

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Penile Inflatable Implant

Device Trade Name: Mentor Alpha I Inflatable Penile Prosthesis

Applicant's Name and Address: Mentor Corporation
201 Mentor Drive
Santa Barbara, California 93111

Premarket Approval (PMA) Application Number: P000006

Date of Good Manufacturing Practice Inspection: May 25, 1999

Date of Notice of Approval to the Applicant: JUL 14 2000

II. INDICATIONS FOR USE

The Alpha I Inflatable Penile Prosthesis is indicated for male patients suffering from erectile dysfunction (impotence) who are considered to be candidates for implantation of a penile prosthesis.

III. CONTRAINDICATIONS

The Alpha I Inflatable Penile Prosthesis is contraindicated in patients who have one or more of the following conditions:

1. Patients with an active infection present anywhere in the body, especially urinary tract or genital infection.
2. Patients with unresolved problems affecting urination, such as an elevated residual urine volume secondary to bladder outlet obstruction or neurogenic bladder.
3. Patients unwilling to undergo any further surgery for device revision.

IV. WARNINGS AND PRECAUTIONS

Warnings:

1. Implantation of the device may make latent natural or spontaneous erections, as well as other interventional treatment options, impossible.
2. Men with diabetes or spinal cord injuries, as well as immunocompromised patients, may have an increased risk of infection associated with a prosthesis.
3. Failure to evaluate and promptly treat erosion may result in a substantial worsening of the condition, leading to infection and loss of tissue.

4. Implantation of a penile prosthesis may result in penile shortening, curvature or scarring.
5. Pre-existing abdominal or penile scarring or contracture may make surgical implantation more complicated or impractical.
6. This device contains solid silicone elastomer. The risks and benefits of implanting this device in patients with lupus (e.g., SLE and DLE), scleroderma (e.g., progressive systemic sclerosis), myasthenia gravis, or documented sensitivity to silicone should be carefully considered. The issue of the possible relationship between silicone (and other implantable materials) and various diseases has been and continues to be the subject of great scientific and medical debate.

Precautions:

Surgery-Related:

1. Surgeons implanting penile prostheses should be familiar with the currently available techniques for measuring the patient, determining implant size, and performing the surgery.
2. Prostheses of incorrect length may result in voiding difficulties, inflammation, pressure necrosis and erosion into the urethra or through the tunica albuginea of the corpus cavernosum, SST deformity, buckling of the cylinders, or malposition of the pump in the scrotum.
3. Do not use narrow cylinders in patients with normal anatomies. Narrow cylinders should only be used in patients with compromised corpora and smaller anatomies. The use of an improper cylinder size increases the risk of an unsuccessful outcome.
4. Improper surgical implantation of the prosthesis could result in unsatisfactory performance or require corrective surgery. Careful technique will minimize the possibility of erosion or perforation of the corpora cavernosa and urethra, and aid in preventing kinked tubing.
5. Improper reservoir placement or filling technique can result in spontaneous unintended inflation or deflation of the cylinders.
6. Each device should be carefully examined prior to surgery and continuously monitored throughout the surgical procedure to ensure the structural integrity of the device is not compromised in any way. A prosthesis which has been damaged or on which repairs have been attempted should not be implanted.
7. The prosthesis should not be handled with pointed, toothed or sharp-cornered instruments, as any nick can be the focus for subsequent failure of the implant. Extreme care should be taken in manipulating the prosthesis with blunt instruments to avoid tearing, warping or nicking.
8. Lint, fingerprints, talc and other surface contaminants can cause foreign body reactions. Utmost caution should be taken to avoid contaminants. Any nick or split in the device is a potential mechanical failure site and can serve as a collection point for debris. Such debris could cause foreign body reactions or be a locus for infection.
9. Removal of an implanted prosthesis without timely reimplantation of a new prosthesis may complicate subsequent reimplantation or may make it impossible.

10. Utmost care must be used with cautery-type devices in or near the area of the implant, as damage to and subsequent leakage of the implant could occur.

Device-Related:

11. Use sterile, isotonic, pyrogen-free Sodium Chloride U.S.P. Solution for Injection to fill the implant.
12. The components of this implant are manufactured and tested for assembly/use with their specified Mentor devices. The use of Mentor components with other manufacturers' components has not been tested and is not recommended.
13. Do not use product that has damaged or opened packaging, as sterility may be compromised.
14. This device is sold sterile for single use only, and should never be resterilized. In the event the product becomes contaminated prior to use, the device should be returned to Mentor for replacement.

