Summary of Safety and Effectiveness Data

ANCURE® Aortoiliac System

Guidant Corporation

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Summary of Safety and Effectiveness Data

ANCURE® Aortoiliac System

Guidant Corporation

1. General Information

Device Generic Name:.....Endovascular Aortoiliac Grafting System

Device Trade Name:.....ANCURE® Aortoiliac System

Applicant's Name and Address:.....Guidant Corporation
1525 O'Brien Drive
Menlo Park, CA 94025

PMA Application Number:.....P990017/S30

Date of Notice of Approval to the Applicant..... April 24, 2002

2. Indications and Usage

The ANCURE Aortoiliac System is indicated for the endovascular treatment of infrarenal abdominal aortic aneurysms or aortoiliac aneurysms (AAA) in patients whose anatomy does not allow the use of a tube or bifurcated device and having:

- adequate iliac/femoral access,
- infrarenal non-aneurysmal neck length of at least 15 mm and a diameter of no greater than 26 mm,
- one distal segment length of at least 20 mm and diameters no greater than 13.4 mm, and
- morphology suitable for endovascular repair.

3. Contraindications

There are no identified contraindications for this device.

4. Warnings and Precautions

See Final Draft Labeling

5. Device Description

The ANCURE Aortoiliac System consists of a graft, which is housed within a delivery catheter. The ANCURE Aortoiliac configuration contains a graft with a single iliac limb segment. The graft is a woven polyester vascular graft with attachment systems affixed to the ends. Each attachment system consists of angled metal attachment hooks and a self-expanding cylindrical metal frame. The attachment systems create an anastomosis between the graft and the vessel wall. Radiopaque markers on the graft assist with the visualization under fluoroscopy. The attachment systems and radiopaque markers are made from metallic alloys.

An earlier version of the ANCURE System, called the EGS System, was used in the clinical trial to support this submission. The EGS and ANCURE grafts are identical except that the aortoiliac ANCURE grafts have suture loops on the superior and inferior attachment systems. These suture loops on the outside of the graft accommodate the deployment mechanism of the ANCURE delivery catheter. In addition, the fuzzy polyester tufts on the superior and inferior ends of the graft which are used to promote attachment site healing were moved slightly closer to the ANCURE graft ends and cut slightly shorter. Pre-clinical testing was used to qualify the new graft design.

The delivery catheter houses the compressed graft and is used to deploy the graft. The delivery catheter consists of 1) a multi-lumen balloon catheter that is used to guide the device over a guidewire and secure the attachment system, 2) a deployment system that controls deployment of the attachment systems, and 3) a jacket that houses the compressed graft. See Figures 1 and 2 for depictions of the ANCURE delivery catheter.

The aortoiliac graft is provided in a range of lengths and diameters to accommodate variations in patient anatomy. Table 1 lists the sizes and model numbers available for the Aortoiliac Endograft prosthesis sizes.

