

P M A M E M O R A N D U M

To: M990022 and P000057 (Volumes 1 and 10 of 13)

From: John S. Goode, Biomedical Engineer, FDA/CDRH/ODE/DGRD/ORDB

Subject: Ascension MCP, metacarpophalangeal total joint prosthesis

Sponsor/Manufacturer: Ascension Orthopedics, Inc.
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Date: July 11, 2001

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PRE-CLINICAL REVIEW: THIS REVIEW MEMO CONTAINS INFORMATION ABOUT:

- The History of Device Development;
- Device Description;
- Device Materials; and
- Pre-Clinical Testing.

This information was contained in the following submissions from Ascension Orthopedics to FDA:

Module 1: M990022 (Volumes 1, 2 and 3)

The sponsor submitted Module 1 to modular PMA M990022. Module 1 was dated 7/28/99 and was received by FDA on 8/2/99. Module 1 contains the following sections:

- Cover Page (General Information)
- Device Description
- Performance Standards
- Non-Clinical Studies
- Environmental Assessment; and
- Bibliography with Answers to items FDA had previously requested:

FDA sent the sponsor a deficiency letter dated 11/22/99 regarding some of the items listed above.

PMA: P000057 (Volumes 1 and 10 of 13)

PMA P000057, dated 12/28/00 was received on 12/29/00.

As part of P000057, the sponsor addressed the items from FDA's deficiency letter dated 11/22/99 (Module M001 and M001/A001).

ASCENSION® MCP DEVELOPMENT HISTORY:

The sponsor stated that the development of a pyrolytic carbon MCP joint implant extended back to the 1970's. Drs. Jerome Klawitter and Stephen Cook performed research on pyrocarbon at Tulane University. Dr. Beckenbaugh of the Mayo Clinic was interested in developing a MCP joint prosthesis. These researchers collaborated and implanted MCP joints in baboons. The sponsor stated that the animal testing was successful in restoring function, mechanics and motion to the MCP joint. So, between 1979 and 1987, 151 pyrolytic carbon MCP implants were put in 53 patients at the Mayo Clinic by Drs. Beckenbaugh and Linscheid. Of these, 147 implants were primary ball-and-cup uncemented pyrocarbon 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 implants (one uncemented and one cemented).

The 53 patients who received 147 primary ball-and-cup uncemented pyrocarbon implants represent the case series upon which the clinical data in this PMA is based. The outcome of the other 4 pyrocarbon implants (2 condylar and 2 revision) are mentioned in the Module 1 and PMA Volume 1 of 13 but are not summarized as part of the clinical data in this PMA or factored into the success/failure criteria for the 53 patients.

In 1992, Ascension Orthopedics, Inc. was founded by Drs. Klawitter and Cook. The sponsor worked with Dr. Beckenbaugh to refine certain aspects of the prosthesis design, resulting in the Ascension® MCP device. The Ascension MCP device is not the one that was used in the animal or clinical study but is the device for which Ascension Orthopedics is requesting approval in their PMA. Similarities and differences between the pyrocarbon implant used in the animal and clinical studies and the Ascension MCP are presented below.

DEVICE DESCRIPTION:

Ascension MCP (device proposed for marketing in this PMA):

The Ascension MCP is a two component, semi-constrained prosthesis consisting of a proximal component with a ball shaped articular surface and a distal component with a cup shaped articular surface. The proximal component is intended to replace the articular surface at the head of the metacarpal (MC) bone, and the distal component is intended to replace the articular surface at the base of the proximal phalanx (PP). Dorsal-volar and medial-lateral translation of the components relative to one another is limited due to the geometry of the articulating surfaces. Therefore, the device is considered semi-constrained. The device is designed to be a press-fit device that achieves fixation by means of implant/bone apposition (osseous integration). The sponsor stated that planar sub-articular collars on both components provide for simple, one-cut planar bone resections. They are inclined to allow 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 motion.

The articulating proximal ball and distal cup surfaces are polished to a mirror finish. Average surface roughness for the articulating surfaces was determined to be $Ra=5.7 \pm 2.3$ microinches (145 \pm 59nm). The stem portion of each component is not polished and has a surface finish of approximately $Ra=15$ microinches (389nm) similar to that produced during the pyrocarbon layer fabrication process.

The devices are available in a range of 5 sizes.