Patient-Related:

15. A thorough preoperative consultation should include a discussion between the patient and physician of all available treatment options and their risks and benefits.
16. Reports in the literature suggest that prophylactic antibiotic treatment for dental procedures may be indicated for patients with a penile prosthesis.
17. Health conditions which hamper sexual activity, such as severe angina, may prevent successful use of this device.
18. The prosthesis should not be implanted in patients who lack the manual dexterity necessary to operate the device.
19. Psychological characteristics, such as inappropriate attitude or motivation, may inhibit the patient's successful use of the device.
20. Trauma to the pelvic or abdominal areas, such as impact injuries associated with sports (e.g., bicycle riding), can result in damage of the implanted device and/or surrounding tissues. This damage may result in the malfunction of the device and may necessitate surgical correction, including replacement of the device.
21. The implantation of this device should only be considered in patients whom the physician determines are adequate surgical risks.

V. DEVICE DESCRIPTION

The Mentor Alpha I Inflatable Penile Prosthesis consists of four inter-connected components: two cylinders implanted within the corpora cavernosa of the penis, a pump implanted within the scrotum, and a fluid reservoir implanted in the lower abdomen. These components are packaged dry, and filled with sterile saline at the time of implantation. The device components can be implanted using either an infrapubic or scrotal incision, depending upon surgeon preference.

To create an erection, the patient repeatedly squeezes the pump bulb to transfer fluid from the reservoir to the cylinders until they become rigid. To make the penis flaccid, the patient squeezes the pump base to open internal check valves and allow fluid to flow from the

cylinders back to the reservoir. More detailed descriptions of each of the components of the Mentor Alpha I Inflatable Penile Prosthesis are as follows:

Cylinders: The cylinders consist of an inflatable shaft constructed from polyurethane elastomer, distal and rear tips constructed from silicone elastomer, and nylon-reinforced silicone tubing for connection to the pump. All components are bonded using silicone elastomer adhesive. The cylinders are available in a variety of diameters and lengths for proper anatomical fit within the corpora cavernosa.

Pump: The pump consists of a pump bulb, valve block, and tubing adapters, each of which is molded from silicone elastomer and bonded using silicone elastomer adhesive. Other components of the pump include nylon-reinforced, silicone tubing for connection to the pump and reservoir, and stainless steel check valves to direct fluid flow. The pump is available in three models, which differ only in the geometry/design of the release mechanism and inlet/outlet tubing.

Reservoir: The reservoir consists of a polyurethane elastomer shell and silicone elastomer tubing adapter, which are bonded using silicone elastomer adhesive. Nylon-reinforced, silicone tubing exits the reservoir at the adapter for connection to the pump. The reservoir is available in a variety of volumes, depending upon the cylinder size used. The reservoir is also available with or without a lockout valve, which prohibits fluid from flowing from the reservoir to the cylinders except when the pump is used.

The following accessories to the Mentor Alpha I Inflatable Penile Prosthesis are available: rear tip extenders, tubing connectors, cylinder protector, flex tip needle, tapered needle, Keith needle, shod tubing, and True-Lock Plug.

The Mentor Alpha I Inflatable Penile Prosthesis and accessories are sold as sterile and labeled for single use only.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

The treatment of erectile dysfunction is based predominately on patient preference and etiology. Current treatment options include: psychological counseling, pharmacological therapy, external penile rigidity devices, intracavernosal injection therapy, vascular surgery, penile rigidity implants, and penile inflatable implants.

VII. MARKETING HISTORY

The applicant submitted this application in response to the proposed rule published in the Federal Register of April 28, 1993 (58 FR 25902) proposing the submission of PMA applications for penile inflatable implants. On April 12, 2000, while this PMA was under review, the final rule announcing the submission of PMAs for penile inflatable implants was published (65 FR 19650). The Mentor Alpha I Inflatable Penile Prosthesis was initially cleared as a preamendments class III device through the premarket notification (510(k)) process in 1989. This devices has been marketed in the United States and 28 other countries since its development, and has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the devices.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

A total of 343 patients were evaluated for adverse events in the clinical investigation of the Alpha I Inflatable Penile Prosthesis. See Table 1 for a complete listing of the adverse events recorded in this study.