Figure 1. ANCURE Delivery Catheter Handle

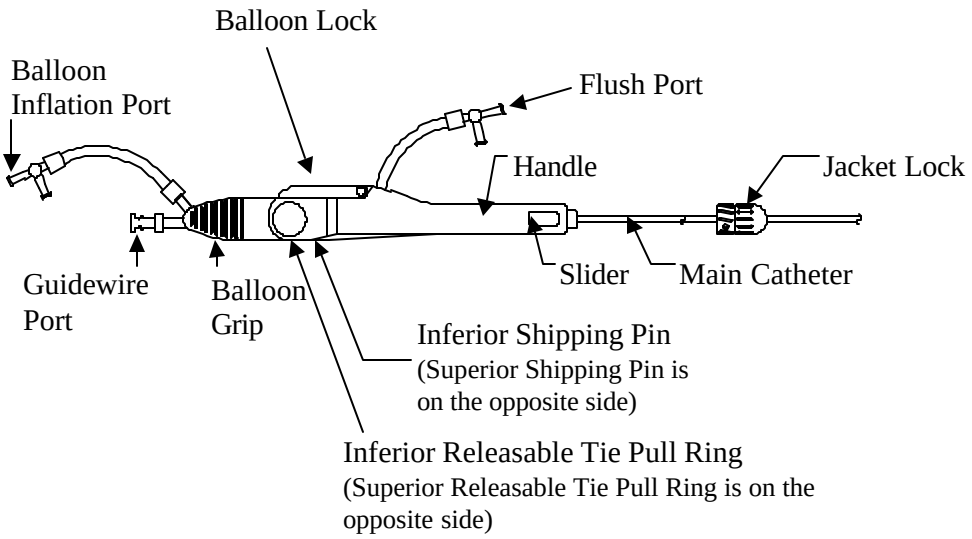

Figure 2. ANCURE Aortoiliac Delivery System

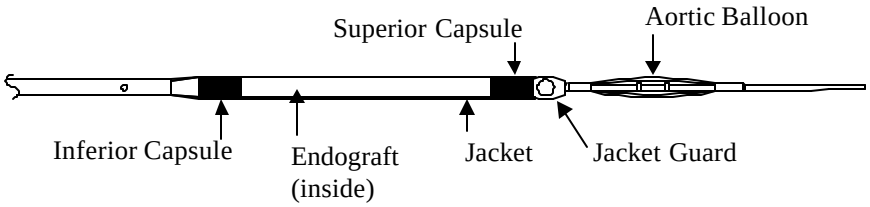

Figure 3. Illustration of ANCURE Aortoiliac Delivery System

Table 1. ANCURE Aortoiliac System Model Numbers

DESCRIPTION	MODEL NUMBER	SIZE
AORTOILIAC	01201210	20 mm X 12.0 cm
AORTOILIAC	01201310	20 mm X 13.0 cm
AORTOILIAC	01201410	20 mm X 14.0 cm
AORTOILIAC	01201510	20 mm X 15.0 cm
AORTOILIAC	01201610	20 mm X 16.0 cm
AORTOILIAC	01201710	20 mm X 17.0 cm
AORTOILIAC	01201810	20 mm X 18.0 cm
AORTOILIAC	01201910	20 mm X 19.0 cm
AORTOILIAC	01202010	20 mm X 20.0 cm
AORTOILIAC	01202110	20 mm X 21.0 cm
AORTOILIAC	01202210	20 mm X 22.0 cm
AORTOILIAC	01202310	20 mm X 23.0 cm
AORTOILIAC	01202410	20 mm X 24.0 cm
AORTOILIAC	01202510	20 mm X 25.0 cm
AORTOILIAC	01221211	22 mm X 12.0 cm
AORTOILIAC	01221311	22 mm X 13.0 cm
AORTOILIAC	01221411	22 mm X 14.0 cm
AORTOILIAC	01221511	22 mm X 15.0 cm
AORTOILIAC	01221611	22 mm X 16.0 cm
AORTOILIAC	01221711	22 mm X 17.0 cm
AORTOILIAC	01221811	22 mm X 18.0 cm
AORTOILIAC	01221911	22 mm X 19.0 cm
AORTOILIAC	01222011	22 mm X 20.0 cm
AORTOILIAC	01222111	22 mm X 21.0 cm
AORTOILIAC	01222211	22 mm X 22.0 cm
AORTOILIAC	01222311	22 mm X 23.0 cm
AORTOILIAC	01222411	22 mm X 24.0 cm
AORTOILIAC	01222511	22 mm X 25.0 cm

DESCRIPTION	MODEL NUMBER	SIZE
AORTOILIAC	01241212	24 mm X 12.0 cm
AORTOILIAC	01241312	24 mm X 13.0 cm
AORTOILIAC	01241412	24 mm X 14.0 cm
AORTOILIAC	01241512	24 mm X 15.0 cm
AORTOILIAC	01241612	24 mm X 16.0 cm
AORTOILIAC	01241712	24 mm X 17.0 cm
AORTOILIAC	01241812	24 mm X 18.0 cm
AORTOILIAC	01241912	24 mm X 19.0 cm
AORTOILIAC	01242012	24 mm X 20.0 cm
AORTOILIAC	01242112	24 mm X 21.0 cm
AORTOILIAC	01242212	24 mm X 22.0 cm
AORTOILIAC	01242312	24 mm X 23.0 cm
AORTOILIAC	01242412	24 mm X 24.0 cm
AORTOILIAC	01242512	24 mm X 25.0 cm
AORTOILIAC	01261213	26 mm X 12.0 cm
AORTOILIAC	01261313	26 mm X 13.0 cm
AORTOILIAC	01261413	26 mm X 14.0 cm
AORTOILIAC	01261513	26 mm X 15.0 cm
AORTOILIAC	01261613	26 mm X 16.0 cm
AORTOILIAC	01261713	26 mm X 17.0 cm
AORTOILIAC	01261813	26 mm X 18.0 cm
AORTOILIAC	01261913	26 mm X 19.0 cm
AORTOILIAC	01262013	26 mm X 20.0 cm
AORTOILIAC	01262113	26 mm X 21.0 cm
AORTOILIAC	01262213	26 mm X 22.0 cm
AORTOILIAC	01262313	26 mm X 23.0 cm
AORTOILIAC	01262413	26 mm X 24.0 cm
AORTOILIAC	01262513	26 mm X 25.0 cm

6. Alternative Practices or Procedures

Currently, the most widely accepted treatment for AAA repair is surgical repair utilizing aneurysmorrhaphy and prosthetic graft interposition through a transperitoneal or retroperitoneal incision.

7. Marketing History

The ANCURE Aortoiliac System has been commercially available in Sweden, France, Australia, Belgium, Greece, Canada, Austria, Spain, United Kingdom, Netherlands, Italy, Germany, Switzerland, Finland, and Israel.

8. Adverse Events

8.1 Observed Adverse Events

A total of 232 patients were enrolled in the EGS clinical study (121 aortoiliac and 111 surgical control). Adverse event data from this study are summarized in alphabetical order in Tables 2 and 3.

In the EGS clinical study, the operative mortality rate was less than five percent in both treatment groups (4.2 % aortoiliac and 2.7% control subjects; not statistically significantly different). In the aortoiliac clinical study, five operative deaths occurred. The 5 operative (defined as < 30 days) deaths are all aortoiliac EGS subjects, 4/5 were male. The causes of the 5 aortoiliac operative deaths are: cardio-respirator failure with pulmonary hypertension (died prior to discharge), exsanguination (died intra-op), cardiac arrest (died 4 days post-discharge), arrhythmia (died prior to discharge), and tension pneumothorax (female subject, died prior to discharge).

In the aortoiliac clinical study, nine late deaths (defined as < 1 year and > 30 days) occurred. Of these nine late deaths, four were cardiac related, three were respiratory related, one was the result of stroke and one was the result of cancer.