Sizes of the Ascension® Orthopedics MCP Device:

Catalog No.	Metacarpal Head Diameter	Metacarpal Stem Length	Phalangeal Stem Length
MCP-100-10	10.0mm	19.3mm	15.6mm
MCP-100-20	11.4mm	23.0mm	16.7mm
MCP-100-30	13.0mm	26.6mm	18.3mm
MCP-100-40	14.8mm	30.2mm	21.2mm
MCP-100-50	16.6mm	33.7mm	22.8mm

The sponsor stated that larger sizes generally would be used on patients with larger bones and in the long and index fingers. Smaller sizes will generally be used in smaller patients and in ring and small fingers. The lengths of the phalangeal and metacarpal stems are intended to fill approximately $\frac{1}{2}$ the length of the intramedullary canal of the proximal phalangeal and metacarpal bones, respectively. Because the articular surfaces of components from different size devices have differing radii of curvature, mating components are not interchangeable between different device sizes. The sub-articular collars are inclined to the long axis of the device at 117.5° for the metacarpal component, and at 85° for the phalangeal component. Maintenance of the soft tissue structures is intended to promote post-operative joint stability. The sponsor stated that the device provides for 20° of hyperextension; 90° of flexion; and 15° of radial and ulnar motion. The sponsor has offset the center of rotation of the articular surface of the metacarpal component from the long axis of the bone in the palmar direction to re-establish the anatomic center of rotation of the joint. To account for offset alignment of the bones of the natural MCP joint, the location of the phalangeal component stem is offset further in the palmar direction. The offset values are as follows:

Stem Offset Values for the Ascension® MCP Device:

Catalog No.	Stem Offset (mm)
MCP-100-10	0.2
MCP-100-20	0.4
MCP-100-30	0.5
MCP-100-40	0.6
MCP-100-50	0.7

Instrumentation:

Instrumentation includes a x-ray overlay-sizing template, alignment guides, cutting guides, broaches, and trial devices.

Original Device Design and Modifications:

The device description outlined above is regarding the Ascension® MCP implant. The Ascension MCP is a modification to the original pyrocarbon MCP implant design that was used in the animal studies and clinical studies.

The sponsor stated that the refinements outlined above were made in order to:

- Simplify the surgical implantation technique; and
- Increase surgical options with respect to implant size selection.

The modifications were made using CAD-CAM design and manufacturing technology. The sponsor provided the following comparative information regarding the original design:

Comparison of the original MCP (pyrolytic carbon device used in the animal study and clinical case series) and the Ascension® MCP device (the device proposed for marketing in this PMA) sizes:

Design	Size	Metacarpal Head Diameter	Metacarpal Stem Length	Phalangeal Stem Length
Original Pyrocarbon Implant	Small	8.2 mm	25 mm	17.8 mm
	Standard	10.2 mm	25 mm	18.0 mm
	Large	12.8 mm	25 mm	19.2 mm
Ascension MCP device	10	10.0mm	19.3mm	15.6mm
	20	11.4mm	23.0mm	16.7mm
	30	13.0mm	26.6mm	18.3mm
	40	14.8mm	30.2mm	21.2mm
	50	16.6mm	33.7mm	22.8mm

The original design was only provided in 3 sizes as compared to the 5 sizes available on the current version.

In addition, the original implant design had bisecting sub-articular collar planes on the MCP component requiring the surgeon to create bisecting osteotomies on the head of the metacarpal bone in order to mate with the component. The sponsor stated that the single, planar attribute of the sub-articular collar on the Ascension® MCP greatly simplifies the osteotomy technique.

In addition to possessing a planar attribute, Ascension® MCP collars are inclined so that minimal resection of bone is necessary at the dorsal aspect of the metacarpal neck, and at the palmar aspect of the proximal phalangeal neck. Minimal bone resection in these areas maintains the anatomic insertion sites for the collateral and accessory ligaments thus providing the surgeon the potential of preserving the soft tissue structures. Other "soft tissue" design refinements 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.

Finally, the anatomic shaped stems of the Ascension® MCP are intended to conform to the anatomic length and shape of the medullary canal of the natural bone in order to more efficiently fill the canal and promote component fixation.

Further Design Comparison of Original and Ascension MCP Devices:

In addition to the device design comparisons outlined above, the sponsor provided comparisons of the pyrocarbon thickness, radial clearance, and sphericity of the original pyrocarbon implant and the Ascension MCP devices.

Pyrocarbon Thickness Comparison

Device	Nominal (inch)	Range	
		Minimum	Maximum
Original pyrocarbon MCP	0.0178" (0.452mm)	0.0159"	0.0214"
Ascension MCP	0.0165" (0.419mm)	0.0150"	0.0180"

The sponsor stated that mechanical strength test experiments conducted during Ascension MCP product development activities revealed that for a given component size, one of the primary attribute affecting fracture load was pyrocarbon thickness.

