

## 1.0 General Information

Device Generic Name: Transcatheter Atrial Septal Defect Occlusion Device

Device Trade Name: GORE HELEX™ Septal Occluder

Applicant's Name and Address: W.L. Gore & Associates, Inc.  
3450 West Kiltie Lane  
Flagstaff, AZ 86001

Premarket Approval Application (PMA) Number: P050006

Date of Panel Recommendation: None

Date of Notice of Approval to Applicant: August 11, 2006

## 2.0 Indications For Use

The GORE HELEX Septal Occluder is a permanently implanted prosthesis indicated for the percutaneous, transcatheter closure of *ostium secundum* atrial septal defects (ASDs).

## 3.0 Contraindications

The GORE HELEX Septal Occluder is contraindicated for use in:

- Patients with extensive congenital cardiac anomalies which can only be adequately repaired by cardiac surgery.
- Patients unable to take anti-platelet or anticoagulant preventative medications such as aspirin, heparin, or warfarin.
- Anatomy where the GORE HELEX Septal Occluder size or position would interfere with other intracardiac or intravascular structures such as cardiac valves or pulmonary veins.
- Active endocarditis, or other infections producing bacteremia, or patients with known sepsis within one month of planned implantation, or any other infection that cannot be treated successfully prior to device placement.
- Patients whose vasculature is inadequate to accommodate a 9 Fr delivery sheath.
- Any patient known to have intracardiac thrombi.

## 4.0 Warnings and Precautions

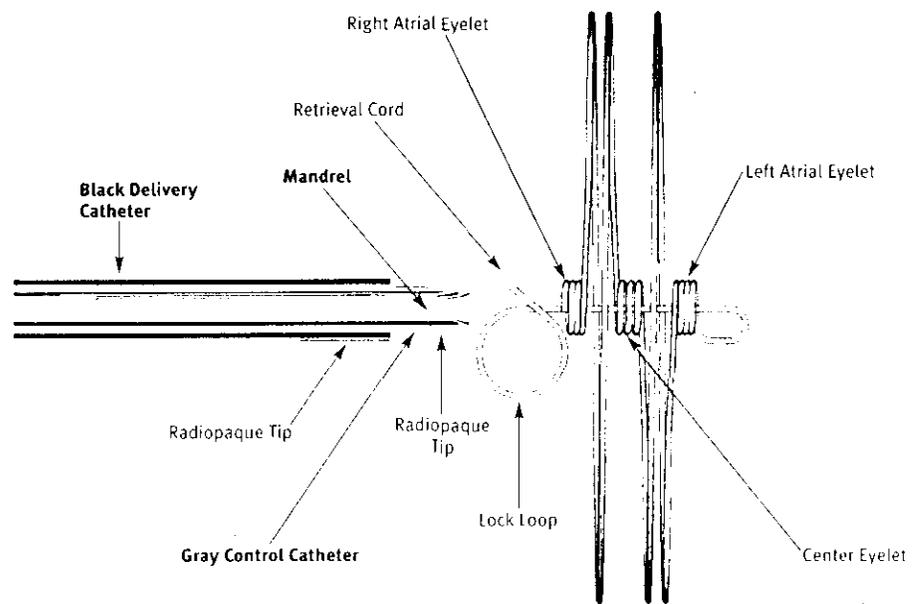
Please refer to the device labeling for a list of warnings and precautions.

## 5.0 Device Description

The GORE HELEX Septal Occluder is comprised of an implantable device and a catheter delivery system which is made up of the following components:

- control catheter,
- delivery catheter, and
- mandrel

**Figure 1** provides a drawing of the implantable device and catheter delivery system.



**Figure 1**

### Occluder

The GORE HELEX Septal Occluder implantable device is comprised of a hydrophilic, expanded polytetrafluoroethylene (ePTFE) patch material supported by a nickel-titanium (nitinol) supporting wire frame. When fully deployed, the occluder takes on a double disc shape and functions by bridging and covering the defect and adjacent tissue with the ePTFE patch supported by the wire frame. Immediately after deployment, the occluder remains in position across the defect by the mild tension created by the wire frame and the blood pressure that pushes the ePTFE patch against the atrial septum. The ePTFE patch will become attached to the atrial septum by cellular penetration through the ePTFE membrane micropores.

The GORE HELEX Septal Occluder is available in five sizes:

- 15 mm
- 20 mm
- 25 mm
- 30 mm
- 35 mm

The GORE HELEX Septal Occluder is deployed from a 9 French outer diameter delivery system.

### **Delivery System**

The delivery system of the GORE HELEX Septal Occluder is a catheter assembly composed of three primary coaxial components: a delivery catheter, a control catheter with retrieval cord, and a mandrel.

The delivery catheter is a black 9 French catheter with a radiopaque tip. Both the control catheter and mandrel are contained within the delivery catheter.

The control catheter is a gray 6 French catheter with a radiopaque tip. The control catheter deploys the occluder implant device from the delivery catheter.

The control catheter is equipped with a white retrieval cord to retrieve the occluder if necessary. A red retrieval cord cap on the proximal end of the control catheter ensures friction at the retrieval cord until device deployment.

The mandrel provides mechanical support to the occluder frame during deployment. In conjunction with the control catheter, the mandrel is used to guide and form the occluder during deployment.

## **6.0 Alternative Practices and Procedures**

Conventional procedures and treatments for atrial septal defects (ASDs) include surgical closure and other transcatheter devices indicated for the closure of *ostium secundum* atrial septal defects (ASD). The expected mortality with surgical closure of ASD generally is accepted as less than 1% in facilities with the appropriate expertise.

## **7.0 Marketing History**

W.L. Gore and Associates received the CE Mark for the GORE HELEX Septal Occluder in June 1999. Currently the GORE HELEX Septal Occluder is commercially available in the following countries:

Western Europe	Uruguay
Argentina	Venezuela
Brazil	India
Barbados	Australia
Bolivia	New Zealand
Chile	Malaysia
Costa Rica	China
El Salvador	Hong Kong
Guatemala	Philippines

Paraguay	Singapore
Panama	Indonesia
Peru	Israel
Trinidad Tobago	Vietnam
Rep. Dominicana	

The GORE HELEX Septal Occluder has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

## 8.0 Summary of Preclinical Testing

Summaries of pre-clinical testing performed on the occluder, delivery system, and complete device system are provided in Table 1. Table 1 also summarizes the pre-clinical testing performed to validate device modifications made during the clinical investigations. Device modifications made during the clinical investigations include:

- The finish of the nitinol wire was changed from mechanically polished to a light oxide finish to improve the mechanical attributes of the wound eyelets.
- The delivery catheter and control catheter wire tip design was changed to reduce deployment friction and increase deployment reliability. A radiopaque marker band was added to the tip material of the delivery catheter for radiopacity, and a soft bumper tip was eliminated and a radiopaque marker band became the tip of the control catheter.
- The material used in the flexible mandrel was changed from black pigmented to nature (non-pigmented) polyimide to reduce the possibility of flexible mandrel particulation during deployment.
- A change to the delivery catheter tip configuration to a tip-over-braid design was implemented for the 35 mm device.
- The mandrel material was changed from non-pigmented polyimide to PEEK™ to provide better control of the delivery system during placement of the occluder.
- The winding pattern of the frame of the device onto the mandrel was changed by 180°. This change allows the lock curvature to keep the left atrial disc overlap closed during deployment.
- A hydrophilic coating was added to the ePTFE material to improve the ultrasound visibility of the occluder during placement.

Preclinical testing demonstrated that the GORE HELEX Septal Occluder meets all design and functional requirements and the device is safe for its intended use.