Table 2. Adverse Events £ 30 days (Listed Alphabetically)

Event	Aortoiliac [1]		Surgical Control [2]	
	%	(n/N)	%	(n/N)
Deaths – Operative	4.2%	(5/118)	2.7%	(3/111)
Other Adverse Events				
Arterial Trauma	9.3%	(11/118)	0.0%	(0/111)
Bleeding	15.3%	(18/118)	39.6%	(44/111)
Bowel	5.9%	(7/118)	8.1%	(9/111)
Cardiac	22.0%	(26/118)	20.7%	(23/111)
Coagulopathy	1.7%	(2/118)	4.5%	(5/111)
Conversions[3] / Cases Aborted	5.8%	(7/121)	N/A	
Deep Vein Thrombosis	1.7%	(2/118)	0.9%	(1/111)
Embolism – Lower Extremity Ischemia	1.7%	(2/118)	0.9%	(1/111)
Hematoma	8.5%	(10/118)	1.8%	(2/111)
Impotence	0.0%	(0/118)	1.8%	(2/111)
Paraplegia/Paraparesis	0.8%	(1/118)	0.0%	(0/111)
Perigraft Flow, Discharge	51.8%	(58/112)	N/A	
Prosthetic Thrombosis	1.7%	(2/118)	0.0%	(0/111)
Reduced Limb Flow [4]	28.3%	(32/113)	N/A	
Renal Insufficiency	6.8%	(8/118)	1.8%	(2/111)
Respiratory	11.9%	(14/118)	22.5%	(25/111)
Stroke	0.8%	(1/118)	0.9%	(1/111)
TIA	0.8%	(1/118)	0.0%	(0/111)
Wound	7.6%	(9/118)	1.8%	(2/111)

1. Of the total 121 aortoiliac subjects, three discontinued their participation at discharge and were alive at that time. These subjects are included in the analysis only through surgical implantation.
2. 94 of the Control subjects were tube subjects and 17 were bifurcated subjects.
3. Three aortoiliac subjects had the treatment abandoned without conversion to open repair.
4. These analyses included only implanted patients.

Table 3. Adverse Events at 12 months (Listed Alphabetically) [1]

Event	Aortoiliac (%)	Surgical Control [2] (%)
Deaths	11.9%	5.4%
Other Adverse Events		
Arterial Trauma	10.2%	1.0%
Bleeding	16.1%	39.6%
Bowel	6.8%	11.0%
Cardiac	38.1%	24.6%
Graft Migration [3]	0.0%	N/A
Perigraft Flow [3]	33.0%	N/A
Renal Insufficiency	8.5%	1.8%
Respiratory	19.5%	24.3%
Wound	9.3%	1.9%

1. Event rates are based on Kaplan Meier methodology.
2. 94 of the Control subjects were tube subjects and 17 were bifurcated subjects.
3. These events were assessed at discrete time points (discharge, 6 mos., 12 mos.), therefore Kaplan Meier estimates of the rates were not performed.

8.2 Potential Adverse Events

The following adverse events (in alphabetical order) may be associated with endovascular AAA repair:

Table 4. Potential Adverse Events

Acute myocardial infarction
Amputation
Anastomotic false aneurysm
Aneurysm rupture
Arrhythmias
Arterial trauma/dissection
Attachment system fractures
Bleeding, requiring transfusion
Bowel ischemia/bowel obstruction/adynamic ileus
Claudication
Coagulopathy
Congestive heart failure
Conversion to standard AAA surgery
Death
Deep vein thrombosis
Drug reactions to antiplatelet agents/contrast medium
Emboli, distal (air, tissue or thrombotic emboli)
Femorofemoral thrombosis
Fistula (aortoenteric, aortocaval)
Graft dilatation
Graft migration
Hypotension/Hypertension
Impotence
Infection and pain at insertion site
Infection
Lymphatic complications
Paraplegia/paraparesis
Perforation
Perigraft flow
Prosthesis extrusion/erosion
Prosthetic infection
Pulmonary embolism
Reduced limb flow
Renal insufficiency/failure
Respiratory failure/atelectasis/pneumonia
Spasm
Stroke/cerebrovascular event
TIA
Thrombosis/occlusion of graft
Wound dehiscence

Hematoma

9. Summary of Pre-Clinical Studies

9.1 Laboratory Studies

The ANCURE System (and the earlier version, the EGS System) was subjected to a pre-clinical testing program in accordance with the FDA draft "Guidance for the Preparation of Research and Marketing Applications for Vascular Graft Prostheses." All test samples were prepared in the same manner as intended for clinical usage.

9.1.1 Biocompatibility, Immunology, and Toxicology Studies

Toxicity and biocompatibility studies were conducted for all graft and delivery catheter materials. The testing was conducted in accordance with Good Laboratory Practices per 21CFR 58 and ISO 10993. The grafts were classified by ISO 10993 as implant devices, blood contact, C - long-term. The delivery catheter was classified as an externally communicating device with circulating blood contact and limited exposure of less than 24 hours. The results as shown in Table 5 support the biocompatibility of the Aortoiliac device for its intended uses.

Table 5. Biocompatibility, Immunology, and Toxicology Studies

Test Performed	Extract(s)	Findings
Ames Salmonella/ Mammalian Microsome Mutagenicity Assay	0.9% USP Sodium Chloride for injection and DMSO extracts	Material is non-mutagenic.
Sister Chromatid Exchange	McCoy's 5A medium	Material is non-genotoxic.
Chromosomal Aberration	McCoy's 5A medium	Material is non-genotoxic.
In Vitro Hemolysis	0.9% Sodium Chloride USP	Material is non-hemolytic.
C3a Complement Activation	Normal Human Serum, NHS, certified HIV (1 & 2) and Hepatitis (B & C) negative	Test article represented activation at 18,472 ng/ml. The materials performed as anticipated.
Determination of Clotting Time using the Lee-White Method	Canis familiaris blood	Material did not have a significant effect on clotting time.
Cytotoxicity	Single strength MEM supplemented with 5% calf serum and 2% antibiotics	Material showed no evidence of cell lysis or toxicity to L-929 mouse fibroblast cells. The material was non-cytotoxic.
Acute Intracutaneous Reactivity Study in the Rabbit	0.9% Sodium Chloride USP Solution and Cottonseed Oil	The Primary Irritation Index Characterization was negligible. There was no evidence of significant irritation or toxicity.
Magnusson and Kligman Method Delayed Contact Sensitization Study in the Guinea Pig, Maximization	0.9% Sodium Chloride USP Solution and Cottonseed Oil	There was no evidence of causing delayed dermal contact sensitization in the guinea pig.