Radial Clearance Comparison

Device	Nominal (inch)	Range	
		Minimum	Maximum
Original pyrocarbon MCP	0.0037	0.0017	0.0062
Ascension MCP			
Size 10	0.026	0.023	0.033
Size 30	0.023	0.008	0.033
Size 50	0.018	0.012	0.023

Sphericity

Device	Nominal (inch)	Range	
		Minimum	Maximum
Original MCP			
Proximal	0.0003	0.0003	0.0003
Distal	0.0003	0.0002	0.0003
Ascension MCP			
Proximal	0.0005	0.0002	0.0008
Distal	0.0008	0.0002	0.0012

The sponsor stated that although the upper limit of the Ascension MCP sphericity ranges extends beyond that of the original MCP, wear tests conducted with final sterilized size 10, and size 50 Ascension MCP components demonstrated that the device exhibits exceptional wear performance superior to that of other commercially available devices.

MATERIALS:**Ascension® MCP Device:**

The sponsor stated that the device is comprised of a pyrocarbon layer approximately 0.0165" (0.419mm) thick encasing a high strength machined graphite substrate.

The pyrocarbon layer is produced by levitating graphite substrates in a fluidized bed reaction chamber heated to 1300-1500°C and introducing a gaseous hydrocarbon (propane). Pyrolysis of the gaseous hydrocarbon occurs producing free carbon atoms, which then recombine and deposit onto the graphite substrate. Components undergo subsequent polishing, cleaning, and inspection operations to insure that parts adhere to component specifications.

The pyrocarbon material in the Ascension® MCP is On-X® Carbon, produced by Medical Carbon Research Institute (MCRI), while the graphite substrate material in the Ascension® MCP is AXF-5Q10W

grade graphite produced by Poco Graphite, Inc. The graphite substrate material in the device is impregnated with 10-wt% of tungsten. The tungsten causes the device to be radiopaque. The On-X® Carbon material has 0% silicone. The sponsor also provided a technical report that identifies the layer plane spacings (approx. 3.48Å), crystallite sizes (approx. 38Å), crystallite-preferred orientation and microstructures of the pure pyrolytic carbons.

The sponsor stated that the physical and mechanical properties of the pyrocarbon correlate with hardness. So, the sponsor stated that it can be easily assured during the manufacture process that optimum properties have been obtained on each lot of pyrocarbon components produced by measuring hardness and ensuring that it falls within a specified range. Thus, for Ascension® MCP components, a specimen from each processing lot is destructively inspected to measure pyrocarbon hardness. The sponsor stated that this ensures that the device components possess strength and hardness properties necessary for optimum endurance and wear resistance.

Properties of Pyrocarbon Surface Material (On-X® Carbon) and Graphite Substrate Material (AXF-5Q10W):

Property	On-X® Carbon Nominal+/- S.D.	On-X® Mechanical Requirements	Graphite Substrate Material: AXF-5Q10W Minimum
Flexural Strength (ksi)*	71.6 +/- 1.7 (493MPa)	50-75 ksi (50ksi min)	8.6 (59MPa)
Density (gm/cm ³)	1.93 +/- 0.01	-	1.85
Strain-to-Failure (%)*	1.58 +/- 0.03	1.2-1.65% (1.1% min)	-
Young's Modulus (Msi)*	4.3 +/- 0.1 (29.6 GPa)	3.8-4.5Msi (3.5Msi min)	1.6
Diamond Pyramid Hardness, 500 gm load	235.9 +/- 3.3	200-250 DPH 200 DPH (min)	-
Compressive Strength (ksi)	-	-	17
Fracture Toughness ksi(in) ^{1/2}	-	1-2.6 (0.9 min)	-
Shore Hardness	-	-	65

*Determined by testing 0.04 x 0.25 x 1.0" polished test slabs in 4-point bend flexure.

Original Pyrocarbon MCP Device Materials (Device used in the Animal Studies and Clinical Trails):

The original device material was Pyrolite carbon (a registered trade name of pyrocarbon material produced by Carbomedics Inc) deposited as a coating on a graphite substrate material.