IX. SUMMARY OF PRECLINICAL STUDIES

Material Characterization Studies:

A series of *in vitro* tests were conducted to characterize the chemical constituents of the materials of the Mentor Alpha I Inflatable Penile Prosthesis. The objectives of this testing were to identify the chemical make-up of these materials and to estimate the exposure of each to the patient. This information was then used to determine the biocompatibility testing scheme. The complete list of material characterization tests performed is as follows:

- chemical analysis of extractables;
- analysis of chemical crosslinking;
- identification and quantification of volatiles and semivolatile extractables;
- molecular weight characterization of nonvolatile extractables;
- polychlorinated biphenyl assessment; and
- heavy metals assessment.

All material characterization tests were performed on finished, sterilized devices.

These tests were found to be adequate for characterizing the materials of the Mentor Alpha I Inflatable Penile Prosthesis.

Biocompatibility Studies:

Using the knowledge gained from the material characterization tests, biocompatibility testing was conducted on the patient-contacting materials of the Mentor Alpha I Inflatable Penile Prosthesis. The objective of this testing was to assess whether these materials are safe for long-term implantation. The complete list of biocompatibility tests performed on the individual patient-contacting materials is as follows:

- cytotoxicity;
- sensitization;
- acute systemic toxicity;
- irritation testing;
- genotoxicity;
- implantation testing (30 and 90 days); and
- hemolysis.

In addition, the following biocompatibility tests were performed on finished, sterilized devices:

- genotoxicity;
- immunological evaluation;
- reproductive toxicity;
- chronic toxicity/carcinogenicity assay; and
- pharmacokinetics assay of silicone monomers and polyurethane degradation products.

This list of biocompatibility tests is consistent with the tests suggested in ISO-10993 for permanent implants. This information demonstrated that the device does not pose a toxicological concern.

Mechanical Testing:

Mechanical testing was conducted to assess the safety, effectiveness, and reliability of the Mentor Alpha I Inflatable Penile Prosthesis. Bench tests were conducted to evaluate all device attributes that are critical to safety, effectiveness, and reliability. Furthermore, additional mechanical bench tests were performed to measure certain other device attributes for characterization purposes. The complete list of mechanical tests performed is as follows:

Material characteristics:

- 200% modulus;
- elongation;
- tensile strength;
- energy;
- tear strength; and
- filling agent permeability.

Full device characteristics/simulated life cycling:

- inflation time;
- inflation rate;
- number of strokes for inflation;
- deflation time;
- deflation rate;
- concentricity;
- column strength;
- radial expansion;
- aneurysm resistance;
- suture pull force;
- restrained burst strength;
- cylinder bladder/base pull force;
- cylinder base/strain relief pull force;
- backpressure test;
- pump strain relief pull force; and
- reservoir/tubing joint bond strength.

Pump characteristics:

- minimum force to affect fluid transfer;
- volume displaced per stroke;
- squeeze force vs. fluid displacement;
- inflation effort;
- uniform discharge to cylinders;
- pressure required to affect valve opening for inflation;
- force required at the pump release mechanism to allow cylinder deflation;
- backpressure required for valve failure;
- maximum pressure differential across closed valve at full inflation;
- leakage rate across closed valve at full inflation;
- pump longevity;
- pump deflation rate;
- pump bulb rebound;
- high pressure (inflate/deflate);

- backpressure test;
- inlet valve test; and
- joint integrity.

Cylinder characteristics:

- radial expansion;
- length expansion;
- column strength;
- aneurysm resistance;
- concentricity;
- unrestrained burst strength;
- restrained burst strength;
- cylinder longevity (10,000 inflation/deflation cycles);
- cylinder longevity (10,000 radial compression cycles);
- cylinder longevity (resistance to forces anticipated *in vivo*);
- joint integrity; and
- suture pull force.

Reservoir characteristics:

- reservoir volume;
- reservoir bladder dimensional symmetry;
- reservoir pressures during inflation/deflation;
- lockout valve extrusion test;
- maximum flow rates to and from the reservoir;
- lockout valve deflation rate and pump bulb rebound;
- lockout valve override pressure;
- fold wear characteristics (4,400 inflation/deflation cycles);
- resistance to external cyclic fatigue (10,000 compressive cycles); and
- joint integrity.

Tubing characteristics:

- tensile strength (with and without tubing connectors);
- kink resistance;
- occlusion resistance with tubing (with connector) and cylinder in shared cavernosa;
- rupture resistance;
- tubing to tubing abrasion resistance (1,000,000 abrasion cycles);
- tubing flex test (1,000,000 flex cycles); and
- hydrostatic pressure test of tubing/connector interface.

Accessory component characteristics:

- tensile strength (with tubing connectors);
- occlusion resistance with tubing (with connector) and cylinder in shared cavernosa;
- hydrostatic pressure test of tubing/connector interface; and
- rear tip extender pull force.

