7.6 years (range 1.0-15.9 years) after implantation; 23 of those 30 implants had a final evaluation > 2 years after implantation. Twenty-one (21) implant outcomes were considered good with a final evaluation occurring at an average of 6.8 years (range 1.3-16.8) after implantation; 11 of those 21 implants had a final evaluation > 2 years after implantation. Thus, 34 of the 51 successful implants had a final evaluation greater than 2 years after implantation, a rate of 67% (34/51).

Under the modified longer-term criteria, successful implants were in 23 of the 45 RA/SLE patients, a rate of 51% (23/45). Of the 23 patients with at least one successful implant, 17 had all their implants considered successful, a rate of 74% (17/23). Therefore, 38% (17/45) of the patients in the RA/SLE cohort had all their implants considered successful when applying longitudinal effectiveness criteria.

For implants demonstrating excellent and good outcomes, the primary treatment objectives for all implants were obtained. There were no reports of implanted joint pain at a final evaluation occurring at an average of 7.0 years (range 1.0-16.8 years) after implantation, and no reports of hand or finger pain. The average extension increase was 33.7 degrees (range of -50 to 125 degrees) with a final evaluation occurring an average of 3.3 years (range 0.1-16.8 years) after implantation. All patients with a primary treatment expectation of increasing extension showed an extension increase. Five implants in 4 patients with a treatment expectation of joint reduction and/or surface replacement and/or pain relief showed an extension decrease, but had good to excellent post-operative range of motion (ROM) averaging 28.0 degrees (range 20 to 40 degrees). Of the 51 implants considered successful, radiographic data showed 43 implants reduced, a rate of 84% (43/51); and 8 implants were subluxed at a final evaluation occurring an average of 4.2 years (range 0.1-13.1 years) after implantation. No successful implants were dislocated in the long-term.

For the group of 73 implants with an unsatisfactory outcome in 25 patients, 20 implants in 10 patients were removed. Two implants were removed due to loosening (1 at 1.5 years and 1 at 4.9 years). The 18 other removed implants were revised due to disease related soft tissue degradation that resulted in flexion contracture (8 implants: 2 each in 2 patients and 4 in another), ulnar deviation deformity and dislocation (3 implants in 1 patient), or subluxation/dislocation (7 implants: 1 in 1 patient, and 2 each in 3 other patients). All removed implants were successfully revised; 15 were replaced with silicone spacers, 4 Pyrocarbon MCP implants were reinserted with bone cement, and 1 new Pyrocarbon MCP implant was inserted.

The other 53 implants with an unsatisfactory outcome in 18 patients were unsuccessful due to extension contracture or flexion lag (13 implants: 1 each in 4 patients, 2 in 1 patient, 3 in 1 patient, and 4 in 1 patient), lack of extension improvement or extension deficit (27 implants: 4 each in 4 patients, 3 in 1 patient, 2 each in 3 patients, and 1 each in 2 patients), recurrent severe ulnar deformity (4 in 1 patient), dislocation (7 implants: 4 in 1 patient, 2 in 1 patient, and 1 in 1 patient), and loss of motion (2 implants in 1). Thus, of the 73 implants with unsatisfactory outcome in 25 patients, only 2 were directly related to implant loosening. All other unsatisfactory outcomes were due to disease related soft tissue degradation leading to reduction or loss of motion, joint dislocation, or recurrent ulnar deformity.

### **Comparison of RA/SLE Effectiveness Results**

The impact of applying the modified longer-term effectiveness criteria to determine effectiveness results for the RA/SLE patient cohort is shown below.

**Table 11. RA/SLE 1-5 Year and Longer Term Effectiveness Results Comparison.**

	1 – 5 Year Criteria		Longer-Term Criteria	
	N	%	N	%
Total	138		138	
Excellent & Good	82 (46 Ex & 36 Gd)	59%	51 (30 Ex & 21 Gd)	37%
Unsatisfactory	37	27%	73	53%
Indeterminate	19	14%	14	10%

When reductions in treatment improvements at evaluation times of greater than five (5) years are considered, the number of successful implants (excellent and good outcomes) decreases from 82/138 (59%) to 51/138 (37%), while the number of implants with unsatisfactory outcome increases from 37/138 (27%) to 73/138 (53%). For the 36 additional implants with unsatisfactory outcome, 6 implants were removed from 2 patients (4 from 1 patient at 5.4 years due to flexion contracture and ulnar deviation deformity, and 2 from another patient at 11.0 years due to subluxation/dislocation); all 6 removed implants were successfully replaced with a silicone spacer. The other 30 additional implants with unsatisfactory outcome were considered failures due to extension lag (15 implants in 6 patients), flexion lag/stiffness (9 implants in 5 patients), dislocation (4 implants in 1 patient), and loss of motion (2 implants in 1 patient). Thus, all 36 additional implants with unsatisfactory outcome under the modified effectiveness criteria were unsuccessful due to disease related soft tissue degradation and attenuation leading to reduction or loss of motion, joint dislocation, or recurrent ulnar deformity.