The sponsor stated that Pyrolite is widely used throughout the prosthetic mechanical cardiac valve industry. Pyrolite carbon is produced by the pyrolysis of a hydrocarbon gas at 1400°C, a temperature that is low compared to the melting point of carbon. Pyrolite carbon is deposited as a coating (approximately ½ mm) onto a graphite substrate. The articulating surfaces of the implants are polished to a supersmooth finish, while the tissue fixation areas are left in the as-deposited condition, which provides a microrough surface for tissue attachment. The sponsor stated that the material properties of Pyrolite are well known and reported by the manufacturer and in the literature. The sponsor provided the following material properties for Pyrolite:

Material Properties of Pyrolite®

Property	Reported Range	Reported Nominal
Flexural Strength (ksi)*	50 - 72	56.4 ± 1.9
Strain-to-Failure (%)*	1.2 - 2.0	1.27 ± 0.06
Young's modulus (msi)*	3.1 - 4.6	3.8 ± 0.09
Diamond Pyramid Hardness	240 - 370	293 ± 13
Density (gm / cm ³)	2.1 - 2.12	2.120 ± 0.005
Crystallite Size (Å)	30 - 50	42 ± 1

* Determined by 4-point bend flexure

In addition, samples of pyrocarbon from two of the six original MCP devices retrieved from clinical use were submitted to AMIA Laboratories for an independent determination of the carbon crystallite size, Lc. Test results indicated that Lc=41-42Å, which is consistent with values reported in the literature.

Graphite Substrate Material:

The sponsor stated that the original device graphite substrate material was made of both AXF-5Q 10W Grade Graphite (impregnated with 10-wt% of tungsten for radio-opacity) and AXF-5Q Grade Graphite without tungsten.

A total of six of the original MCP devices implanted in patients at Mayo Clinic and then removed during subsequent revision operations were returned to Ascension Orthopedics, Inc. Fragments from two of these devices were metallographically sectioned, mounted and polished in order to examine the underlying graphite substrate material. These metallographic mounts were submitted to Poco Graphite, Inc., the manufacturer of the graphite material, to confirm the grade of graphite in each of the fragments. Based on EDX and microstructure analysis, it was concluded that one of the fragments contained tungsten and thus was AXF-5Q 10W Grade Graphite, while the other fragment did not contain tungsten and thus was AXF-5Q Grade Graphite. Thus, the original device graphite substrate material was made of both AXF-5Q 10W Grade Graphite with tungsten and AXF-5Q Grade Graphite.

Material Properties of Original MCP device graphite substrate material (Note: the Ascension MCP device has a graphite substrate composed of AXF-5Q10W Grade Graphite):

Material Properties	AXF-5Q Grade Graphite	AXF-5Q10W Grade Graphite
Property	Minimum	Minimum
Flexural Strength (ksi)	10	8.6
Compressive Strength (ksi)	18	17
Shore Hardness	70	65
Density (gm / cm ³)	1.77	1.85

SUMMARY OF PRE-CLINICAL STUDIES (including animal testing, mechanical testing, and biocompatibility):**Animal Testing Summary:**

The devices used in the animal study and the clinical study were made of Pyrolite (a trademark of Carbomedics Inc.) carbon coating over a graphite substrate and had a different design than the devices proposed in this PMA. This information is outlined above in the device description and materials sections.

Five of the original pyrocarbon MCP implants and one Steffee design (metal/polyethylene) were implanted into the long finger MCP joints of four baboons. One baboon received a noncemented Pyrolite carbon implant in the right hand and a cemented PE/metal (Steffee) implant on the left. One received a non-cemented Pyrolite carbon implant in the right hand and a cemented Pyrolite carbon implant in the left. The remaining two baboons received one non-cemented Pyrolite carbon implant each in the right hand. The implants remained in place for 9 months. X-rays were taken at 3, 6 and 9 months post-op. Microscopic examination of the soft tissue structures was performed on 2 of the prostheses, and microradiographic and histologic evaluation were performed on 3 of the prostheses. The sponsor reported that of the 4 devices implanted without bone cement, one had direct bone fixation along the medullary stem while the other 3 had a combination of bone fixation with an interposing fibrous tissue membrane. The sponsor stated that there was no evidence of bone resorption around the stems and functional fixation was obtained with all of the uncemented pyrocarbon implants. No foreign body reaction was observed in the soft tissues, and no evidence of intracellular particles was present. The sponsor reported that the pyrocarbon device implanted with bone cement showed evidence of bone resorption at the cement-bone interface around one component, and intermittent lucent lines around the cement-bone interface of the other. Evidence of bone resorption and gross implant loosening was observed in the cemented metal-polyethylene Steffee implant. The sponsor concluded that the result of this animal study demonstrated the potential for biological fixation of pyrocarbon implants in bone and confirm the clinical suitability of the uncemented, semi-constrained Ascension® MCP implant design.