**Table 1 Summary of Results from GORE HELEX Septal Occluder Pre-Clinical Testing**

Testing Performed	Purpose of Study	Summary of Results	
<b>OCCLUDER TESTING</b>			
Finite Element Analysis (FEA)	Septal Defect Closure Device (SDCD) Finite Element Analysis of <i>In Vivo</i> Loading	To determine the maximum stresses and strains, and their location in the nitinol structure when subjected to worst case physiologic loads to help predict the theoretical fatigue life of the GORE HELEX Septal Occluder.  Finite analysis was conducted on 15 mm and 35 mm Helex occluder diameters. The peak mean and peak alternating strains were evaluated. Results of the fatigue analysis showed higher mean and alternating strains in the 15mm implant than the 35mm implant. Comparison of the fatigue results with the experimental Goodman plot showed an acceptable safety factor of greater than 2, predicting an acceptable fatigue life of the implant.	
Nitinol Wire Testing	<b>Mechanical</b>		
	<b>Hardness</b>	This testing was done to determine if significant differences in hardness attributes of mechanically polished and light oxide nitinol wire exist.	The surface hardness attributes of the mechanically polished and light oxide nitinol wire groups are equivalent.
	<b>Fatigue Strength</b>	To determine the fatigue strength of the nitinol wire used in the GORE HELEX Septal Occluder, and to compare the results to FEA predictions of <i>in vivo</i> strain levels.	Nitinol wire was tested under fully reversed (zero mean) and non-zero mean cyclic strain conditions. Endurance limit alternating strain amplitude has been shown to be well above the highest predicted <i>in vivo</i> alternating strain.
	<b>Fatigue Strength (Hydrophilic Coating)</b>	To determine the fatigue strength of the nitinol wire used in the GORE HELEX Septal Occluder, and to compare the results to FEA predictions of <i>in vivo</i> strain levels.	Nitinol wire was heat treated and separated into 2 groups of 15 samples. One group was subjected to the hydrophilic coating and the other group was left in the heat-treated condition. Each group was then fatigue tested using a rotating/bending alternating strain method to 100,000 cycles or until fracture. Inspection via SEM photomicroscopy and the results of subsequent fatigue tests confirm that the hydrophilic coating process is not detrimental to wire fatigue.
	<b>Elastic Modulus</b>	To determine the elastic modulus at ambient conditions for the light oxide nitinol wire used in the GORE HELEX Septal Occluder.	Testing demonstrated that the elastic modulus of light oxide nitinol wire (5.85 Msi) is sufficiently equivalent to mechanically polished wire (5.34 Msi).

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Table 1 Summary of Results from GORE HELEX Septal Occluder Pre-Clinical Testing - continued

Testing Performed	Purpose of Study	Summary of Results	
<b>OCCLUDER TESTING</b>			
<b>Mechanical</b>			
<b>Nitinol Wire Testing</b>	<b>Dimensional Properties</b>	To characterize the dimensional properties of light oxide nitinol wire as compared to mechanically polished wire.	The dimensional properties of devices made with light oxide nitinol wire are equivalent to or exceed those of devices made with mechanically polished wire.
	<b>Tensile Properties</b>	To characterize the tensile properties of light oxide nitinol wire as compared to mechanically polished wire.	Five samples of each wire type were evaluated. The tensile properties of light oxide nitinol wire (ultimate tensile strength of $1645.6 \pm 5.5$ MPa and % elongation of $11.30 \pm 0.35$ ) are equivalent to or exceed that of mechanically polished wire (ultimate tensile strength of $1536.4 \pm 3.65$ MPa and % elongation of $11.24 \pm 0.11$ ).
	<b>A<sub>p</sub> / A<sub>r</sub> Austenitic Transformation Temperature</b>	To characterize the austenitic transformation temperature of the light oxide nitinol wire as compared to mechanically polished wire.	The transformation temperatures of light oxide nitinol wire (mean A <sub>p</sub> of $3.5 \pm 2.66^\circ\text{C}$ and mean A <sub>r</sub> of $29.6 \pm 0.65^\circ\text{C}$ ) are equivalent to or exceed that of mechanically polished wire (mean A <sub>p</sub> of $5.7 \pm 0.81^\circ\text{C}$ and mean A <sub>r</sub> of $28.2 \pm 0.51^\circ\text{C}$ ).
	<b>Chemical</b>		
	<b>Chemical Composition</b>	To evaluate change in surface composition and morphology of electropolished nitinol wire.	The analytical methods used for this study were Electron Spectroscopy for Chemical Analysis (ESCA), X-ray Diffraction (XRD), X-ray Fluorescence (XRF), Auger Electron Spectroscopy (AES) and Atomic Force Spectroscopy (AFS). Electropolishing reduces both the elemental concentration of nickel found near the wire surface, and the quantifiable surface roughness.
	<b>Corrosion</b>	To quantify the uniform and stress corrosion of mechanically polished nitinol wire.	There is no significant loss of nickel or titanium due to corrosion, nor was there any evidence of localized corrosion.

**Table 1 Summary of Results from GORE HELEX Septal Occluder Pre-Clinical Testing - continued**

Testing Performed	Purpose of Study	Summary of Results
Nitinol Wire Testing	Nickel Extraction	<p>To determine the amount of nickel extracted from the nitinol wire (both mechanically polished and light oxide).</p> <p>Nickel extracted from mechanically polished wire was below the recommended safe level of exposure to nickel (35µg/day for periods greater than 28 days). Results showed an initial release of nickel at 24 hours, which tapered off significantly at 48 hours, and even further at 7 days. Negligible nickel amounts were detected at later timepoints.</p> <p>Nickel extraction from light oxide nitinol wire was substantially less than the process monitor limit of ≤10ppm.</p>
	Nickel Leachability	<p>To determine elutable attributes of finished GORE HELEX Septal Occluder devices using light oxide nitinol wire.</p> <p>Nickel leachability rates are significantly below the recommended safe level of exposure (35µg/day for periods greater than 28 days).</p>
	<b>Strength</b>	
	Eyelet Tensile	<p>To confirm that the proximal eyelet of the GORE HELEX Septal Occluder nitinol wire frame has sufficient strength margin during retrieval of an implanted device so that it does not break.</p> <p>Testing was conducted on 24 samples of all 5 sizes. The proximal eyelet of the wire frame has sufficient strength (mean eyelet strength greater than 3 times) to withstand the force applied to it during retrieval of a device from a septal defect (mean 0.261 kg). There is at least a 99.7% probability that the eyelet will not fail when retrieval is attempted.</p>
ePTFE Leaflet Porosity and Strength	<p>To confirm that the material's porosity is appropriate for promotion of tissue in-growth and that the ePTFE leaflet material has sufficient tensile strength to withstand the atrial trans-septal pressure gradient for 100 years.</p>	<p>The ePTFE leaflet material's porosity was evaluated by measuring the bubble point of leaflet material specimens using isopropyl alcohol as the wetting agent. The bubble points ranged from 1.6 to 3.9 psi, which is appropriate for promotion of tissue in-growth. The tensile strength of the ePTFE leaflet material is adequate to withstand the atrial trans-septal pressure differential for 100 years with a 19-fold safety margin.</p>

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**Table 1 Summary of Results from GORE HELEX Septal Occluder Pre-Clinical Testing - continued**

Testing Performed	Purpose of Study	Summary of Results
Accelerated Cyclic Durability	To demonstrate that GORE HELEX Septal Occluder devices will withstand the equivalent of 10 years of simulated cardiac cycles with fatigue fracture of the nitinol wire frame.	Testing was conducted on 18 of the 15 mm and 35 mm occluder diameters. GORE HELEX devices successfully completed 400 million cycles of accelerated durability testing, the equivalent of 10 years <i>in vivo</i> , at a peak pressure pulse significantly higher than the typical human atrial pressure differential.
Finished Device Pressure	To confirm that the GORE HELEX Septal Occluder will withstand short-term and long-term pressurization in a mock septal defect without failure due to leaflet material rupture, wire fracture, leaflet lacing hole pullout, or embolization through the defect.	The GORE HELEX Septal Occluder has been shown to withstand the highest expected <i>in vivo</i> atrial trans-septal pressure differential without structural failure or embolization through the defect.
Magnetic Resonance Imaging (MRI) Testing	To determine the presence of magnetic field interactions and heating for the GORE HELEX Septal Occluder with the use of a MR system.	The device has been shown to be MRI safe at field strengths of 3.0 Tesla or less and a maximum whole body averaged specific absorption rate (SAR) of 3.0w/kg for 15 minutes of MRI.
Particulation / Wet Out	To demonstrate that the hydrophilic coating of the GORE HELEX Septal Occluder wets out as specified, and does not release any particulation as a result of the hydrophilic coating following deployment.	Testing was conducted on 6 devices; 3 with the hydrophilic coating and 3 without. Particulation from the hydrophilic-coated GORE HELEX Septal Occluder devices was not statistically different from the control devices. The particulate count range for 40-200µ particle size was 15-28 for the coated devices and 17-21 for the uncoated devices. The particulate count range for the 200-1000µ particle size was 1-2 for the coated devices and 2-3 for the uncoated devices. The particulate count for the 1000-2000µ particle size was 0 in both groups.
180° Opposed Wind Deployment	To confirm that opposed wind results in reduced left side intra-disk separation of GORE HELEX Septal Occluder.	Reduction of left atrial intra-disc separation has been demonstrated by updating the frame winding pattern of the GORE HELEX Septal Occluder by 180°.