Test Performed	Extract(s)	Findings
Magnusson and Kligman Method Delayed Contact Sensitization Study in the Guinea Pig, Maximization Method (Positive Control)	1-Chloro -2,4-Dinitrobenzene (DNCB)	The known sensitizer DNCB showed significant evidence of causing delayed dermal contact sensitization.
Rabbit Pyrogen	0.9% Sodium Chloride USP Solution	Material is non-pyrogenic.
USP Systemic Toxicity Study in the Mouse	0.9% Sodium Chloride USP Solution and Cottonseed Oil, NF (CSO)	There was no evidence of significant systemic toxicity.
Sub-Chronic (14 days) Intravenous Toxicity Study in the Rat	0.9% Sodium Chloride USP Solution	There was no evidence of significant systemic toxicity
Muscle Implantation Study in the rabbit with Histopathology (surgical method 13 weeks)	N/A	There was no evidence if material toxicity in the surrounding animal tissues.

9.1.2 Graft Mechanical Testing

Although there are no specific applicable standards for endovascular aortoiliac grafts, mechanical tests were conducted on the EndoWeave-65 tube graft, as representative of the aortoiliac graft. Two sources for the EndoWeave-65 material were qualified. A summary of the mechanical testing conducted is presented in Table 6. The data demonstrates the mechanical properties of the graft are suitable for its intended use and are within manufacturing capabilities.

Table 6. Graft Mechanical Testing Summary

Attribute	Source A EndoWeave-65 Graft Material	Source B EndoWeave-65 Graft Material	Guidant Specification (EndoWeave-65)
Water Permeability ($ml/cm^2/min$)	Avg: 177 S.D.: 30.8	Avg.: 186 S.D.: 39.8	Average must be between 50 and 300 $ml/cm^2/min$
Modified Tensile Strength (lbs.)	Avg: 112.0 S.D.: 6.91	Avg.: 112.5 S.D.: 6.27	Average must be $\geq$95 lbs.
Balloon Burst Strength (Hoop Stress) (p.s.i.)	Avg: 9573 S.D.: 557	Avg.: 10199 S.D.: 665	$\geq$5732 PSI
Compliance (%)	Avg: 0.0100 S.D.: 0.00145	Avg .: 0.0088 S.D.: 0.00121	0.00 – 0.03%
Longitudinal Tensile Strength (lb./inch)	Avg: 86.1 S.D.: 3.02	Avg.: 84.5 S.D.: 18.35	$\geq$60 lb./in
Suture Retention Strength (grams-force)	Avg: 1682 S.D.: 366	Avg.: 2243 S.D.: 166	$\geq$800 grams-force
Suture Hole Elongation (inches)	Avg: 0.006” S.D.: 0.0038	Avg.: 0.009” S.D.: 0.0038	$\leq$0.039”
Kink Radius (inches)	Avg. Limbs: 0.234” S.D.: 0.010	Avg. Limbs: 0.235” S.D.: 0.005	<0.65”

Crush Resistance (grams)	Avg. Limbs: 52.5 S.D.: 2.5	Avg. Limbs: 78.3 S.D.: 12.5	≥50 grams-force
Usable Length (% elongation)	Avg. (100mm Hg): 18.6% S.D.: 3.60 Avg. (full): 22.3% S.D.: 3.28%	Avg. (100mm Hg):15.9% S.D.: 2.0% Avg. (full): 22.1% S.D.: 2.5%	8 – 20% at 100mm Hg 20 – 27% at full elongation

9.1.3 Graft Durability Testing

Objective: Testing was conducted on the EndoWeave-65 graft material to evaluate its mechanical integrity.

Methods: Testing was completed on graft material samples to an equivalent of 10 years or 400 million cycles. A cycle is considered a simulation of pulsatile blood flow. A modified tensile test was performed on one sample each following 100 million, 200 million, 300 million and 400 million cycles. Following cycling, the samples were cut into two pieces and pulled to failure.

Results: Durability results are shown in Table 7.

Table 7. Graft Durability Testing Summary

Peak Tensile Force (lbf) after 100 Million Cycles (n=2)	Peak Tensile Force (lbf) after 200 Million Cycles (n=2)	Peak Tensile Force (lbf) after 300 Million Cycles (n=2)	Peak Tensile Force (lbf) after 400 Million Cycles (n=2)
113.2 ± 2.33	99.3 ± 7.92	102 ± 1.06	81.83 ± 16.65

Theoretical burst strength was calculated from the tensile force data. After the equivalent of 10 years *in vivo* the EndoWeave-65 graft material exhibited a theoretical burst strength of 106.5 psi, which far exceeds the estimated *in vivo* loads of 2 – 5 psi. The compliance of the Endo-Weave-65 graft material before and after 400 million cycles was 0.0100% and 0.0083%, respectively.

Conclusions: These data indicate the EndoWeave-65 graft material has sufficient strength and compliance for its intended use throughout its intended lifetime.

9.1.4 Aortoiliac Graft Attachment System Studies

9.1.4.1 Estimation of In vivo Loads

Although there are no specific applicable standards for endovascular aortoiliac grafts, three estimation methods (clinical extrapolation, a flow model, and a fluid mechanics model) were used to model the aortoiliac graft *in vivo* axial loads. Aortic axial loads experienced in an aortoiliac graft were found to be similar to axial loads in the tube and bifurcated grafts.

The iliac attachment system mean diameter *in vivo* was determined for all sizes of graft diameters. Radial loads were estimated based on the cyclic diameter change experienced by the iliac arteries. The *in vivo* mean diameters and cyclic diameter changes were used in combination with finite element analysis to determine the *in vivo* mean and alternating stresses of the aortic and iliac attachment systems due to arterial diameter change loading.