Explanted device characteristics:

- radial expansion;
- aneurysm resistance;
- column strength;
- concentricity;
- suture pull force;
- restrained burst strength;
- unrestrained burst strength;

- cylinder longevity (10,000 inflation/deflation cycles);
- cylinder longevity (10,000 radial compression cycles);
- joint integrity;
- high pressure (inflate/deflate);
- backpressure test;
- inlet valve test; and
- reservoir bladder dimensional symmetry.

All mechanical tests were performed on finished, sterilized devices, device components, or material samples, and test conditions simulated *in vivo* conditions wherever appropriate. The sample sizes used for each test were statistically justified, and representative samples of each device model and size range were evaluated. This information demonstrated that the device functions according to the stated design specifications.

In addition to the above tests, stability testing was performed on aged samples of all device components except the reservoir with the lockout valve. This testing justified the 5-year shelf life proposed for the tested components.

X. SUMMARY OF CLINICAL STUDIES

Objectives:

The objectives of the clinical study were to assess the safety and effectiveness of the Mentor Alpha I Inflatable Penile Prosthesis in the treatment of erectile dysfunction.

The primary effectiveness objective was evaluation of the ability of the device to provide an erection suitable for sexual intercourse. Secondary effectiveness objectives were evaluation of (i) the effects of the device on patient quality of life and (ii) the incidence of complications and device malfunction, including the incidence of cancer and connective tissue diseases.

Study Design:

A baseline-controlled, multicenter, prospective clinical study was conducted to evaluate the safety and effectiveness of the Mentor Alpha I Inflatable Penile Prosthesis, with the pre-implant experience of patients serving as the comparison for the assessment of device outcome. The design of this clinical study is consistent with the recommendations contained in the Proposed Rule for Premarket Approval of the Penile Inflatable Implant (58 FR 25902), as well as the recommendations of the FDA guidance document entitled "Draft Guidance for Preparation of PMA Applications for Penile Inflatable Implants."

Patients were implanted at 15 institutions in the United States, beginning in August 1996. Initially, the PMA reported the clinical results of 326 patients, which corresponded to a database closure date of May 1, 1999. Although these data are sufficient for the evaluation of the device implantation information and effectiveness results, a more recent database closure date was requested to obtain thorough safety data. As a result, the analyses of adverse events and revision rate are based on a revised database closure date of December 31, 1999, corresponding to 343 implanted patients.

Clinical Endpoints:

Evaluation of the safety and effectiveness of the Mentor Alpha I Inflatable Penile Prosthesis is based on 18-month evaluation of the following clinical endpoints:

Effectiveness:

- Physician measurement of penile rigidity.
- Physician assessment of cosmetic appearance, device function, and ease of use.
- Patient assessment of sexual function (Derogatis Sexual Functioning Inventory Score) and quality of life (Rosenberg Self-Esteem Scale, Medical Outcome Study Instrument, and Extended Satisfaction with Life Scale).

Safety variables:

- Rates of device revision, explantation, and malfunction.
- Incidence of adverse events, including cancer and connective tissue diseases.

Patient Selection:

Adult male patients diagnosed with erectile dysfunction were enrolled into the study. All subjects had decided to be implanted with a Mentor Alpha I Inflatable Penile Prosthesis after having been given information pertaining to alternative therapies for erectile dysfunction, and provided valid informed consent. Exclusion criteria for the study included: patient had an active infection (e.g., UTI) or abscess; patient has uncontrolled or severe diabetes reducing their wound healing ability; patient was HIV positive; patient had health conditions which may prevent successful use of the device; patient had any medical condition contraindicated for penile prosthesis implantation; patient had any prior silicone implant, including a prior penile implant or other urogenital silicone implant; and patient was diagnosed with systemic lupus erythematosus, discoid lupus, or scleroderma. Furthermore, patients who did not speak English were excluded, due to their potential inability to use the survey instruments and adequately understand the informed consent document.

Prior to enrollment, patients received routine clinical assessments to document the presence and etiology of erectile dysfunction. This evaluation included snap-gauge testing and measurement of serum testosterone. After implantation, all study subjects were scheduled for follow-up examinations at 3-6 weeks, 6 months, 1 year, 18 months, 2 years, 3 years, 4 years, and 5 years post-implantation.

Patient Accountability:

Of the 343 patients implanted through December 31, 1999, 164 received 18-month follow-up, 114 were not due for their 18-month follow-up, 55 prematurely discontinued the study prior to 18-month follow-up, and 10 were excluded from the analysis due to device explantation. Reasons for study discontinuation at 18 months are patient moved/lost-to-follow-up/missed visit (n=30); patient refused further follow-up (n=12); investigator discontinued study (n=4); insurance does not cover visits (n=4); death (n=3); and protocol violation/does not meet selection criteria (n=2). The use of 18-month follow-up data for the review of this PMA permits a thorough assessment of device function and adverse events, and also provides preliminary information regarding the rate of revision surgeries. Based on this information, coupled with the concurrence of the Gastroenterology and Urology Devices Advisory Panel at a prior meeting, reliance on 18-month follow-up data is clinically justified.

Demographic Data:

The 343 study patients had a mean age of 61 years, ranging from 25 to 86. The majority of these patients were married.

Over one-third of patients had a significant history of smoking. These patients also had significant medical histories, with 58.2% of patients reporting at least one pre-existing general health problem unrelated to their erectile dysfunction.

Diabetes was present in approximately one quarter of patients enrolled into the study, and was a contributing etiology of erectile dysfunction in 20.2% of the patients. Other etiologies of erectile dysfunction listed for these patients were vascular (67.4%), prostatectomy (15.5%), Peyronie's disease (12.3%), unknown organic cause (10.6%), neurogenic (2.9%), psychogenic (0.6%), and other (7.0%).

The majority of study patients reported a duration of erectile dysfunction of at least 3 years. Approximately two-thirds of patients had tried at least one previous treatment for their erectile dysfunction prior to entering the study.

Although pooling analyses revealed statistically significant differences between the investigational sites in patient age and primary etiology, these differences were judged not to be clinically significant.

Device Implantation/Surgical Information:

Information regarding the device implantation of the Mentor Alpha I Inflatable Penile Prosthesis is based on the cohort of 326 patients implanted through May 1, 1999.

The implanted devices included the typical range of cylinders lengths and reservoir sizes. All Mentor Alpha I Inflatable Penile Prosthesis accessories were used in the trial. The implantation surgeries were predominantly performed on an outpatient basis, with a mean hospitalization duration of 0.7 days. The majority of devices were implanted using either a scrotal approach (61.7%) or an infrapubic approach (38.3%). Nearly all investigators (96.3%) used prophylactic antibiotics prior to and/or during the implantation procedure. Consistent with standard clinical practice, patients typically received either general (56.1%) or spinal (41.4%) anesthesia. A total of 80 patients underwent 84 concurrent surgeries at the time of device implantation, most commonly penile straightening (n=22), circumcision (n=19), and "other" (e.g., penile modeling, incision of penile ligament) (n=41).

A total of 26 operative difficulties were reported (i.e., 14 dilations, 1 bleeding, 1 crural perforation, and 10 "other" difficulties). During the immediate post-operative period, 22 adverse events were reported (i.e., 8 urinary retentions, 6 fevers, 1 bleeding, and 7 "other"). These intra/post-operative complications were considered to be related to the surgical procedure, and none were serious. Overall, a total of 93.1% and 91.4% of patients were free from intra-operative and post-operative complications, respectively.

Authorization to use the device for sexual intercourse was given at the 3-6 week exam in 80.6% of patients. The remaining patients received authorization at a later follow-up exam.

Data Analysis and Results:

Effectiveness Endpoints:

The evaluation of device effectiveness is based on the results of the 326 patients who were implanted with the Mentor Alpha I Inflatable Penile Prosthesis through May 1, 1999. Of these 326 patients, 140 were due for 18-month follow-up, of whom 107 were available for analysis.

The primary effectiveness endpoint for this clinical trial was physician measurement of the rigidity of the fully inflated device at 18-months post-implantation. This assessment consisted of measuring the differences in penile length between (1) 100 g and 550 g axial loads, and (2) 550 g and 650 g axial loads. Insufficient rigidity was defined as a length reduction of greater than 1.5 cm between either sets of loads. This method of evaluating penile rigidity was performed using a standard protocol at all study centers. This objective

assessment is based on data in the literature demonstrating that the penis must withstand a minimum axial load of 500-550 g to successfully achieve sexual intercourse. At the 18-month exam, 99.0% of patients demonstrated adequate penile rigidity with the inflated prosthesis (i.e., penile length reduction ≤ 1.5 cm) when comparing the 100 g and 550 g loads. Of these patients, all continued to demonstrate adequate penile rigidity with the 550 g and 650 g comparison. These results demonstrate that nearly all patients receiving the Mentor Alpha I Inflatable Penile Prosthesis and not explanted during the 18-month follow-up period were capable of achieving adequate penile rigidity for sexual intercourse. The rigidity results obtained at other follow-up exams (i.e., 6, 12, and 24 months) were equivalent to those reported at 18-months, providing further evidence of device effectiveness.