**Table 1 Summary of Results from GORE HELEX Septal Occluder Pre-Clinical Testing - continued**

Testing Performed		Purpose of Study	Summary of Results
<b>DELIVERY SYSTEM TESTING</b>			
Control Catheter	Control Catheter Retrieval Cord Attachment Strength	To measure the tensile strength of the retrieval cord attachment on the control catheter to ensure adequate attachment strength during device loading and retrieval.	Testing was conducted on 8 samples and results demonstrated an average load to failure of 1.5 kg ± 0.2 kg. The control catheter retrieval cords that were tested meet the specification for the attachment strength.
	Control Catheter Tip Attachment Strength	To confirm the tensile strength of the tip attachment of the control catheter meets specification.	Testing was conducted on 8 samples and results demonstrated an average load to failure of 4.5 kg ± 0.1 kg. The control catheter tip meets the specification for the attachment strength.
	Control Catheter Hub Attachment Strength	To confirm the tensile strength of the hub attachment of the control catheter meets specification.	Testing was conducted on 8 samples and results demonstrated an average load to failure of 7.4 kg ± 0.5 kg. The control catheter hub meets the specification for the attachment strength.
	Control Catheter Pressure	To confirm that there is no leakage in the control catheter when subjected to the specification injection pressure of 300 kPa for 30 seconds.	Control catheter meets the specification for pressure loading.
Delivery Catheter Testing	Delivery Catheter Tip Attachment Strength	To confirm the tensile strength of the tip attachment of the delivery catheter meets specification.	Testing was conducted on 8 samples and results demonstrated an average load to failure of 3.8 kg ± 0.3 kg. The delivery catheter tip meets the specification for the attachment strength.
	Delivery Catheter Hub Attachment Strength	To confirm the tensile strength of the hub attachment of the delivery catheter meets specification.	Testing was conducted on 8 samples and results demonstrated an average load to failure of 10.9 kg ± 0.4 kg. The delivery catheter meets the specification for the attachment strength.
	Delivery Catheter Pressure	To confirm that there is no leakage in the delivery catheter when subjected to the specification injection pressure of 300 kPa for 30 seconds.	Delivery catheter hub meets the specification for pressure loading.
PEEK™ Mandrel Deployment		To confirm that change from polyimide to PEEK mandrels does not negatively impact device deployment.	Testing was conducted on 20 assembled occluder devices assembled with PEEK mandrels and delivery systems. The GORE HELEX Septal Occluder devices with PEEK mandrels deployed successfully.

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**Table 1 Summary of Results from GORE HELEX Septal Occluder Pre-Clinical Testing - continued**

Testing Performed	Purpose of Study	Summary of Results
<b>SYSTEM TESTING</b>		
Finite Element Analysis of Catheter Loading Conditions	To determine the maximum stresses and strains, and their location, in the nitinol structure when loaded in the delivery catheter to help predict shelf life of the implants and to confirm that the nitinol wire is not strained beyond the safe limit.	Peak strains are in the lock loop loaded in the mandrel. This peak strain value of 10.62% is within the acceptable range and no permanent damage to the wire is expected.
Device Storage and Nitinol Wire Stress Relaxation Test	To demonstrate that GORE HELEX Septal Occluder devices made with light oxide nitinol wire can be stored over a wide range of temperatures without loss of shape memory.	Testing was conducted in accordance with ASTM 4169-96 and 4169-94.* Functional integrity of the device is maintained throughout shipping, receipt, and handling following sterilization and 6-month accelerated aging.
Device Deployment Reliability	Three tests were conducted to evaluate deployment reliability. First test established reliability of the original design, second test evaluated deployment reliability of the 35mm device with the tip-over-braid delivery catheters, and the third test confirmed deployment reliability of new delivery and control catheters with PEEK mandrels.	<p><b>First Test:</b> Results demonstrated a 95% confidence with 95% reliability of a successful deployment of the GORE HELEX Septal Occluder.</p> <p><b>Second Test:</b> All 35mm GORE HELEX Septal Occluder devices were successfully deployed.</p> <p><b>Third Test:</b> Results demonstrated a 95% confidence with 95% reliability of a successful deployment of the GORE HELEX Septal Occluder.</p>
Device Deployment Reliability (Hydrophilic Coating)	To confirm that the addition of a hydrophilic coating to the implantable device does not affect deployment or particulation.	Results demonstrated a 95% confidence with 95% reliability of a successful deployment of the GORE HELEX Septal Occluder. Devices passed particulation and wet out testing.
Device Deployment Reliability (180° Opposed Wind)	To confirm deployment reliability of the GORE HELEX Septal Occluder with 180° opposed wind.	Results demonstrated a 95% confidence with 95% reliability of a successful deployment of the GORE HELEX Septal Occluder.

\* Standard Practice for Performance Testing of Shipping Containers and Systems (1994 and 1996)

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## 8.1 Biocompatibility

Table 2 summarizes the biocompatibility testing performed on the GORE HELEX Septal Occluder.

**Table 2 Summary and Results of Biocompatibility Testing.**

Device Section	Test Name	Test Method	Results
Delivery System	Cytotoxicity	Minimum Essential Medium (MEM)	Non-cytotoxic
	Cytotoxicity	Agarose Overlay	Non-cytotoxic
	Sensitization	Skin Sensitization Kligman Maximization	Produced no reaction
	Irritation / Intracutaneous	Intracutaneous Injection	Negligible irritant
	Acute Systemic Toxicity	Systemic Injection	Test negative
	Hemocompatibility*	Direct contact – Rabbit blood	Non-hemolytic
	Pyrogenicity	Rabbit Pyrogen	Non-pyrogenic
Implant Device	Cytotoxicity	Minimum Essential Medium (MEM)	Non-cytotoxic
	Cytotoxicity	Agarose Overlay	Non-cytotoxic
	Sensitization	Skin Sensitization Kligman Maximization	Produced no reaction
	Irritation / Intracutaneous	Intracutaneous Injection	Negligible irritant
	Acute Systemic Toxicity	Systemic Injection	Test negative
	Implantation	Short-term intramuscular implantation	Non-toxic
	Hemocompatibility*	Direct contact – Rabbit blood	Non-hemolytic
	Pyrogenicity	Rabbit Pyrogen	Non-pyrogenic
	Genotoxicity	<i>S. typhi</i> and <i>E. coli</i> Reverse Mutation <i>In-vivo</i> Chromosomal Aberration Study in Mammalian Cells Mouse Bone Marrow Micronucleus study 0.9% Sodium Chloride/Sesame oil extracts	Non-genotoxic

\* Separate testing for in vivo thrombogenicity was not performed because the *in vivo* animal studies of the finished device included evaluations for the absence of thrombus formation or thromboembolism. Additionally, separate complement activation testing was not required because the materials in the occluder and delivery catheter have been used in other approved products and the clinical evaluation did not reveal any instances of anaphylactic shock.

## 8.2 Animal Studies

Three animal studies were conducted utilizing the GORE HELEX Septal Occluder:

1. The purpose of the initial study was to evaluate the deployment and the chronic *in-vivo* performance at 1, 3, 6, 12, and 24 months. Twenty-six mixed breed hounds were entered into this study. ASDs were created and devices were implanted using transesophageal echocardiography (TEE) and fluoroscopy for guidance. Post-operative TEE with color flow Doppler (CFD) was used to evaluate residual shunting and device orientation. Two animals died during ASD creation and 1 animal died 4 days post-procedure due to causes unrelated to the device. Implants were retrieved at 1, 3, 6, 12, and 24 months post-procedure. Gross and histological examinations of the explants were performed and materials were evaluated for evidence of wear.

There were 24 successful implants with complete ASD closure. There was 1 animal with a wire break resulting from a wire kink during deployment using an earlier delivery system prototype. With all 23 devices, there was acceptable tissue incorporation, benign tissue response, no evidence of thrombogenicity, and no evidence of material fatigue or wear.

2. The purpose of the second animal study was to evaluate mechanical wear of nitinol and ePTFE with multiple overlapping devices and the effects that this deployment configuration would have, if any, on the biologic response with specific reference to healing and thrombosis. Twelve mixed breed hounds were entered into this study. Double ASDs were created and 2 devices were implanted to cover the defects. Post-operative TEE with CFD was used to evaluate residual shunting and device orientation. One animal died during ASD creation and another animal with a partially locked device was maintained for 139 days. Implants were retrieved at 3 and 6 months post-procedure. Gross and histological examinations of the explants were performed, and materials were evaluated for evidence of wear.

There were 10 successful implants of 2 overlapping devices with complete closure of all double ASDs. With all 20 devices (10 animals), there was acceptable tissue incorporation, benign tissue response, no evidence of thrombogenicity, and no evidence of material fatigue or wear. The presence of overlapping devices had no adverse effect on material or biologic response.