9.1.4.2 Finite Element Analysis

Results from the finite element analysis for the tube EGS graft attachment system were used to represent the aortoiliac EGS graft aortic attachment system frame, since the aortic end of the aortoiliac EGS graft attachment system is identical to that of the tube EGS graft attachment system. A finite element analysis was used to estimate the *in vivo* stresses of the aortoiliac EGS V-hooks. The V-hook model showed stress as linearly proportional to the attachment system diameter change over the *in vivo* diameter range. Stresses were dominated by bending stresses. Axial and torsional stresses were low.

Finite element analysis was used to estimate the *in vivo* mean and alternating stresses of the attachment system frame and V-hook. Two analyses were conducted on the bifurcated EGS graft iliac attachment system to estimate hook stresses using elastic finite element analysis. The results from these tests were used to represent the aortoiliac EGS graft, since the iliac attachment systems for these two devices are identical. In the first analysis, the iliac attachment system frame stresses were estimated using a radially loaded model that was compressed from a 15mm-free diameter to the estimated *in vivo* systolic and diastolic diameters. A second analysis was conducted to estimate hook stresses using a radially and axially loaded model that was compressed from a 15mm-free diameter to the estimated *in vivo* systolic and diastolic changes. The results for both analyses showed that stresses are linearly proportional to attachment system diameter changes over the *in vivo* diameter range. Stresses were dominated by bending stresses. Axial and torsional stresses were low. A similar analysis was performed on each diameter for iliac attachment systems yielding similar results.

9.1.4.3 Fatigue Testing

The estimated *in vivo* mean and alternating stresses and R-ratios in the aortic attachment systems and V-hooks for the tube graft attachment systems were utilized to represent the aortoiliac graft aortic attachment system frame and V-hooks, with one exception. While the V-hook design on the aortoiliac graft is identical to the tube design, the estimated *in vivo* stress for the aortoiliac V-hook tip is slightly higher. A fatigue test was therefore conducted on the aortoiliac V-hook. These data were used in estimating fatigue life using the Goodman fatigue diagrams.

Table 8. Aortoiliac Attachment System Fatigue Analyses

Test Performed	Methods	Findings
Fatigue lifetime of the iliac attachment system hook tip bend	Estimations by plotting alternating load versus cycles to failure at several different loads. Results were extrapolated from a fatigue curve and compared to the *in vivo* force.	The iliac hook tip bend was determined to meet the product requirement of a 15-year *in vivo* lifetime.

Test Performed	Methods	Findings
In vivo life of the iliac frame apex	Estimated using cyclic displacement loading applied to test specimens representing the iliac attachment frame apex in a corrosive environment. A fatigue curve was generated.	The iliac frame apex was determined to meet the product requirement of a 15-year *in vivo* lifetime.
In vivo life of the iliac hook weld	Estimated using cyclic displacement loading applied to test specimens representing the iliac attachment frame hook weld in a corrosive environment at three different test conditions. A fatigue curve was generated.	The iliac hook weld was determined to meet the product requirement of a 15-year *in vivo* lifetime.
Fatigue of aortic frame closure weld	Cyclic displacement at different loading was applied to test specimens in a corrosive environment using Cantilever Beam Equipment. Results were extrapolated to long term *in vivo* lifetimes.	The aortic frame closure weld was determined to meet the product criteria of a 15-year *in vivo* lifetime.
Fatigue of iliac frame closure weld	Cyclic displacement at different loading was applied to test specimens in a corrosive environment using Cantilever Beam Equipment. Results were extrapolated to long term *in vivo* lifetimes.	The iliac frame closure weld was determined to meet the product criteria of a 15-year *in vivo* lifetime.

9.1.5 Delivery System Mechanical Testing

Mechanical joint and component testing was conducted on the ANCURE delivery catheter. Deflation rate and burst testing was conducted for the balloon and balloon catheter components of the delivery catheter. The maximum anticipated *in vivo* loads for the delivery catheter was estimated and used as conservative design criteria for mechanical testing. The early estimates were found to be appropriate during the clinical trials.

All of the bonded joints and engagements were tested for the ANCURE delivery catheter. All results indicated that at a 95% confidence level that 99.9% of the bonded strength joints were greater than the expected maximum *in vivo* forces. The burst strength of the balloons was determined to be at least 51 psi, which compared favorably with the rated burst pressure of 30 psi.

9.2 Animal Studies

A series of animal studies were conducted to evaluate the tube, bifurcated and aortoiliac EGS and ANCURE Systems. Both EGS and ANCURE animal data are presented since the EGS and ANCURE grafts are nearly identical in design making both relevant to an evaluation of the ANCURE graft.

Table 9. Animal Studies Summary

Animal Study	No./Type Animals Studied	Test Article	Methods	Results/Conclusions
Acute and Chronic Study of Tube Graft	19 sheep	Scaled-down tube EGS system consisting of a delivery catheter with a helically wound, longitudinal flexible capsule containing the compressed graft.	Five animals each implanted for periods of 1, 2, and 6 months, at which time they were sacrificed. Four additional animals were later added to 6-month group. Implant sites were evaluated macro and microscopically.	All grafts successfully deployed. Grafts remained patent with no evidence of thrombosis, migration, twist, or compression. All animals displayed morphologic evidence of normal graft healing.
Acute Healing Study of Bifurcated Graft	15 bovine	Full-scale EGS delivery catheters & EGS bifurcated graft.	Fifteen animals assessed for delivery catheter deployment & acute implantation. Chronic evaluation was planned but terminated early due to animal model difficulties resulting from bovine vasculature. See next study for chronic healing.	Excellent acute results of the delivery catheter and graft. All grafts were patent.
Chronic Healing Study of Bifurcated Graft	7 sheep	Iliac portion of bifurcated EGS graft	Two animals implanted with the bifurcated graft with a shortened contralateral limb. Five animals were implanted bilaterally with a short tube with iliac attachment system using modified delivery catheters.	Acute implantation was successful in all animals. All grafts were patent with good distal perfusion. There were no signs of twisting, migration, kinks or longitudinal compression. Healing was normal and similar to those found in sheep at one month.
Acute Evaluation of the Aortoiliac EGS System	3 bovine	Aortoiliac EGS delivery catheter and aortoiliac EGS graft	Animals implanted with aortoiliac EGS graft. Following implantation each animal was sacrificed and a necropsy of the graft was performed.	Acute implantation successful with unobstructed flow through the graft. While the catheters performed flawlessly, some refinements were later incorporated to the jacket lock and inferior control handle. A swing-lock, jacket lock design was implemented. The prosthesis was patent and free from thrombus. The aortic attachment system hooks all penetrated the aortic arterial wall with effective results. The current iliac attachment system hooks all penetrated the iliac arterial wall with effective results.
Acute Evaluation of ANCURE System	5 bovine	ANCURE delivery catheter w/ ANGIOSCALE catheter	Grafts were deployed using ANCURE tube, bifurcated, and aortoiliac delivery catheters. A necropsy was performed following animal sacrifice.	Acute implantation was successful and all grafts were patent, with no evidence of migration, twist, or compression. Minor technical issues encountered with the delivery catheter, which were corrected by subsequent device changes.