**Safety Analysis (RA/SLE)**

The frequency and severity of the following events were evaluated for purposes of determining device safety:

- Intraoperative implant fracture
- Non-intraoperative implant fracture
- Unstable intraoperative bone fracture
- Post operative bone fractures
- Implant related infection
- Adverse biological reaction to implant

**Safety Results (RA/SLE)**

Intraoperative implant fractures occurred in two patients during implantation of the device. In one patient the fractured component was removed and a new Pyrocarbon MCP component was inserted successfully while in the other patient the fractured fragment was left *in situ* and a silicone spacer was successfully inserted. In addition, 6 components fractured in 3 patients during revision. As noted above, all implants that fractured during removal were successfully revised; silicone spacers were inserted in 2 patients, and the fractured Pyrocarbon MCP implant removed from the third patient was reinserted with bone cement. Similar to the OA/Trauma cohort, there were no other reported occurrences of the implant safety criteria listed above. A complete list of adverse events for the entire study population was provided in Table 6.

## **OA/TRAUMA PATIENTS**

### **Treatment objectives (OA/Trauma)**

The OA/Traumatic Arthritis patients presented with damaged or destroyed articular surfaces and almost always had pain and limited motion. Most of these patients needed treatment in only one MCP joint; only one patient required treatment in multiple MCP joints.

For the OA/TRAUMA cases, the physician had the expectation that total joint arthroplasty would relieve pain, maintain reasonable joint range of motion (ROM), and maintain joint reduction.

### **Success/Failure Analysis (OA/Trauma)**

For the OA/TRAUMA group, effectiveness criteria were defined for a greater than 2 year treatment outcome analysis. Two (2) years was set as the minimum amount of time that the surgical improvement must be maintained to be deemed successful.

### **Effectiveness Analysis (OA/Trauma)**

For the OA/Trauma cohort, the following effectiveness criteria were applied on an implant basis to determine the treatment outcome category for each implant. An implant with an Excellent or Good outcome was considered a Success while an implant with an Unsatisfactory outcome was considered a Failure.

#### Excellent

1. Physical exam, ROM and radiographic data > 2 years indicating:
  - a. Pain free implant at last follow-up;
  - b. Increase in range of motion (ROM) from baseline, or ROM > 50 degrees<sup>29</sup>; and
  - c. Reduced implant position.

#### Good

1. Physical exam, ROM and radiographic data < 2 years indicating:
  - a. Increase in ROM from baseline, or ROM > 50 degrees; and
  - b. Reduced implant position; and
2. Physical exam or telephone conversation with a physician > 2 years indicating:
  - a. pain free implant; and
  - b. implant survival

#### Unsatisfactory

1. Implant related pain at last evaluation;
2. Implant loosening or removal;
3. Post-operative implant fracture;
4. Decrease in ROM from baseline with ROM < 50 degrees; or
5. Implant subluxation or dislocation.

#### Indeterminate

1. No information > 2 years or insufficient information > 2 years to indicate maintenance of the improvements.

### **Effectiveness Results (OA/Trauma)**

In the OA/Trauma cohort, the effectiveness analysis revealed the following:

**Table 12. OA/Trauma Effectiveness Results.**

	<b>Implants (N = 9)</b>	<b>Patients (N = 8)</b>
“Success”	7 (78%) (6 Excellent, 1 Good)	--
“Failure”	1 (11%)	--
“Indeterminate”	1 (11%)	--
Patients w/ All Implants “Success”	--	6 (75%)
Patients w/ All Implants “Failure”	--	1 (12.5%)
Patients w/ All Implants “Indeterminate”	--	1 (12.5%)

Seven of the nine (78%) implants in this cohort were determined to be a “Success” while only 1 implant (11%) was a “Failure”. Six implants had an excellent outcome, 1 implant had a good outcome, 1 implant was unsatisfactory, and 1 implant was indeterminate.

The implant with an unsatisfactory result was removed due to loosening at 1.1 years and revised with a new Pyrocarbon MCP implant with cement. No other implants in this cohort loosened or were removed.

The 6 implants that had an excellent outcome had their last evaluation ranging from 3.5 to 16.0 years, and all but 1 implant demonstrated an increase in ROM. For the 1 implant that did not show increased ROM, the post-operative ROM was very good at 65 degrees.

The implant with a good outcome had a last evaluation indicating implant survival at 17 years, while the implant with indeterminate outcome had a 0.5-year evaluation demonstrating good improvement. All implants demonstrated no joint pain at final evaluation except for the unsatisfactory implant that had pain secondary to loosening.

**Safety Analysis (OA/Trauma)**

The frequency and severity of the following events were evaluated for purposes of determining device safety in the OA/Trauma group:

- Intraoperative implant fracture
- Non-intraoperative implant fracture
- Unstable intraoperative bone fracture
- Post operative bone fractures
- Implant related infection
- Adverse biological reaction to implant

**Safety Results (OA/Trauma)**

There were 2 intraoperative implant fractures that occurred in 2 patients in this cohort. Both fractures occurred during implantation, and both fractured implants were removed and a new Pyrocarbon MCP implant was inserted without sequelae. There were no other reported occurrences of the implant safety criteria listed above. A complete summary of adverse events for the entire study population was provided in Table 6.

## XI. Conclusions Drawn from the Studies

FDA believes that the results of the clinical case series and animal testing of the Pyrocarbon MCP can be applied to the Ascension MCP. This conclusion is based on the results of the pre-clinical bench testing.

Therefore, based on the bench, animal, and clinical case series, it is reasonable to conclude that the benefits of the use of the Ascension MCP for the target population outweigh the risk of illness or injury when used in accordance with the directions for use.

## XII. Panel Recommendations

At an advisory meeting held on August 9, 2001, the Orthopedic and Rehabilitation Devices Panel recommended that Ascension Orthopedics, Inc.'s PMA for the Ascension MCP be approved subject to submission to, and approval by, the Center for Devices and Radiological Health (CDRH) of revised labeling in which the following additional information is provided to the physician:

- (1) Do not use the Ascension MCP in a joint where soft tissue reconstruction cannot provide adequate stabilization. Because soft tissue reconstruction may be unable to maintain joint stability, the Ascension MCP is not recommended for use in joints:
  - (a) where it is not possible to reconstruct the radial-collateral ligament, or
  - (b) in joints that exhibit extension lag greater than 45 degrees,
  - (c) ulnar deviation greater than 30 degrees, or
  - (d) severe subluxation and/or shortening greater than 1 centimeter.
- (2) Special attention should be given to soft tissue reconstruction and joint stability in the ring and small fingers.
- (3) Corrective wrist surgery may be required prior to use of the Ascension MCP. In patients with severe intercarpal supination and radial deviation of the wrist, ulnar deviation of the digits may not be correctable with MCP joint soft tissue reconstruction alone. In these instances, it is recommended that corrective wrist surgery be performed first at a separate setting, and
- (4) Training is available, but not required, prior to device use.

## XIII. CDRH Decision

CDRH reviewed portions of the pre-market application submission under the Modular PMA process (M990022). Acceptance letters for one of the two modules was sent on December 2, 1999. The remaining module was incorporated into the review of the PMA. The PMA was filed on February 20, 2001 and granted expedited review status. The Ascension MCP was granted expedited review status because it may offer significant advantages in safety and effectiveness over existing alternatives; such as, increased biomechanical hand function and a lower rate of

implant fracture.

CDRH concurred with the Orthopedic and Rehabilitation Devices Panel recommendation of August 9, 2001. Several labeling revisions were requested by CDRH and the applicant submitted the requested information.

CDRH believes that the applicant must conduct a post-approval study to evaluate the effect of a revised post-operative rehabilitation protocol in the early follow-up period (i.e., 1 year) at a minimum of 4 sites and 100 patients. This information is to be collected on patients for whom this device is indicated. Also, should there be any implant revisions necessary during the first year of follow-up, another objective is to evaluate the revised device removal procedures and instrumentation. The sponsor agreed to this post-approval condition.

The applicant's manufacturing facility was inspected on April 16-18, 2001, and was found to be in compliance with the device Good Manufacturing Practice regulations.

CDRH has determined that based on the data submitted in the PMA, the use of this device for the labeled indications has been shown to be safe and effective and issued an approval letter on

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#### XIV. 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 Restrictions: See approval order.

#### XV. References

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