3. The purpose of the third animal study was to assess:
  - The ultrasonic visibility of the GORE HELEX Septal Occluder with a hydrophilic coating (HPL) by demonstrating that the device was easily visible by TEE during deployment.
  - The safety of the HPL-coated device by evaluating thrombogenicity and atrial tissue response to the device.

In each of the 6 canines entered into this study, a 20 mm HPL-coated device was implanted for 30 days. Within 31 days post-procedure, all animals demonstrated complete fibrous connective tissue coverage of the left and right atrial discs. There was no adverse effect on thrombogenicity or atrial tissue response. No evidence of thromboemboli was found on the device surfaces, with the cardiac chambers and coronary vessels, or within the lungs, brain, or kidney of any animal in the study.

The HPL-coating improved the ultrasonic visibility and ease-of-use during deployment.

### **8.3 Sterilization, Packaging and Shelf Life Testing**

The GORE HELEX Septal Occluder is sterilized using 100% Ethylene Oxide (ETO) cycle that has been validated to achieve a Sterility Assurance Level (SAL) of  $10^{-6}$  in accordance with ANSI/AAMI/ISO 11135-1994 (Sterilization of health care products - Ethylene oxide - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices). Sterilization residual limits meet the requirements of ANSI/AAMI/ISO 10993-7:1995 (Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals).

Product and package stability testing of the GORE HELEX Septal Occluder was performed and validated a 3-year shelf life.

## 9.0 Adverse Events

### 9.1 Clinical Summary

The GORE HELEX Septal Occluder was evaluated in a feasibility study (two center, single arm), a pivotal study (multi-center, non-randomized), and a continued access study (multi-center, single arm, prospective). The feasibility study included 51 subjects treated with the device. The pivotal study compared the device to surgical closure of *ostium secundum* atrial septal defects. Investigators were required to complete 3 device training cases. The pivotal study included 119 non-training subjects treated with the device and 128 subjects treated with surgical closure. The continued access study included 113 non-training subjects treated with the device as of December 15, 2005, of which 77 subjects completed the 12-month follow-up evaluation.

These subjects form the basis of the observed adverse event data reported in the following section. An independent Data Safety Monitoring Board (DSMB) reviewed all reported adverse events to determine device/procedure relationship and event severity (major or minor). An event was considered major if it required reintervention, readmission to the hospital or resulted in permanent damage or deficit. For the GORE HELEX Septal Occluder studies, reintervention was defined as chronic medical, and acute surgical or interventional cardiology therapies.

### 9.2 Deaths

There was one post-operative death in the surgical control treatment arm of the pivotal study. This subject died of complications related to post-pericardiotomy syndrome on Day 10 post surgery. No deaths have been reported in the device subjects in the feasibility, pivotal, and continued access studies.

### 9.3 Observed Adverse Events

Major adverse events reported through the 12-month follow-up for the feasibility, pivotal and continued access studies are presented in **Table 3**.

**Table 3**  
**Number of Subjects with Successful Device Delivery by Category of Major Adverse Events**

**GORE HELEX Septal Occluder Studies**  
**Events Reported Through 12-Month Follow-up**

	Pivotal Study				Continued Access Study
	Feasibility Study	Device Arm	Surgery Arm	Difference (95% CI) <sup>1</sup>	
<b>Subjects Evaluable for Safety</b>	51	119	128		77
<b>Deaths (Any Cause)</b>	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
<b>Subjects With One or More Major Adverse Events</b>	2 ( 3.9%)	7 ( 5.9%)	14 ( 10.9%)	-5.1% (-12.1%, 1.9%)	3 ( 3.9%)
<b>Cardiac</b>	1 ( 2.0%)	2 ( 1.7%)	10 ( 7.8%)	-6.1% (-11.5%, -0.8%)	2 ( 2.6%)
Arrhythmia	1 ( 2.0%)	0	0		0
Bleeding (treatment required)	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Device Embolization (post- procedure) <sup>2</sup>	0	2 ( 1.7%)	na	na	2 ( 2.6%)
Pulmonary Edema	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Post-Pericardiotomy Syndrome	na	na	8 ( 6.3%)	na	na
<b>Integument (Skin)</b>	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Allergic reaction	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
<b>Neurologic</b>	1 ( 2.0%)	2 ( 1.7%)	0	1.7% (-0.6%, 3.9%)	0
Migraine (new)	0	2 ( 1.7%)	0	1.7% (-0.6%, 3.9%)	0
Paresthesia	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Seizure	1 ( 2.0%)	0	0		0
<b>Pulmonary (Respiratory)</b>	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Stridor	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
<b>Vascular</b>	0	1 ( 0.8%)	1 ( 0.8%)	0.1% (-2.2%, 2.3%)	0
Hemorrhage (treatment or intervention required)	0	1 ( 0.8%)	1 ( 0.8%)	0.1% (-2.2%, 2.3%)	0
<b>Wound</b>	0	0	2 ( 1.6%)	-1.6% (-3.8%, 0.7%)	0
Hernia	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Scarring or scar related	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
<b>Device (HELEX Septal Occluder)</b>	0	3 ( 2.5%)	na	na	1 ( 1.3%)
Allergic reaction	0	1 ( 0.8%)	na	na	0
Device size inappropriate	0	2 ( 1.7%)	na	na	0
Device removal due to fracture	0	0	na	na	1 ( 1.3%)
<b>Other</b>	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Anemia	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0

NOTE: Analysis includes all Feasibility subjects, nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

na – not applicable

<sup>1</sup> Differences between Pivotal device and surgery groups and associated 95% confidence intervals

<sup>2</sup> The 4 embolized devices were removed by transcatheter technique

Minor adverse events reported through the 12-month follow-up for the feasibility, pivotal and continued access studies are presented in **Table 4**.

**Table 4**  
**Number of Subjects with Successful Device Delivery by Category of Minor Adverse Events**

**GORE HELEX Septal Occluder Studies**  
**Events Reported Through 12-Month Follow-up**

	Pivotal Study				Continued Access Study
	Feasibility Study	Device Arm	Surgery Arm	Difference (95% CI) <sup>1</sup>	
<b>Subjects Evaluable for Safety</b>	<b>51</b>	<b>119</b>	<b>128</b>		<b>77</b>
<b>Subjects With One or More Minor Adverse Events</b>	<b>19 ( 37.3%)</b>	<b>34 ( 28.6%)</b>	<b>36 ( 28.1%)</b>	<b>0.4% (-10.9%, 11.8%)</b>	<b>21 ( 27.3%)</b>
<b>Cardiac</b>	<b>7 ( 13.7%)</b>	<b>14 ( 11.8%)</b>	<b>26 ( 20.3%)</b>	<b>-8.5% (-17.8%, 0.7%)</b>	<b>2 ( 2.6%)</b>
Arrhythmia	3 ( 5.9%)	10 ( 8.4%)	5 ( 3.9%)	4.5% (-1.5%, 10.5%)	2 ( 2.6%)
Chest Pain	1 ( 2.0%)	2 ( 1.7%)	0	1.7% (-0.6%, 3.9%)	0
Embolus – air	1 ( 2.0%)	0	2 ( 1.6%)	-1.6% (-3.8%, 0.7%)	0
Hemopericardium	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Hypotension	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Palpitations	1 ( 2.0%)	0	0		0
Pericardial effusion	1 ( 2.0%)	1 ( 0.8%)	5 ( 3.9%)	-3.1% (-6.9%, 0.8%)	0
Pneumopericardium	0	0	3 ( 2.3%)	-2.3% (-5.1%, 0.4%)	0
Post-Pericardiotomy Syndrome	na	na	10 ( 7.8%)	na	na
Syncope	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Vaso-vagal reaction	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
<b>Integument</b>	<b>0</b>	<b>0</b>	<b>0</b>		<b>1 ( 1.3%)</b>
Abrasion	0	0	0		1 ( 1.3%)
<b>Neurologic</b>	<b>7 ( 13.7%)</b>	<b>8 ( 6.7%)</b>	<b>0</b>	<b>6.7% (2.3%, 11.1%)</b>	<b>7 ( 9.1%)</b>
Dizziness	2 ( 3.9%)	0	0		0
Headache	4 ( 7.8%)	5 ( 4.2%)	0	4.2% (0.7%, 7.7%)	7 ( 9.1%)
Migraine (new)	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Paresthesia	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Visual field disturbance or defect	1 ( 2.0%)	2 ( 1.7%)	0	1.7% (-0.6%, 3.9%)	0
<b>Pulmonary (Respiratory)</b>	<b>0</b>	<b>1 ( 0.8%)</b>	<b>8 ( 6.3%)</b>	<b>-5.4% (-10.1%, -0.7%)</b>	<b>1 ( 1.3%)</b>
Atelectasis	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Congestion	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Dyspnea	0	0	0		1 ( 1.3%)
Pleural effusion (not requiring drainage)	0	0	3 ( 2.3%)	-2.3% (-5.1%, 0.4%)	0
Pneumothorax	0	0	4 ( 3.1%)	-3.1% (-6.3%, 0.0%)	0
Pneumonia	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
<b>Renal &amp; Uro-Genital</b>	<b>0</b>	<b>1 ( 0.8%)</b>	<b>0</b>	<b>0.8% (-0.8%, 2.4%)</b>	<b>0</b>
Urinary retention	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
<b>Anesthesia</b>	<b>1 ( 2.0%)</b>	<b>3 ( 2.5%)</b>	<b>1 ( 0.8%)</b>	<b>1.7% (-1.4%, 4.9%)</b>	<b>5 ( 6.5%)</b>
Abdominal Pain	0	0	0		1 ( 1.3%)
Corneal abrasion	0	0	0		1 ( 1.3%)
Emesis	0	1 ( 0.8%)	1 ( 0.8%)	0.1% (-2.2%, 2.3%)	1 ( 1.3%)
Nausea	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Nausea with emesis	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	3 ( 3.9%)
Paresthesia	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Sore throat	1 ( 2.0%)	0	0		0
<b>Drug-Related</b>	<b>5 ( 9.8%)</b>	<b>6 ( 5.0%)</b>	<b>2 ( 1.6%)</b>	<b>3.5% (-1.0%, 7.9%)</b>	<b>4 ( 5.2%)</b>
Allergic response	1 ( 2.0%)	0	2 ( 1.6%)	-1.6% (-3.8%, 0.7%)	0
Bruising / Ecchymosis	2 ( 3.9%)	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	1 ( 1.3%)
Gastric irritation	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Nosebleed	1 ( 2.0%)	4 ( 3.4%)	0	3.4% (0.2%, 6.5%)	3 ( 3.9%)
Rectal Bleeding	1 ( 2.0%)	0	0		0