9.3 Additional Studies

This device contains no software or electrical components.

10. Summary of Clinical Studies

Purpose: The Aortoiliac EGS clinical study compared the rates of (proportions of patients with) major complications for patients treated with the Aortoiliac EGS system to the standard surgical treatment for AAA. Primary outcome measures were: 1) the rate of complications; 2) the length of hospital stay; and 3) the rate of aneurysm enlargement and rupture in the first 12 months.

Study Design: This prospective, multi-center, non-randomized clinical study compared patients treated with the Aortoiliac EGS system to a concurrent surgical control group. All patients had an infrarenal AAA and were candidates for surgical treatment of AAA. The concurrent surgical control group included patients whose vascular anatomy may not have been suitable for endovascular AAA repair based on arterial access size and proximal and distal neck lengths. Patients were followed at 6 weeks and 6 and 12 months from surgery. Aneurysm diameter changes and graft patency were evaluated by core laboratory assessment of contrast enhanced CT scans, abdominal ultrasounds, and x-rays. A total of 15 centers participated in the Aortoiliac EGS study. The study enrolled 121 Aortoiliac and 111 Surgical Control patients.

Vascular surgeons, as well as an interventional radiologist, served as principal investigators in the clinical study. When the interventional radiologist performed the procedure, a vascular surgeon performed the cutdown and closure and was available during the procedure in the event that conversion to standard surgical repair was necessary.

10.1 Description of Patients Studied and Gender Bias

Table 10. Demographics

Variable	Aortoiliac (N=121) n	%	Surgical Control (N=111) [1] n	%
Male	112	(92.6%)	85	(76.6%)
Age (yrs) Mean ±SD	73.2 ± 7.1		71.6 ± 7.0	
Race (Caucasian)	113	(93.4%)	108	(97.3%)
CAD	79	(65.3%)	68	(61.3%)
MI	56	(46.3%)	43	(38.7%)
Arrhythmia [2]	45	(37.8%)	21	(18.9%)
Valvular Heart Disease	14	(11.6%)	10	(9.0%)
CHF	21	(17.4%)	8	(7.2%)
Stroke	11	(9.1%)	13	(11.7%)
Hypertension	76	(62.8%)	79	(71.2%)
PAOD	31	(25.6%)	12	(10.8%)
COPD	48	(39.7%)	33	(29.7%)
Smoking [3]	109	(90.8%)	100	(90.1%)
Diabetes	15	(12.4%)	11	(9.9%)
Anesthesia Risk				
I	0	(0.0%)	1	(0.9%)
II	16	(13.2%)	14	(12.6%)
III	86	(71.1%)	79	(71.2%)
IV	19	(15.7%)	17	(15.3%)

1. 94 of the Control subjects were tube subjects and 17 were bifurcated subjects.
2. N=119
3. N=120

10.1.1 Evaluation of Gender Bias

Study inclusion and exclusion criteria were designed and the study was conducted in a manner to avoid gender bias in the subject population. The selection criteria in the study were based on identifying subjects with the appropriate anatomy for endovascular surgery.

Table 11 displays the percentage of males and females in each study and the differences between groups. Overall, more men were enrolled in both treatment groups. This finding reflects the actual incidence of AAA in the general population; men are more likely to have AAAs than women. The Control group included a statistically significantly (p=0.0008) higher percentage of female subjects (23.4%) compared to the Aortoiliac group (7.4%). This finding was anticipated as women tend to have smaller peripheral vasculature than men and Aortoiliac subjects were required to have a femoral artery of sufficient size to accommodate the 23 French EGS System Delivery Catheter. There were no other statistically significant differences between the treatment groups in regard to demographic characteristics.

Table 11. Comparison of Gender Between the Aortoiliac and Control Groups

Treatment Group	Males		Females		Difference: [95% CI]
	(%)	n/N	(%)	n/N	
Aortoiliac	(92.6%)	112/121	(7.4%)	9/121	16.0% [6.8, 25.2] [1]
Sx Control	(76.6%)	85/111	(23.4%)	26/111	--

1. p<0.01

10.1.2 Aneurysm Diameter Distribution

Table 12. Aneurysm Diameter Distribution

Diameter Range	Aortoiliac (N=121)		Surgical Control [1] (N=102)	
	n	%	n	%
< 30 mm	0	(0.0%)	0	(0.0%)
30 mm – 39 mm	2	(1.7%)	2	(2.0%)
40 mm – 49 mm	24	(19.8%)	28	(27.5%)
50 mm – 59 mm	50	(41.3%)	42	(41.2%)
60 mm – 69 mm	29	(24.0%)	21	(20.6%)
70 mm – 79 mm	15	(12.4%)	6	(5.9%)
80 mm – 89 mm	1	(0.8%)	3	(2.9%)
≥ 90 mm	0	(0.0%)	0	(0.0%)

1. Of the total 111 surgical control subjects, data is missing for nine subjects. These subjects were not included in the distribution of aneurysm diameter above.