The secondary endpoints of device effectiveness were assessment of patient self esteem, health-related quality of life, extended satisfaction with life, and sexual function. Additionally, information regarding patient satisfaction with the device and physician assessment of device function was obtained. Each of these endpoints was evaluated by patient self-report (except for the physician assessment) using standardized surveys at baseline, 6 months, 1 year, and 18 months. The results of these effectiveness endpoints are individually described below:

Self-Esteem: Patient self-esteem, as measured by the Rosenberg Self-Esteem Scale, was not statistically significantly different between the baseline and 18-month evaluations.

Health-Related Quality of Life: Health-related quality of life, as measured by the Medical Outcomes Study Health Survey (MOS-20), was not statistically significantly reduced from baseline to 18-months evaluations.

Extended Satisfaction with Life: Patient satisfaction with their sex life, self, relationship/marriage, and general life, as measured by the Extended Satisfaction with Life Scale, was statistically significantly improved between the baseline and 18-month evaluations, primarily in the subscale in sex life.

Sexual Function: Patient sexual function, as measured by the Derogatis Sexual Functioning Inventory, was statistically significantly improved from the baseline to 18-month evaluation.

Satisfaction with Device: Patient satisfaction, as rated using a standard set of questions, recorded the following 18-month results: > 80% would recommend the procedure to a friend, > 75% would undergo the procedure again, > 90% stated that they have been able to perform sexual intercourse as, or better than, expected, > 50% indicated that they had intercourse more frequently than before implantation, > 90% are neutral to completely satisfied with the ease of inflation/deflation, > 90% are neutral to completely satisfied with penile girth, > 80% are neutral to completely satisfied with penile length, and > 85% are neutral to completely satisfied with the implant's concealability.

Physician Assessment: Physician assessments of the device, as rated using a standard set of questions, recorded the following 18-month results: 100% of assessments were satisfied with device inflation/deflation, rigidity, symmetry, and flaccidity; > 99% were satisfied with other cosmetic aspects related to the device and its placement; and 99.0% rated penile rigidity sufficient for intercourse.

These results demonstrate that the Mentor Alpha I Inflatable Penile Prosthesis significantly improves patient sexual function and the subscale of sex life, is associated with a high degree of patient satisfaction, and is functional and cosmetically acceptable as rated by the

physician. As anticipated, no decrease in patient self-esteem or health-related quality of life was observed.

Safety Endpoints:

The evaluation of device safety is based on the results of the 343 patients who were implanted with the Mentor Alpha I Inflatable Penile Prosthesis through December 31, 1999.

The primary safety endpoint for this clinical trial was assessment of the rate of revision surgeries at 18-months post-implantation. A revision was defined as any urogenital surgical intervention after device implantation. In all, a total of 34 patients experienced a revision surgery during the study period. Of these 34 revision cases, 17 were device explantations, 5 were device repair surgeries, and 12 were "other surgeries" that did not involve explantation or repair of the device (e.g., circumcision, inguinal hernia repair). Using a Kaplan-Meier Survival Analysis, the probability of a patient being free of a revision at 18 months was 88.5% (lower bound of 95% confidence interval = 84.5%). Similarly, the probability of a patient being free of device explantation at 18 months was 94.6% (lower bound of 95% confidence interval = 91.9%). Based upon information provided by the applicant, these rates of revision and explantation are consistent with those reported in the published literature for inflatable penile prostheses.

The majority of revision surgeries (31/34; 91.2%) occurred within 18 months post-implantation, over half (17/31; 54.8%) of which occurred in the first 6 months. The reasons reported for the 17 explantation surgeries were as follows: infection (n=6), autoinflation (n=3), cylinder aneurysm (n=2), chronic pain (n=2), split tubing/fluid loss (n=2), cylinder erosion (n=1), and inability to inflate (n=1). The reasons for the five device repair surgeries were: erosion with or without Gortex sock placement (n=2), autoinflation (n=1), split tubing (n=1), and excessive scar tissue formation (n=1). As stated above, the reasons for the 12 "other surgeries" were varied, and were unrelated to device function.

Although 99% of devices evaluated at the 18-month evaluation provided sufficient rigidity for intercourse (described under "Effectiveness Endpoints"), investigators reported a total of 16 "mechanical malfunctions" in 15 patients during the study period. These events included 6 reports of autoinflation, 5 reports of cylinder aneurysm/dilation, 3 reports of fluid loss/split tubing, 1 report of reservoir herniation, and 1 report of inability to inflate. These 16 cases of mechanical malfunction required surgical correction in 10 cases, non-surgical treatment in 3 cases, and no treatment in 3 cases.

The secondary device safety endpoint was assessment of all adverse events recorded from the day of surgery through the 18-month follow-up exam. Table 1 summarizes the adverse events reported during the clinical study.

**Table 1 – ADVERSE EVENTS: Incidence and Onset
(n=343 patients)**

Adverse Event Category	Number (%) of Patients	Mean (Range) Onset Time in Days
Scrotal swelling	42 (12.2%)	27 (0-543)
Autoinflation	38 (11.1%)	112 (4-584)
Discomfort	37 (10.8%)	32 (0-322)
Angulation/curvature	19 (5.5%)	87 (0-329)
Edema	17 (5.0%)	36 (0-239)
Device malfunction	15 (4.4%)	214 (7-1096)
Chronic pain	11 (3.2%)	69 (1-248)
Difficulty with ejaculation	11 (3.2%)	274 (8-743)
Transient urinary retention	11 (3.2%)	1 (0-6)
Fever	10 (2.9%)	22 (0-167)
Migration	10 (2.9%)	140 (24-365)
Patient dissatisfaction	10 (2.9%)	174 (38-789)
Infection - site	10 (2.9%)	112 (38-248)
Deflation	9 (2.6%)	157 (29-431)
Hematoma/seroma	8 (2.3%)	3 (0-11)
Wound leakage	7 (2.0%)	37 (0-167)
Bleeding	5 (1.5%)	221 (0-608)
Delayed wound healing	5 (1.5%)	59 (6-184)
Phimosis	5 (1.5%)	197 (2-635)
Sensory loss	5 (1.5%)	221 (34-557)
Cylinder aneurysm	4 (1.2%)	339 (101-667)
Fibrous capsule formation	4 (1.2%)	103 (28-169)
Over/under inflation	4 (1.2%)	91 (41-183)
Erosion	3 (0.9%)	39 (6-59)
Scrotal erythema	3 (0.9%)	67 (5-183)
Genital change	2 (0.6%)	272 (89-454)
Infection – wound	2 (0.6%)	106 (28-184)
Inguinal hernia	2 (0.6%)	458 (370-546)
Other device-related events	55 (16.0%)	N/A

The following 55 "other device-related events" were reported during the study: hematuria (n=5), difficulty voiding (n=3), reduced penile length (n=3), nausea (n=2), slow urinary stream (n=2), urgency (n=2), adhesion at pump (n=1), allergic reaction to contract medium (n=1), corporal rupture (n=1), cylinder buckling (n=1), cystitis (n=1), deformity (n=1), difficulty working pump (n=1), difficulty working prosthesis (n=1), drainage from incision (n=1), drug reaction (n=1), dysuria (n=1), extrusion (n=1), fluid loss (n=1), hematospermia (n=1), iliac vein injury (n=1), incontinence (n=1), induration (n=1), inflamed glans (n=1), lymphadenopathy (n=1), mild redness (n=1), pain with intercourse (n=1), popped suture (n=1), pump hardness (n=1), pump stuck in scrotum (n=1), rash (n=1), scar tissue formation (n=1), scrotal abscess (n=1), scrotal discomfort/redness (n=1), scrotal heaviness (n=1), SST deformity (n=1), suture sticking out (n=1), testicular pain (n=1), ulceration (n=1), urethroscrotal fistula (n=1), urge incontinence (n=1), urinary frequency (n=1), UTI (n=1), and ventral chordee (n=1).

With the exception of the complications that led to revision surgery (described earlier), all device-related complications either resolved or were judged by the patient not to require further treatment. The complication rates observed in this study are consistent with those reported in the literature for inflatable penile prostheses.