**Table 4 cont**  
**Number of Subjects with Successful Device Delivery by Category of Minor Adverse Events**

**GORE HELEX Septal Occluder Studies**  
**Events Reported Through 12-Month Follow-up**

	Pivotal Study				Continued Access Study
	Feasibility Study	Device Arm	Surgery Arm	Difference (95% CI) <sup>†</sup>	
<b>Wound</b>	<b>2 ( 3.9%)</b>	<b>1 ( 0.8%)</b>	<b>4 ( 3.1%)</b>	<b>-2.3% (-5.8%, 1.3%)</b>	<b>1 ( 1.3%)</b>
Access site bleeding	0	1 ( 0.8%)	0	0.8% (-0.8%, 2.4%)	0
Access site pain	1 ( 2.0%)	0	0		0
Hematoma (not requiring treatment or intervention)	1 ( 2.0%)	0	0		1 ( 1.3%)
Scarring or scar related	0	0	2 ( 1.6%)	-1.6% (-3.8%, 0.7%)	0
Suture related	0	0	1 ( 0.8%)	-0.8% (-2.4%, 0.8%)	0
Sternal wire	na	na	1 ( 0.8%)		na
<b>Delivery System</b>	<b>2 ( 3.9%)</b>	<b>1 ( 0.8%)</b>	<b>na</b>	<b>na</b>	<b>0</b>
Mandrel Kink	1 ( 2.0%)	0	na	na	0
Retrieval cord break	1 ( 2.0%)	0	na	na	0
Retrieval cord detachment	0	1 ( 0.8%)	na	na	0
<b>Device (HELEX Septal Occluder)</b>	<b>3 ( 5.9%)</b>	<b>6 ( 5.0%)</b>	<b>na</b>	<b>na</b>	<b>5 ( 6.5%)</b>
Fracture-wire frame	3 ( 5.9%)	6 ( 5.0%)	na	na	5 ( 6.5%)
<b>Non-Investigational Device Related</b>	<b>0</b>	<b>0</b>	<b>0</b>		<b>1 ( 1.3%)</b>
Contrast reaction	0	0	0		1 ( 1.3%)

NOTE: Analysis includes all Feasibility subjects, nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05.

na – not applicable

<sup>†</sup> Differences between Pivotal device and surgery groups and associated 95% confidence intervals

#### 9.4 Potential Device or Procedure-Related Adverse Events

Adverse Events associated with the use of the GORE HELEX Septal Occluder may include, but are not limited to:

- Repeat procedure to the target ASD
- Postprocedure device embolization
- New arrhythmia post-procedure
- Surgical intervention for device failure or ineffectiveness
- Access site complications requiring surgery, interventional procedure, transfusion, or prescription medication
- Neurological problems resulting in permanent deficit
- Thrombosis or thromboembolic event resulting in clinical sequelae
- Permanent loss of arterial pulse
- Perforation of a cardiovascular structure by the device
- Device fracture resulting in clinical sequelae or surgical intervention
- Pericardial tamponade
- Cardiac arrest
- Renal failure
- Sepsis
- Pneumothorax requiring chest tube evacuation
- Significant pleural or pericardial effusion requiring drainage
- Significant bleeding
- Endocarditis
- Death

## 10.0 Summary of Clinical Studies

### 10.1 Feasibility Study

The GORE HELEX Septal Occluder was evaluated in a single arm, prospective feasibility study intended to provide an initial evaluation of the safety and performance of the GORE HELEX Septal Occluder for closure of *ostium secundum* atrial septal defects (ASDs). Two U.S. sites participated in the study and enrolled 63 subjects. The median subject age was 11 years (range: 6 months to 65 years) and 65% of the subjects were female. The median estimated defect size was 12 mm (range: 4.5 to 20 mm), in subjects with a delivery attempt (n=59), the median stretched defect size was 18 mm (range 6 to 26 mm).

The GORE HELEX Septal Occluder was successfully implanted in 86.4% (51/59) of subjects with a delivery attempt. Subjects with a successful device delivery were followed for 12 months. No deaths, device embolizations, thrombus on the device, or erosions requiring surgery were reported through the 12-month follow-up. There were no repeat procedures to the target ASD in the study population.

Of subjects evaluated for 12-month ASD closure by independent echocardiography core laboratory review, 94.6% (35/37) had a successful defect closure (complete occlusion or clinically insignificant leak). Clinically significant leaks were present in two subjects (5.4%) at the 12-month follow-up evaluation. Clinical success, a composite of safety (no major AE or repeat procedure) and efficacy (clinical closure at 12 months), was achieved in 89.5% of subjects (34/38) available for evaluation.

**Table 5**  
**GORE HELEX Septal Occluder Feasibility Study**  
**Principal Safety and Effectiveness Results**

	Feasibility
<b>Technical Success<sup>1</sup></b>	51 / 59 (86.4%)
<b>Clinical Closure Success<sup>2</sup></b>	
Pre-Discharge	49/51 (96.1%)
6 Months	30/31 (96.8%)
12 Months	35/37 (94.6%)
<b>Principal Safety Measures</b>	
Major Adverse Events 12 Months	2/51 (3.9%)
Minor Adverse Events 12 Months	19/51 (37.3%)
Survival at 365 Days (K-M)	100%
<b>Composite Clinical Success 12 Months<sup>3</sup></b>	34/38 (89.5%)

<sup>1</sup> Technical Success defined as successful delivery of the device

<sup>2</sup> Clinical Closure Success defined as defect that is either Completely Occluded or Clinically Insignificant Leak. Leak status was evaluated by the investigational sites at pre-discharge and 6 months and by the echocardiography core laboratory at 12 months

<sup>3</sup> Composite Clinical Success defined as no major adverse event or repeated procedure and clinical closure success at 12 months

### 10.2 Purpose - Pivotal and Continued Access Studies

The purpose of the pivotal study was to evaluate the safety and effectiveness of the GORE HELEX Septal Occluder for the closure of *ostium secundum* atrial septal defects. The purpose of the continued access study was to evaluate design modifications to the GORE HELEX Septal

Occluder. The design modifications incorporated into the GORE HELEX Septal Occluder were implemented based on investigator input and feedback given during the feasibility and pivotal trials.

### 10.3 Patient Selection

#### 10.3.1 Pivotal Study

The pivotal study enrolled 143 non-training subjects in the device treatment arm and 128 subjects in the surgical control arm at 14 clinical sites within the U.S. Investigators who did not participate in the feasibility study were required to complete 3 device training cases. Fifty subjects were enrolled as training cases and these subjects were excluded from the primary endpoint analyses.