10.2 Summary of the Aortoiliac EGS Study

Table 13. Principle Safety and Effectiveness Results (Comparison Measures)

Outcome Measure	Treatment Group	%	(n/N)	Aortoiliac EGS -Control [1] Difference [95% CI]
Operative Mortality (≤ 30 days)	Aortoiliac [2]	4.2%	(5/118)	1.5% [-5.7, 9.8]
	Sx Control	2.7%	(3/111)	--
Major Complications [3] (≤ 30 days)	Aortoiliac [2]	35.6%	(42/118)	-8.6% [-21, 4.0]
	Sx Control	44.1%	(49/111)	--
Need for ICU Stay (%)	Aortoiliac	38.9%	(44/113)	-57.7% [-59.1, -55.6]
	Sx Control	96.3%	(104/108)	--
Thrombosis/Occlusion	Aortoiliac [2]	1.7%	(2/118)	1.7% [-3.6, 9.8]
	Sx Control	0.0%	(0/111)	--
		Median	**(N)**	
Hospital Stay (days)	Aortoiliac [2]	3	(113)	-3.0 [-3.0, -2.0]
	Sx Control	6	(108)	--
ICU Stay (hours) [4]	Aortoiliac [2]	24.0	(44)	-6.0 [-12.2, -1.0]
	Sx Control	27.0	(104)	--
Operative Time (min)	Aortoiliac [2]	240.0	(118)	77.0 [62.0, 92.0]
	Sx Control	167.0	(111)	--
Operative Blood Loss (cc)	Aortoiliac [2]	400	(118)	-400 [-500, -300]
	Sx Control	800	(111)	--

1. Confidence intervals for differences in percentages were calculated by the exact (binomial) method; confidence intervals for differences in medians center on the Hodges-Lehmann estimator.
2. Of the total 121 aortoiliac subjects, three discontinued their participation at discharge and were alive at that time. These subjects are included in the analysis only through surgical implantation.
3. Major Complications = significant respiratory, cardiac, bleeding, bowel, wound, renal, arterial trauma, neurological and ischemic complications, and death.
4. ICU Stay duration includes only subjects who went to the ICU.

Table 14. Principle Safety and Effectiveness Results for Aortoiliac EGS System at 12 months (Other Measures)

Outcome Measure	n/N	% [95% CI]
Intraop Conversions [1]	7/121	5.8% [2.4, 11.6]
Postop Conversions	0/113	0.0% [0, 0.03]
Aneurysm Rupture	0/113	0.0% [0, 0.03]
Reduced Limb Flow [3]	34/113	30.1% [21.6 38.5]
Perigraft Flow, Discharge	58/112	51.8% [45.2, 61.0]
Perigraft Flow	33/100	33.0% [23.8, 42.2]
Increased Aneurysm Size (≥ 5 mm)	4/98	4.1% [0.2, 8.0]
Decreased Aneurysm Size, (≥ 5 mm)	46/98	46.9% [37.1, 56.8]
Graft Migration	0/113	0.0% [0, 0.03]

1. Intraop Conversions = access failure or failure to deploy. Protocol required these subjects to undergo standard AAA repair.
2. There were four aortoiliac intraoperative conversions; in three subjects the implant procedure was abandoned.
3. Reduced Limb Flow = intraoperative or postoperative intervention during the first 12 mos. to treat reduced limb patency.

Table 15. Claudication Complications versus Site of Distal Attachment and Contralateral Occlusion for Aortoiliac Subjects at £ 30 days [1]

Configuration	N=110	Leg Claudication		Buttock/Thigh Claudication	
		n	%	n	%
Landing zone in common, contra occlusion in common; fem-fem; both internal iliac arteries remain patent.	54	0	0%	1	1.9%
Landing zone in common, contra. occlusion in external and internal, fem-fem; the ipsilateral internal iliac artery remains patent.	13	0	0%	1	7.7%
Landing zone in external, contra. occlusion in common, fem-fem; the contralateral internal iliac artery remains patent.	32	0	0%	7	21.9%
Landing zone in external, contra. occlusion in external and internal, fem-fem.	6	0	0%	0	0%
Any landing zone, preexisting contra. occlusion	5	0	0%	0	0%

1. 113 patients successfully implanted; missing data for three subjects.

Table 16. Conversions to Standard Surgical Repair

Reason for Conversion	Aortoiliac Conversions (N=121) n	% [95% CI]
Conversion (Total)	**7**	**5.8% [2.9, 11.6]**
Failure to Access	4	3.3% [1.4, 8.3]
Failure to Accurately Place (Total)	**2**	**1.7% [0.5, 5.8]**
Arterial Trauma	0	0.0% [0.0, 3.0]
Failure to Retract Jacket	0	0.0% [0.0, 3.0]
Improper Graft Position	0	0.0% [0.0, 3.0]
Perigraft Flow	0	0.0% [0.0, 3.0]
Twist	0	0.0% [0.0, 3.0]
Unable to Remove Delivery Catheter	2	1.7% [0.5, 5.8]
Change in anatomy	1	0.8% [0.2, 4.5]
Late Conversion (Total)	**2**	**1.7% [0.5, 5.8]**
Perigraft Flow and Aneurysm Enlargement	1	0.8% [0.0, 4.5]
Reduced Limb Flow	1	0.8% [0.0, 4.5]

Table 17. Perigraft Flow for Aortoiliac EGS Subjects Over Time[1]

