



NOV 22 1999

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Jerome J. Klawitter, Ph.D.
President and CEO
Ascension Orthopedics, Inc.
8200 Cameron Road, Suite C-140
Austin, Texas 78754

Re: M990022 / Module 1
Device: Acension® MCP, metacarpophalangeal total joint
replacement
Received: August 2, 1999
Amended: October 1, 1999

Dear Dr. Klawitter:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of the following sections of your premarket approval (PMA) application modular submission:

- Cover Page (General Information)
- Device Description
- Performance Standards
- Non-Clinical Studies
- Environmental Assessment; and
- Bibliography

However, we have not completed our review of Volume 1, Section 2 of your submission containing a discussion of how the clinical study was conducted. Please be advised that this section of Module 1 is still under review and you may be asked to provide additional information once our review is completed.

The following deficiencies have been identified and require responses prior to acceptance and closure of this module.

Pre-Clinical Testing

1. On p.377, the wear testing protocol stated that testing was conducted on ball and cup specimens that were "not implantable joint components but rather axisymmetric components which have articular surfaces of a form and

size that are virtually identical to the articular surfaces of the size 10 MCP device components." In addition, on p.378, you stated that size 10 MCP components were used in your wear testing because these components have the smallest radius of curvature and highest contact stresses. You stated that because of high contact stresses the smallest components should have the greatest material removal and represent the worst case wear couple.

We believe that all device testing should be performed on final sterilized devices you intend to market. In addition, we believe that testing components with the highest contact stresses may provide worst-case results in terms of fatigue wear; however, for abrasive wear we believe the component with the largest contact area and the lowest contact stresses exhibit the highest wear rates. This is why 32mm femoral heads have higher abrasive wear rates than 22mm femoral heads when articulating against polyethylene acetabular components in a total hip prosthesis. Therefore, please provide the following information regarding your wear testing:

- a. Please identify the similarities and differences between the tested and subject device components; and
 - b. Either provide a complete wear testing report including testing on final sterilized size 50 MCP components intended for marketing or provide a rationale for why the results of the wear testing already performed are representative of the results expected for the subject device components.
2. Regarding the mechanical testing to determine fatigue endurance of the metacarpal and phalangeal components, you stated that all components survived the cyclic fatigue load for 10 million cycles. However, you did not specify the type(s) of analysis (e.g., dye penetrant, SEM, optical microscopy) performed to determine the extent of component damage (e.g., cracking, deformation, chipping) after 10 million cycles. Therefore, please either provide a complete test report including a damage analysis of these components or provide a rationale for not performing this analysis.

3. In the article you provided by Cook, et al., "Long-Term Follow-up of Pyrolytic Carbon Metacarpophalangeal Implants," JBJS, 81-A, May 1999, it stated that one patient had a fracture of the distal stem of one of the MCP implants. Please:
 - a. Clarify if there were any additional fractures of the MCP components in the clinical study;
 - b. Identify where the fracture occurred and the failure mode for each failed component; and
 - c. Provide a comparison of the clinical fracture location and failure mode to the fracture location and failure mode identified in your bench testing.
4. Regarding the mechanical testing to determine strength of the metacarpal components, phalangeal components, and phalangeal components that were fatigue tested, please identify where the fracture occurred and the failure mode for each component tested.
5. Please provide contact area and stress measurements for the original and subject MCP device components over a range of flexion/extension angles.

Animal Study

6. In the literature article regarding the use of the pyrocarbon MCP device in several baboons, Cook et al., "Pyrolite Carbon Implants in the Metacarpophalangeal Joint of Baboons," the researchers stated that there were several cortical perforations. Please clarify why each cortical perforation occurred and outline any modifications (e.g., device design, surgical technique) that were made to minimize the risk of this complication in the clinical study.
7. Please provide the following information regarding the devices explanted in the baboon animal study:
 - a. Volumetric and linear wear on the articulating surfaces;
 - b. Wear patterns on the articulating surfaces including photomicrographs; and
 - c. The extent of damage to the articulating and stem surfaces of the metacarpal and phalangeal components.

8. In the fabrication of the components used for testing, there were several protocol deviations regarding coating thickness tolerances and chips in component's stems. Please clarify why each deviation from protocol occurred and outline any and all modifications that were made to minimize the potential for these problems in the fabrication of the final device components.

Biocompatibility

9. Per ISO 10993-1, chronic toxicity and implantation testing are recommended for devices with permanent contact with tissue and bone. On p.85, you stated that a systemic injection test and a rabbit pyrogen test were conducted on extracts of the pyrocarbon material to address these concerns. FDA disagrees that the acute systemic toxicity and material-mediated pyrogenicity testing address the need for chronic toxicity and implantation testing. Please provide test protocols and results from chronic toxicity and implantation testing, or provide a rationale for why this testing is not necessary. A test protocol rationale, a representative sample of color photo micrographs and associated pathology reports from your baboon study should be provided, and may address these concerns. FDA recommends that ASTM F981-93 "Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Bone," and ISO 10993-6 "Tests for Local Effects after Implantation" be used to help format your response.
10. For the Salmonella Typhimurium Reverse Mutation Assay, provided on pp.231-243, please address the following:
 - a. FDA recommends that in addition to the 4 strains used in your study, investigators also study one of the following test strains: TA 1538, TA 102, WP2uvrA or WP2uvrA(pKM101). Therefore, please repeat the testing using one of the recommended test strains or provide a scientific justification for the *E. Coli* test strains used in your assay; and
 - b. FDA recommends that a non-polar extract also be tested. Therefore, please repeat your testing using a non-polar extract or provide a scientific justification for the use of only a sodium chloride test extract.