Enrolled patients had echocardiographic evidence of an *ostium secundum* atrial septal defect and right heart volume overload (or as indicated by a  $Q_p:Q_s$  ratio of  $\geq 1.5:1$  for the device treatment arm). Patients enrolled in the device treatment arm had a defect size of 22 mm or less as measured by balloon sizing and an adequate rim to retain the device present in  $\geq 75\%$  of the circumference of the defect. Patients enrolled in the surgical control arm had surgical intervention within 12 months of Institutional Review Board (IRB) approval for the study, a minimum body weight of 8kg at the time of surgery, and a pre-operative, non-anesthetized echocardiogram performed within 6 months of the ASD surgery date. Exclusion criteria included:

- Patient had concurrent cardiac defect(s) that were associated with potentially significant morbidity or mortality that could elevate morbidity/mortality beyond what is common for ASD or that is expected to require surgical treatment within 2 years for the device treatment group or 5 years for the surgical control group.
- Patient had systemic or inherited conditions that would significantly increase patient risk of major morbidity and mortality during the term of the study.
- Patient had an uncontrolled arrhythmia.
- Patient had history of stroke.
- Patient was pregnant or lactating.
- Patient had contraindication to antiplatelet therapy (device treatment arm).
- Patient had a pulmonary artery systolic pressure greater than half the systemic systolic arterial pressure unless the indexed pulmonary artery resistance was  $< 5$  Woods units (device treatment arm).
- Patient had significant atrial septal aneurysm (device treatment arm).
- Patient had multiple defects that would require placement of  $>1$  device (device treatment arm).
- Patient had an atrial septum  $>8$ mm thick (device treatment arm).
- Patient had an attempted transcatheter septal defect closure device placement within 1 month of surgery (surgical control arm).
- Patient had significant pulmonary hypertension at the time of surgery (surgical control arm).
- Patient had already completed a routine 12-month post-operative evaluation (surgical control arm).

### 10.3.2 Continued Access Study

The continued access study enrolled 156 non-training subjects at 13 clinical sites within the U.S. as of December 15, 2005. Investigators who did not participate in the feasibility and pivotal studies were required to complete 3 device training cases and these cases were excluded from the primary analyses. Enrolled subjects met the same inclusion and exclusion criteria as the pivotal study subjects.

### 10.4 Demographics

The median age of the 143 subjects enrolled in the device treatment arm of the pivotal study was 6.5 years (range: 1.4 to 72.4 years) and 65.7% of the subjects were female. The median estimated defect size was 10 mm (range: 1.3 to 25 mm) and in subjects with a delivery attempt (n=134), the median stretched defect size was 14 mm (range 5 to 24 mm).

The median age of the 128 subjects enrolled in the surgical control arm of the pivotal study was 4.7 years (range: 0.6 to 70.4 years), and 63.3% of the subjects were female. The median estimated defect size was 15 mm (range: 1.5 to 42 mm).

The median age of the 156 non-training subjects enrolled in the continued access study was 5.5 years (range: 0.8 to 51.4 years) and 66.0% of the subjects were female. The median estimated defect size was 10 mm (range: 1.7 to 20.0 mm). In subjects with a delivery attempt (n=129), the median stretched defect size was 14 mm (range: 4 to 22 mm).

**Table 6**  
**GORE HELEX Septal Occluder Studies**  
**Subject Demographics**

	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI) <sup>1</sup>	
<b>Number of Subjects</b>	143	128		156
<b>Gender</b>				
Male	49 (34.3%)	47 (36.7%)	-2.5% (-13.9%, 9.0%)	53 (34.0%)
Female	94 (65.7%)	81 (63.3%)	2.5% (-9.0%, 13.9%)	103 (66.0%)
<b>Subject Ethnicity</b>				
White or Caucasian	95 (66.4%)	84 (65.6%)	0.8% (-10.5%, 12.1%)	106 (67.9%)
Black or African American	15 (10.5%)	9 (7.0%)	3.5% (-3.2%, 10.2%)	9 (5.8%)
Hispanic or Latino	26 (18.2%)	23 (18.0%)	0.2% (-9.0%, 9.4%)	20 (12.8%)
Asian	3 (2.1%)	7 (5.5%)	-3.4% (-8.0%, 1.2%)	5 (3.2%)
Other	3 (2.1%)	3 (2.3%)	-0.2% (-3.8%, 3.3%)	9 (5.8%)
Unknown	1 (0.7%)	2 (1.6%)	-0.9% (-3.4%, 1.7%)	7 (4.5%)
<b>Subject Age (years)</b>				
N	143	128		156
Mean (Std Dev)	12.4 (14.0)	9.2 (12.2)	3.2 (0.1, 6.4)	8.2 (8.3)
Median	6.5	4.7		5.5
Range	(1.4, 72.4)	(0.6, 70.4)		(0.8, 51.4)
<b>Weight (kg)</b>				
N	143	128		156
Mean (Std Dev)	35.6 (26.0)	27.5 (22.4)	8.2 (2.3, 14.0)	27.9 (20.5)
Median	23.0	17.5		19.0
Range	(9.2, 132.5)	(8.3, 135.0)		(6.9, 105.5)
<b>Body Surface Area (BSA)</b>				
N	143	128		156
Mean (Std Dev)	1.08 (0.51)	0.91 (0.46)	0.2 (0.1, 0.3)	0.92 (0.44)
Median	0.89	0.72		0.77
Range	(0.32, 2.61)	(0.38, 2.01)		(0.33, 2.07)
<b>Estimated ASD Size (mm)</b>				
N	141	124		155
Mean (Std Dev)	10.7 (3.8)	15.5 (6.3)	-4.8 (-6.1, -3.6)	10.0 (3.2)
Median	10.0	15.0		10.0
Range	(1.3, 25.0)	(1.5, 42.0)		(1.7, 20.0)

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

<sup>1</sup> Differences between Pivotal device and surgery groups and associated 95% confidence intervals

**Table 7**  
**GORE HELEX Septal Occluder Studies**  
**Subject Medical History**

	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI) <sup>1</sup>	
<b>Subjects Enrolled</b>	143	128		156
<b>General Medical History</b>				
Previous Cardiac Surgery	8 ( 5.6%)	4 ( 3.1%)	2.5% (-2.4%, 7.3%)	7 ( 4.5%)
ECG Abnormalities	72 ( 50.3%)	89 ( 69.5%)	-19.2% (-30.6%, -7.7%)	91 ( 58.3%)
Cardiac Arrhythmia(s)	12 ( 8.4%)	3 ( 2.3%)	6.0% (0.8%, 11.3%)	4 ( 2.6%)
Chromosomal Abnormalities	4 ( 2.8%)	7 ( 5.5%)	-2.7% (-7.4%, 2.1%)	12 ( 7.7%)
Emotional or Psychiatric Problems	5 ( 3.5%)	0 ( 0.0%)	3.5% (0.5%, 6.5%)	6 ( 3.8%)
Epilepsy	0 ( 0.0%)	0 ( 0.0%)	0.0% (0.0%, 0.0%)	1 ( 0.6%)
Failure to Thrive	1 ( 0.7%)	5 ( 3.9%)	-3.2% (-6.8%, 0.4%)	8 ( 5.1%)
Migraines	3 ( 2.1%)	1 ( 0.8%)	1.3% (-1.5%, 4.1%)	1 ( 0.6%)
Neurological Deficits/Symptoms	7 ( 4.9%)	5 ( 3.9%)	1.0% (-3.9%, 5.9%)	9 ( 5.8%)
Other (non-ASD) Cardiac Disease	15 ( 10.5%)	5 ( 3.9%)	6.6% (0.5%, 12.6%)	18 ( 11.5%)
Other Vascular Disease	2 ( 1.4%)	1 ( 0.8%)	0.6% (-1.8%, 3.1%)	2 ( 1.3%)
Pre-Term Baby	6 ( 4.2%)	8 ( 6.3%)	-2.1% (-7.4%, 3.3%)	12 ( 7.7%)
Respiratory Difficulties	14 ( 9.8%)	13 ( 10.2%)	-0.4% (-7.5%, 6.8%)	18 ( 11.5%)
Hepatitis	0 ( 0.0%)	0 ( 0.0%)		0 ( 0.0%)
Other	29 ( 20.3%)	43 ( 33.6%)	-13.3% (-23.8%, -2.8%)	68 ( 43.6%)
<b>Current Medication Pre-Procedure</b>				
Anti-arrhythmic	7 ( 4.9%)	2 ( 1.6%)	3.3% (-0.8%, 7.5%)	0 ( 0.0%)
Anti-coagulant	2 ( 1.4%)	0 ( 0.0%)	1.4% (-0.5%, 3.3%)	1 ( 0.6%)
Anti-hypertensive	4 ( 2.8%)	2 ( 1.6%)	1.2% (-2.2%, 4.7%)	0 ( 0.0%)
Anti-platelet	10 ( 7.0%)	2 ( 1.6%)	5.4% (0.7%, 10.1%)	13 ( 8.3%)
Diuretic	5 ( 3.5%)	5 ( 3.9%)	-0.4% (-4.9%, 4.1%)	3 ( 1.9%)
Other	36 ( 25.2%)	29 ( 22.7%)	2.5% (-7.6%, 12.7%)	42 ( 26.9%)

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

<sup>1</sup> Differences between Pivotal device and surgery groups and associated 95% confidence intervals

## 10.4 Design

### 10.4.1 Pivotal Study

The Multicenter Pivotal Study of the GORE HELEX Septal Occluder was a non-randomized, controlled trial comparing safety and efficacy outcomes of the GORE HELEX Septal Occluder with traditional (open) surgical repair of atrial septal defects.