The following events occurred during the clinical study but were judged by the investigators not to be related to the device or the implantation surgery: cardiovascular disease/surgery (n=18), cancer (n=11), arthritis/joint pain (n=7), hypertension (n=7), incontinence (n=7), angina/chest pain (n=6), flu/cold (n=6), back pain/injury (n=5), BPH (n=5), ophthalmic surgery (n=4), prostatitis (n=4), sinus infection (n=4), upper respiratory infection (n=4), bladder neck contracture (n=3), dermatophyte (n=3), diabetes (n=3), pneumonia (n=3), rising PSA (n=3), skin lesion (n=3), urinary frequency (n=3), abdominal pain (n=2), allergy to drug (n=2), back surgery (n=2), bladder stones (n=2), chest congestion (n=2), cholecystectomy (n=2), constipation (n=2), cyst at joint (n=2), depression (n=2), diarrhea (n=2), difficult/slow urination (n=2), gastric ulcer (n=2), gout (n=2), leg/foot edema (n=2), Parkinson's disease (n=2), peripheral neuropathy (n=2), renal cyst (n=2), swollen joint (n=2), urethral stricture (n=2), anemia (n=1), anxiety (n=1), asthma (n=1), bronchitis (n=1), bladder injury (n=1), bladder lesion (n=1), blood clot (n=1), breast mass (n=1), chondyloma (n=1), cyst on back (n=1), detached retina (n=1), diabetic toe infection (n=1), dissatisfaction (n=1), diverticulitis (n=1), dry skin (n=1), dyspnea (n=1), epididymitis (n=1), enlarged spleen (n=1), esophageal reflux (n=1), extended hospitalization (n=1), fatigue (n=1), folliculitis (n=1), foot muscle tear (n=1), foot pain (n=1), GI infection (n=1), growth in mouth (n=1), growth on eyelid (n=1), hematuria (n=1), herpes (n=1), hydrocele (n=1), indigestion (n=1), ingrown toenail (n=1), knee surgery (n=1), leg injury (n=1), lipoma (n=1), low platelet count (n=1), lump on neck (n=1), nausea (n=1), nocturia (n=1), orchitis (n=1), paralysis (n=1), penile warts (n=1), peripheral vascular surgery (n=1), phlebitis in arm (n=1), prostatectomy (n=1), pulled muscle (n=1), rash (n=1), respiratory difficulty (n=1), sickle cell complications (n=1), shoulder injury (n=1), sleep apnea (n=1), snoring (n=1), sore throat (n=1), stomach problems (n=1), stroke (n=1), suprapubic pain (n=1), tendonitis (n=1), tetanus (n=1), tonsillectomy (n=1), TURP (n=1), urgency (n=1), urosepsis (n=1), UTI (n=1), vertigo (n=1), and wrist surgery (n=1).

The following risks of inflatable penile implants or their materials have been reported in the medical literature but did not occur during the prospective study: adhesions requiring lysis, gangrene, granuloma formation, immune-related connective tissue disorders, ischemia, necrosis, perforation, vascular compromise, and ventral band formation.

There were five patient deaths during the course of the study period. None of these deaths were attributed to the device or the implantation surgery.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Preclinical testing of the Mentor Alpha I Inflatable Penile Prosthesis adequately characterized the device's materials, demonstrated that the materials of this device are biocompatible, and verified that the device is mechanically reliable.

Clinical testing of the device demonstrated that the Mentor Alpha I Inflatable Penile Prosthesis is safe and effective. Specifically, the results of clinical testing demonstrated that the device:

- provided sufficient penile rigidity for sexual intercourse in 99% of patients at the 18-month follow-up examination;
- resulted in a significant improvement in sexual function (using the Derogatis Sexual Function Inventory) and the domain of sex life (of the Extended Satisfaction with Life Scale) at 18 months, as compared to baseline;
- was not associated with a decrease in self-esteem or health-related quality of life at 18 months, as compared to baseline;
- was associated with a high degree of patient satisfaction, and was subjectively rated by the physician as functional and cosmetically acceptable in nearly all cases;
- had 18-month surgical revision and device explantation rates that are consistent with those reported in the literature for penile inflatable prostheses; and

- was associated with a risk profile that is consistent with that reported in the literature for penile inflatable prostheses.

Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

XII. PANEL RECOMMENDATION

Pursuant to section 515(c)(2) of the Food, Drug, and Cosmetic Act (the act) as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

Based upon the PMA review, CDRH believes that these data provide reasonable assurance that the device is safe and effective when used as indicated in accordance with the directions for use. Therefore, CDRH believes that the Mentor Alpha I Inflatable Penile Prosthesis can be approved with the following postapproval requirement: continued follow-up of a minimum of 125 patients out to 5 years post-implantation, consistent with the existing protocol, for assessment of device function and adverse events.

The applicant's manufacturing facility was inspected on May 25, 1999, and was found to be in compliance with the device Quality Systems regulations.

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the labeling (attached).

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.