The sponsor reported that several cortical perforations occurred in the animal study for primarily two reasons:

- Custom surgical instrumentation such as sizing templates, broaches, and implant sizing trial components were not available to aid in surgical planning or the surgical implantation of the prostheses. Removal of the metacarpal head was accomplished using a rongeur, and medullary reaming was performed using a dental drill.
- The stem sizes that were used (similar in size to the small version implanted in patients at the Mayo Clinic) were too large for the animal's hands. In order to implant the prostheses, it was necessary to enlarge the medullary cavities sufficiently to accept the stem of the pyrocarbon implants; this resulted in cortical perforations on some of the animals.

The sponsor has taken the following steps to minimize the risk of cortical perforation when using the Ascension MCP prosthesis:

- Five implant sizes allow for a broad range of size selectivity to meet patient needs;
- X-ray templates for proper sizing;
- Custom surgical instruments; and
- Surgical technique for the physicians.

Measurements allowing for determination of volumetric or linear wear of the pyrocarbon MCP implants used in the baboon study were not performed. The sponsor stated that an examination of the implant site by the surgeon investigator at the time the implants were removed revealed no evidence of wear debris. No reports or remarks of damage to the articular surfaces of the pyrolytic carbon prostheses have been found in any notes or records.

Tissue samples excised from anatomic structures in baboons surrounding pyrocarbon MCP total joint prostheses during implant removal were examined by an independent, third party pathologist. The investigator concluded that no foreign body granuloma or other negative foreign body reactions were seen in any of the sections examined. None of the sections showed evidence of debris or foreign material of any kind. No sections showed evidence of inflammation or necrosis. Since there were no indications of negative tissue reaction due to the presence of the pyrocarbon implants, the report concludes that the histopathologic toxicity rating for the pyrocarbon MCP implants is "non-toxic."

Mechanical Testing Summary:**Literature Review to Support Methods for Mechanical Testing:**

To ensure proper test conditions for mechanical evaluation of the Ascension® MCP, an extensive review of the biomechanics literature was conducted to establish the magnitude and direction of the joint reaction force (JRF) at the MCP joint resulting from daily hand function. From the sponsor's literature review, they concluded the following:

- Average grasp strength for normal and female dominant hand is 85.4lb (range 34-142lb) and 51.2 (range 17.9-87lb), respectively;
- Average pinch strength for the index finger of the normal male dominant hand is 13.5lb (range 7.7-17.1lb);
- Average pinch strength for normal female hand is approximately 70% of the strength of the male hand;
- Relative strength of the fingers for the normal male and female hand: Index=1.0, Long=1.0, Ring=0.67, and Little=0.47.
- The pinch strength of the diseased arthritic hand has been observed to range from 1.1-4.5lb, or about 10%-30% of normal strength.
- MCP joint flexion for isometric hand function is 60°.
- Magnitude of MCP JRF for isometric hand function is 78.7lb.
- Direction of MCP JRF is 20 degrees dorsal angle (see figure 7-2).
- Magnitude of MCP JRF for dynamic hand function is 4.5lb.
- Maximum sliding velocity for MCP joint is 200mm/second (7.87"/second)

Mechanical Testing:

Mechanical testing was performed on the device to be marketed. The device to be marketed has been modified from the original device that was used in the animal testing and human clinical trials. Similarities and differences of the original pyrocarbon MCP and Ascension MCP device designs and materials were summarized in the designated sections above.

In Vitro mechanical tests were designed and carried out to evaluate three (3) distinct performance characteristics of the Ascension® MCP: wear, strength; cyclic endurance (fatigue). Strength tests and contact tests were conducted on size 10, 30 and 50 proximal and distal components. Size 10 components only were used for cyclic endurance tests because it was the smallest size Ascension MCP device available and because the size 10 components exhibited the lowest fracture strength compared to the larger sizes. For strength, cyclic endurance, coronal load strength, and contact tests, components were held with the distal 2/3 of the stem rigidly supported. The testing results were as follows:

Test	Size & Component	Results
Wear Test	Ascension MCP size 10 Ascension MCP size 50	Size 10 and Size 50 Ascension MCP devices exhibited identical wear behavior. Measurable wear did not occur on Ascension MCP components (sensitivity 0.0002 inch).
	For comparison, wear testing of Avanta Orthopaedics, Inc. SR MCP (Cobalt Chrome metal on polyethylene) size "XL" and size "SM" was performed.	Measurable wear did not occur on the CoCr components (sensitivity 0.0002 inch). Wear on UHMWPE components ranged from 0.0018 to 0.0040 inches.
	For comparison, wear testing of an axisymmetric CoCr metal on UHMWPE MCP device was performed (sizes similar to Ascension MCP size 10 and size 50)	Measurable wear did not occur on the CoCr components (sensitivity 0.0002 inch). Wear on UHMWPE components ranged from 0.0019 to 0.0043 inches.