The primary study endpoint was clinical success, a composite evaluation of safety and efficacy, which was evaluated at 12 months post-procedure. Clinical success was defined as: 1) A residual defect classified as either completely occluded or clinically insignificant leak as determined by echocardiography core lab assessment; 2) No repeat procedure to the target ASD; and 3) No major device- or procedure-related adverse events. The study was designed to demonstrate that the clinical success rate of the GORE HELEX Septal Occluder was not inferior to the clinical success rate for surgical closure of ASDs.

Additional safety endpoints included the proportion of subjects experiencing one or more major and minor device-related and/or procedure-related adverse events through 12 months post-procedure. Additional efficacy endpoints included delivery (technical) success, defined as successful deployment and accurate placement of the GORE HELEX Septal Occluder to the target ASD, and treatment efficacy, defined as the proportion of subjects with a final residual defect assessment of clinically successful closure (completely occluded or clinically insignificant leak).

#### 10.4.2 Continued Access Study

The continued access study was a prospective, single-arm trial intended to evaluate design modifications to the GORE HELEX Septal Occluder. The design modifications incorporated into the GORE HELEX Septal Occluder were implemented based on investigator input and feedback given during the feasibility and pivotal trials. The continued access study endpoints were the same as those of the pivotal study and were evaluated at 12 months.

### 10.5 Method

#### 10.5.1 Pivotal Study - Device Treatment Arm

For patients enrolled in the device treatment arm of the pivotal study, dimensional verification and characterization of the ASD and surrounding cardiac structures were performed per the investigator's standard methods. An initial static measurement of the septal defect was obtained during echocardiographic visualization. A second measurement was taken utilizing a balloon to gently stretch the defect and measure the balloon's waist (narrowest portion of the balloon), and the balloon stretched defect size was used to determine the optimal size of the GORE HELEX Septal Occluder per Instructions for Use (IFU) recommendations. Fluoroscopic and echocardiographic guidance were used throughout the procedure for placement of, and at the completion of each procedure to assess the status of, the GORE HELEX Occluder.

There was no requirement for prior therapy or medical management. All subjects were placed on the investigator's choice of antiplatelet therapy for 6 months following implantation of the GORE HELEX Septal Occluder, and on prophylactic, post-procedure antibiotic therapy consistent with the investigator's routine procedure.

Follow-up evaluations, which included a physical exam, ECG, and an assessment of the residual defect status by transthoracic echocardiography (TTE), were performed at hospital discharge, and at 1, 6, and 12 months post-procedure. If the TTE was inconclusive, a TEE or angiography may have been performed. At the 6 and 12 month follow-up visits, fluoroscopic examinations were performed to assess device integrity.

#### 10.5.2 Pivotal Study - Surgical Control Arm

Investigators identified surgical control subjects at their respective sites who had undergone an open-heart surgical ASD closure within 12 months of IRB approval of the pivotal study, and who also met the inclusion/exclusion criteria for the control arm. Open-heart surgical ASD repair was performed per the investigator's standard procedure, and was achieved by suturing the defect edges or by implantation of autologous or synthetic patch materials over the defect.

Subjects were placed on antiplatelet therapy and prophylactic, post-procedure antibiotic therapy at the investigator's discretion and consistent with investigator's standard method.

Follow-up evaluations, which included a physical exam, ECG, and an assessment of the residual defect status by TTE, were performed at hospital discharge and at 12 months. If the TTE was inconclusive, a TEE or angiography may have been performed.

### 10.5.3 Continued Access Study

The methodology and follow-up of the continued access study was the same as that of the device treatment arm of the pivotal study.

## 10.6 Results

### 10.6.1 Pivotal Study - Device Treatment Arm

The GORE HELEX Septal Occluder was successfully implanted in 88.1% (119/135) of subjects with a delivery attempt. No deaths, device-related thrombus, perforations, or erosions requiring surgery were reported. Major adverse events were reported in 5.9% of subjects with a successful delivery through the 12-month follow-up. Clinically successful closure (complete occlusion or clinically insignificant leak), as determined by echocardiographic core laboratory review, was achieved in 98.1% of subjects evaluated at 12 months post-procedure. The primary clinical success endpoint was achieved in 91.7% of subjects evaluated.

### 10.6.2 Pivotal Study - Surgical Control Arm

Major adverse events were reported in 10.9% of control subjects. One death resulting from complications of post-pericardiotomy syndrome was reported. Clinically successful closure, as determined by echocardiographic core laboratory review, was achieved in 100% of subjects evaluated at 12 months post-procedure. Clinical success was achieved in 83.7% of subjects evaluated.

### 10.6.3 Continued Access Study

The GORE HELEX Septal Occluder was successfully implanted in 85.6% of subjects with an attempt. No deaths, device-related thrombus, perforations, or erosions requiring surgery were reported. Major adverse events were reported in 3.9% of subjects with a successful delivery who have been evaluated through 12 months. Clinically successful closure, as determined by echocardiographic core laboratory review, was achieved in 98.0% of subjects who have been evaluated at 12 months post-procedure. The primary clinical success endpoint was achieved in 92.6% of subjects evaluated.

### 10.6.4 Tables of Safety and Effectiveness Results

The principal safety and effectiveness results through 12 months and the procedure outcomes for the pivotal and continued access studies are reported in **Tables 8 and 9**.

**Table 8**  
**GORE HELEX Septal Occluder Studies**  
**Principal Safety and Effectiveness Results**

Study Outcomes	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI) <sup>4</sup>	
<b>Technical Success<sup>1</sup></b>	119/135 (88.1%)	na	na	113 / 132 (85.6%)
<b>Clinical Closure Success<sup>2</sup></b>				
Pre-Discharge	115/118 (97.5%)	123/123 (100%)	-2.5% (-5.4%, 0.3%)	110/112 (98.2%)
Month 6	99/101 (98.0%)	na	na	80/80 (100%)
Month 12	103/105 (98.1%)	82/82 (100%)	-1.9% (-4.5%, 0.7%)	50/51 (98.0%)
<b>Principal Safety Measures</b>				
Major Adverse Events 12 Months	7/119 (5.9%)	14/128 (10.9%)	-5.1% (-11.9%, 1.8%)	3/77 (3.9%)
Minor Adverse Events 12 Months	34/119 (28.6%)	36/128 (28.1%)	0.4% (-10.8%, 11.7%)	21/77 (27.3%)
Survival at 365 Days (K-M)	100%	99.1%		100%
<b>Composite Clinical Success 12 Months<sup>3</sup></b>	100/109 (91.7%)	72/86 (83.7%)	8.0% (-1.3%, 17.4%)	50/54 (92.6%)

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

<sup>1</sup> Technical Success defined as successful delivery of the device in subjects with a delivery attempted

<sup>2</sup> Clinical Closure Success defined as residual defect that is either Completely Occluded or Clinically Insignificant Leak. Leak status was evaluated by the investigational sites at pre-discharge and 6 months and by the echocardiography core laboratory at 12 months

<sup>3</sup> Composite Clinical Success defined as no major adverse event or repeated procedure and clinical closure success at 12 months

<sup>4</sup> Differences between Pivotal device and surgery groups and associated 95% confidence intervals

**Table 9**  
**GORE HELEX Septal Occluder Studies**  
**Procedural Outcomes**

	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI) <sup>1</sup>	
<b>Subjects with Delivery Attempt/Surgery</b>	135	128		132
<b>Total Time Under Fluoroscopy (minutes)</b>				
N	134	na		127
Mean (Std Dev)	28 (21)			23 (16)
Median	22			19
Range	(6, 148)			(5, 116)
<b>Total Time Under Anesthesia (minutes)</b>				
N	133	128		125
Mean (Std Dev)	168 (63)	205 (43)	-37.1 (-50.3, -23.9)	157 (61)
Median	160	202		153
Range	(55, 360)	(30, 330)		(30, 380)
<b>Days in Hospital for Procedure</b>				
N	135	128		129
Mean (Std Dev)	1 (0)	3 (1)	-1.9 (-2.1, -1.7)	1 (0)
Median	1	3		1
Range	(0, 4)	(1, 9)		(0, 2)

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

<sup>1</sup> Differences between Pivotal device and surgery groups and associated 95% confidence intervals

**Table 10** presents the number of devices attempted and number of those successfully delivered for each device size overall and by subject age at procedure for combined device subjects from the pivotal and continued access studies.

**Table 10**  
**GORE HELEX Septal Occluder Studies**  
**Number of Devices Attempted and Successfully Delivered**  
**By Device Size and Subject Age at Procedure**

	HELEX 15 mm (N <sub>S</sub> /N <sub>A</sub> ) <sup>1</sup>	HELEX 20 mm (N <sub>S</sub> /N <sub>A</sub> ) <sup>1</sup>	HELEX 25 mm (N <sub>S</sub> /N <sub>A</sub> ) <sup>1</sup>	HELEX 30 mm (N <sub>S</sub> /N <sub>A</sub> ) <sup>1</sup>	HELEX 35 mm (N <sub>S</sub> /N <sub>A</sub> ) <sup>1</sup>	Overall (N <sub>S</sub> /N <sub>A</sub> ) <sup>1</sup>
<b>Subject Age</b>						
Infant (< 2 yrs)	1 / 1	3 / 4	2 / 5	0	0	6 / 10
Child (2-5 yrs)	5 / 5	21 / 35	53 / 100	27 / 64	4 / 12	110 / 216
Child (6-11 yrs)	3 / 4	10 / 12	15 / 24	23 / 41	4 / 12	55 / 93
Adolescent (12-20 yrs)	2 / 2	6 / 9	11 / 15	10 / 16	12 / 22	41 / 64
Adult (21+ yrs)	0	0	5 / 6	7 / 8	9 / 13	21 / 27
<b>Overall</b>	<b>11 / 12</b>	<b>40 / 60</b>	<b>86 / 150</b>	<b>67 / 129</b>	<b>29 / 59</b>	<b>233 / 410</b>

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

<sup>1</sup> N<sub>S</sub> = Number of successful device deliveries, N<sub>A</sub> = number of devices attempted.

**Table 11** presents the frequency of reported medications at follow-up visits for combined device subjects from the pivotal and continued access studies.

**Table 11**  
**GORE HELEX Septal Occluder Studies**  
**Summary of Reported Medications for Device Subjects**

	Pre- Procedure	Pre-Discharge	Six Months	Twelve Months
<b>Medications</b>				
Anti-Platelet	23/300 (7.8%)	200/231 (86.6%)	122/183 (66.7%)	14/177 (7.9%)
Anti-Arrhythmic	7/300 (2.3%)	6/231 (2.6%)	5/183 (2.7%)	4/177 (2.3%)
Anti-Hypertensive	4/300 (1.3%)	2/231 (0.9%)	3/183 (1.6%)	3/177 (1.7%)
Anti-Coagulant	3/300 (1%)	12/231 (5.2%)	2/183 (1.1%)	3/177 (1.7%)
Diuretic	8/300 (2.7%)	2/231 (0.9%)	2/183 (1.1%)	2/177 (1.1%)

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

**Table 12** presents a summary of procedural fluoroscopy time by device delivery success and number of devices attempted for combined device subjects from the pivotal and continued access studies.

**Table 12**  
**GORE HELEX Septal Occluder Studies**  
**Summary of Procedural Fluoroscopy Times for Device Subjects**

	N	Median (minutes)	Range (minutes)
<b>Subjects with Successful Delivery</b>	232	18.7	(5.3, 92.1)
<b>One Device Attempted</b>	161	15.7	(5.3, 46.6)
<b>Two Devices Attempted</b>	49	28.6	(9.8, 76.1)
<b>Three or More Devices Attempted</b>	22	40.0	(24.0, 92.1)
<b>Subjects with Unsuccessful Delivery</b>	35	36.2	(13.4, 148.0)
<b>One Device Attempted</b>	17	27.3	(13.4, 51.3)
<b>Two Devices Attempted</b>	9	34.9	(31.3, 56.2)
<b>Three or More Devices Attempted</b>	9	72.4	(41.5, 148.0)

NOTE: Analysis includes all nontraining Pivotal subjects and Continued Access subjects enrolled and evaluated through 12 month follow-up as of database closure on 12/15/05

## 10.7 Conclusions

The clinical success outcomes satisfied the primary, non-inferiority hypothesis for the pivotal study ( $p < 0.001$  using two-sample binomial proportions test with non-inferiority margin of 10%) and indicated that the clinical success rate of the GORE HELEX Septal Occluder is not inferior to surgical closure.

## 11.0 Device Malfunctions

- Wire frame fractures have been identified in 19 subjects evaluated through the 12-month follow-up, which includes both training and non-training subjects. Two additional fractures were reported in the Feasibility Study after the 12 month follow-up (Year 2 and Year 4 follow-up visits). Two of the fractures occurred in the lock loop, all other fractures were in the circumferential wire frame.

After reviewing case reports the DSMB determined that frame fractures without complications were classified as minor adverse events. With the exception of the transcatheter removal of one device in the Continued Access study, which was classified as a major adverse event, no other adverse events or clinical sequela have been attributed to frame fracture.

In a review of all source documents, provided from all studies;

- A total of 17 mandrel or catheter kink-related malfunctions were reported in all studies.
- Retrieval cord break or entanglement/detachment was reported in 25 cases. Nine cord breaks and 16 cord entanglements/detachments were reported. There were no clinical sequelae associated with any of these malfunctions.
- A total of 39 events involving premature lock release (34) and missed eyelets (5) were reported. There were no clinical sequelae associated with any of these malfunctions.

## 12.0 Conclusions Drawn From the Studies

The GORE HELEX Septal Occluder is a reasonably safe and effective treatment for *ostium secundum* atrial septal defects as demonstrated by:

- Clinical success (defined as a residual defect classified as either completely occluded or clinically insignificant leak, no repeat procedure to the target ASD, and no major device- or procedure-related adverse events) in 91.7% of subjects evaluated at 12 months post-procedure.
- A low occurrence of major adverse events (5.9%) at 12 months post-procedure.
- Wire frame fractures discovered at the 6 or 12-month follow-up have not been associated with clinical sequelae.

The clinical studies demonstrated that the GORE HELEX Septal Occluder operates as designed and is reasonably safe and effective for its intended use.

## 13.0 Panel Recommendation

In accordance with the provisions of section 515(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this Panel.

## 14.0 CDRH Decision

CDRH issued two letters to W.L. Gore & Associates on May 9, and June 27, 2006 advising that the PMA was approvable subject to changes to the labeling, and post-approval study protocols. W.L. Gore addressed the requested changes to the labeling and post-approval study protocols in their responses to the approvable letters. The applicant also concurred to the following conditions of approval:

1. The long-term safety and effectiveness of the GORE HELEX™ Septal Occluder will be further characterized by following for 5 years the first 50 subjects enrolled in your continued access study, as the data from the first 50 subjects were provided in the premarket application to support approval of device modifications. At least 80% of these subjects should be available for follow-up out to 2 years. These data should be gathered in accordance with the continued access protocol provided in your submission dated August 8, 2006. Summary reports should be submitted to the Agency annually and a final report should be submitted at the end of the study. Please be advised that the long-term study data should be incorporated into the labeling when the study is complete.
2. The long-term safety and effectiveness of the device will be further characterized by following for 5 years at least 200 subjects that do not include the first 50 subjects enrolled in your continued access study. At least 80% of these subjects should be available for follow-up out to 2 years. These data

should be gathered in accordance with the postapproval study protocols provided in your submission dated August 8, 2006. Summary reports should be submitted to the Agency annually and a final report should be submitted at the end of the study. Please be advised that the postapproval study data should be incorporated into the labeling when the study is complete.

FDA issued an approval order on August 11, 2006.

The applicant's manufacturing facility was inspected on October 11-13, 2005 and was found to be in compliance with the Quality System Regulation (21 CFR 820).

## **15.0 Approval Specifications**

Directions for Use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.

Post-Approval Requirements and Restrictions: See approval order.

8-11-06