	Discharge		6 Months		12 Months	
	n/N	% [95% CI]	n/N	% [95% CI]	n/N	% [95% CI]
Attachment Site Flow	8/112	7.1 [2.4, 11.9]	6/88	6.8% [2.5, 14.37]	4/100	4.0% [0.2, 7.8]
Branch Flow	35/112	31.3% [22.7, 39.8]	23/88	26.1% [17.3, 36.6]	19/100	19.0% [11.3, 26.7]
Contralateral Occlusion Site Flow	8/112	7.1% [2.4, 11.9]	10/88	11.4% [5.6, 19.9]	7/100	7.0% [2.0, 12.0]
Source Unknown	7/112	6.3% [1.8, 10.7]	3/88	3.4% [0.7, 9.6]	3/100	3.0% [0.0, 6.3]
	24 Months		**36 Months**		**48 Months**	
	n/N	**%**	**n/N**	**%**	**n/N**	**%**
Attachment Site Flow	1/67	1.5%	0/37	0.0%	0/12	0.0%
Branch Flow	18/67	26.9%	6/37	16.2%	3/12	25.0%
Contralateral Occlusion Site Flow	2/67	3.0%	0/37	0.0%	0/12	0.0%
Source Unknown	3/67	4.5%	2/37	5.4%	0/12	0.0%

1. Includes implanted subjects with data available at each time period.

Table 18. Change in Aneurysm Diameter [1]

	Aortoiliac (N=98) Discharge to 12 months			Aortoiliac (N=65) Discharge to 24 months		
	n	% [95% CI]	Mean Change (mm)	n	%	Mean Change (mm)
Increase (+ ≥5 mm)	4	4.1% [0.2, 8.0]	+8.7	2	3.1%	+15.8
No Change (± <5 mm)	48	49.0% [39.1, 58.9]	-1.4	22	33.8%	-1.5
Decrease (- ≥5 mm)	46	46.9% [37.1, 56.8]	-11.3	41	63.1%	-14.1
	Aortoiliac (N=36) Discharge to 36 months			**Aortoiliac (N=11) Discharge to 48 months**		
	n	**%**	**Mean Change (mm)**	**n**	**%**	**Mean Change (mm)**
Increase (+ ≥5 mm)	2	5.6%	+17.9	1	9.1%	+6.6
No Change (± <5 mm)	12	33.3%	-2.0	2	18.2%	-2.6
Decrease (- ≥5 mm)	22	61.1%	-16.9	8	72.7%	-16.3

1. Includes implanted subjects who have follow-up data at each time period.

Table 19. Aneurysm Diameter by Perigraft Flow Status

Perigraft Flow Status	Aneurysm Diameter Change					
	Decrease (³ 5 mm)		No Change (± <5 mm)		Increase (³ 5 mm)	
	n/N	% [95% CI]	n/N	% [95% CI]	n/N	% [95% CI]
12 months						
No Perigraft Flow	33/62	53.2% [40.8, 65.6]	29/62	46.8% [34.4, 59.2]	0/62	0.0% [0.0, 0.05]
Perigraft Flow	12/33	36.4% [20.0, 52.8]	17/33	51.5% [24.5, 68.6]	4/33	12.1% [1.0, 23.3]
24 months						
No Perigraft Flow	29/37	78.4 %	8/37	21.6 %	0/37	0.0 %
Perigraft Flow	9/23	39.1 %	12/23	52.2 %	2/23	8.7 %
36 months						
No Perigraft Flow	17/22	77.3 %	5/22	22.7 %	0/22	0.0 %
Perigraft Flow	2/8	25.0 %	4/8	50.0 %	2/8	25.0 %

Table 20. Types of Interventions to Optimize Aortoiliac Graft Limb Flow

	Intraoperative		Postoperative		Total	
	n/N	% [95% CI]	n/N	% [95% CI]	n/N	% [95% CI]
Stent[1]	19/113	16.8% [9.9, 23.7]	12[2]/113	10.6% [4.9, 16.3]	31/113	27.4% [19.2, 35.7]
PTA only	4/113	3.5% [0.1, 6.9]	0/113	0.0% [0, 0.03]	4/113	3.5% [0.1, 6.9]
Surgical[3]	1/113	0.9% [0.0, 2.6]	2/113	1.8% [0, 4.2]	3/113	2.7% [0.0, 5.6]
Other	0/113	0.0% [0, 0.03]	0/113	0.0% [0, 0.03]	0/113	0.0% [0, 0.03]
(Total)	**24/113**	**21.2%**	**14/113**	**12.4%**	**38/113**	**33.6%**

1. Includes some subjects who had PTA or thrombolysis and stent.
2. One of these subjects had one stent placed intraoperatively. Another subject had a surgical limb attachment intraoperatively.
3. Includes Femoro-Femoral Bypass and surgical revision. Includes some subjects who may have had stents, PTA, or other non-surgical interventions.

11. Conclusions Drawn from the Studies

The data establish that all delivery catheter components will withstand the expected *in vivo* loads and the implants have at least a 15-year useful life. The clinical benefits of these systems are the reduced risk of several serious complications including bleeding, cardiac, respiratory, and bowel, and the less invasive nature of the devices which lead to reduced need for post-operative care and shorter hospitalization. The risks include the increased risk of renal and arterial trauma complications and device-related phenomenon such as perigraft flow and increases in aneurysm size. FDA determined that the data provide valid scientific evidence of reasonable assurance of safety and clinical benefit to the patient when used as indicated.

12. FDA Decision

FDA determined that this PMA supplement did not require a panel meeting. FDA also determined that the application was approvable with the condition that all patients in the original PMA cohort be followed for five years after implantation. CDRH issued an approval order on April 24, 2002.

13. Approval Specifications

Directions for Use: See Final Draft Labeling (Instructions for Use)

Hazards to Health from Use of the Device: See INDICATIONS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE EVENTS in the Final Draft Labeling (Instructions for Use).

Post-approval Requirements and Restrictions: See Approval Order