11. For the Intracutaneous Reactivity test, provided on p.259, the table title indicated that a NaCl extract was used, but the table itself identifies CSO as the extraction vehicle. Please clarify the discrepancy, and provide results from the NaCl extract if they have not yet been submitted to this application.
12. Please provide a scientific justification for the test article to extract ratio (slabs/ml) used in the acute systemic toxicity, intracutaneous reactivity, and material-mediated pyrogenicity tests provided in M990022/M1/V2 Appendix 4.
13. For the Ultem™ material used to fabricate the Metacarpal and phalangeal sizing trial sets, please address the following:
 - a. Identify the supplier model number for the particular Ultem™ used in this device
 - b. Provide a material safety data sheet;
 - c. Provide a product technical information sheet;
 - d. Provide processing information to explain how your processing differs from the supplier recommended processing, and explain how these processing steps could affect biocompatibility of the final sterilized device. Any additives that you incorporate into the processing or formulation (such as color, etc.) should be addressed in this rationale; and
 - e. Either perform cytotoxicity, sensitization, and irritation (or intracutaneous reactivity) testing for this product, as recommended by ISO 10993-1 for externally communicating devices in contact with tissue and bone for a limited (<24 hr) duration or provide a scientifically valid rationale for not conducting these tests.
14. FDA is unaware of 17-7PH and 17-4PH stainless steels being used for medical device instrumentation. Please address the following:
 - a. Identify all of the differences and similarities between Type 300 and 400 stainless steels which have a long history of use as medical device instrumentation, and the 17-7PH and 17-4PH stainless steels proposed for the subject instrumentation.

- b. Provide a scientifically valid rationale for why these materials are appropriate for use in medical device instrumentation, and why additional material biocompatibility and physical property testing are not necessary or provide the results of such testing.
15. For each of the biocompatibility tests, please explain how the biocompatibility test article differs from the final, sterilized, finger joint prosthesis. Please format your response according to the attached Biocompatibility Certification.

Materials

16. In Tables 4-4 and 4-5 on pp.49 and 50, you provided material properties for On-X® Carbon and AXF-5Q10W Grade Graphite. Please provide these same material properties for the pyrocarbon and graphite materials used to make the original MCP device used in the baboon study and the clinical study. In addition, please identify the carbon crystallite size for the original device material.
17. On p.50 you stated that the compressive strength of the AXF-5Q10W Grade Graphite is 2.5 ksi. However, on p.202, the minimum compressive strength value identified by Poco Graphite, Inc. was 17ksi. Please rectify this apparent discrepancy.

Responses to FDA Questions, Volume 1, Section 2

18. Per our telephone conversation on November 10, 1999 regarding the FDA questions you answered in Volume 1, Section 2, please:
 - a. Provide a copy of the form that documented approval of the use of the device by the Mayo Clinic Human Studies Committee, if available;
 - b. Identify the IRB chairman who approved the use of this device at the Mayo Clinic including name and address, if available;
 - c. Identify what patients (i.e., identified by patient number or identifier and not by name) provided written consent and what patients provided verbal consent over the course of the study;
 - d. In your response on p.21 to our request for a table of all adverse events including time to event and the number of patients available at each time point, you stated that you have not yet completed your

collection, collation, and analysis of the data. Please provide this information once your collection, collation, and analysis has been completed.

Intended Use and Device Description

19. Please clarify if this device is intended for use in the MCP joint of the thumb.
20. Regarding the original MCP device used in the baboon study and the clinical study, please identify:
 - a. The thickness of the pyrocarbon coating including manufacturing tolerances;
 - b. The radial clearance including manufacturing tolerances; and
 - c. The sphericity of the metacarpal and phalangeal components.
21. Regarding the Ascension® MCP device, please identify:
 - a. The radial clearance including manufacturing tolerances; and
 - b. The sphericity of the metacarpal and phalangeal components.
22. The engineering drawings provided on pp.41 and 100 contain dimensions for metacarpal head diameter and metacarpal stem length that are inconsistent with one another. Please clarify this apparent discrepancy by providing either revised engineering drawings or an adequate rationale.

Device Labeling and Draft Surgical Technique

23. You provided labeling information and a draft surgical technique in Appendix 6 of Volume 2. This information cannot be adequately review without the results from your clinical study. Therefore, please be advised that you will need to resubmit this information in your PMA along with your clinical data. FDA will not review this information until that time.

If you intend to address the deficiencies prior to the submission of your PMA application, you should submit the information in the form of an amendment to the module. CDRH may extend the review time by an additional ninety days once your response is received. However, we will continue to

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communicate promptly to resolve any remaining issues. Please submit 6 copies to the address below, referencing the above PMA Shell and Module numbers:

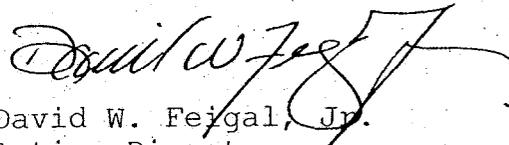
Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

Otherwise, your future PMA application should incorporate by reference the information contained in the module and should include your response to the remaining deficiencies, as well as any additional changes to the content of the module.

Please be advised that depending on your responses to items 18a-d above, we may request additional information regarding the conduct of the clinical study.

If you have any questions concerning this letter, please contact Mr. John Goode at (301) 594-2035 x155.

Sincerely yours,



David W. Feigal, Jr.
Acting Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure