Summary of Safety and Effectiveness Data

A. General Information

Device Generic Name:	Vascular Hemostasis Device
Device Trade Name:	Mynx Vascular Closure Device
Applicant:	Access Closure, Inc. 645 Clyde Avenue Mountain View, CA 94043
Premarket Approval Application (PMA) Number:	P040044/S001
Date of Panel Recommendation:	None

Date of Notice of Approval to Applicant: May 16, 2007

The original PMA application (P040044) for the Matrix VSG System was approved on August 17, 2005. Information from the original application is applicable to the current supplemental application for the Mynx Vascular Closure Device, and is incorporated by reference. Please refer to the SSED via the CDRH website at http://www.fda.gov/cdrh/pmapage.html. Written requests for copies can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852 under Docket #05M-0359.

B. Indications for Use

Mynx is indicated for use to seal femoral arterial access sites while reducing times to hemostasis and ambulation in patients who have undergone diagnostic or interventional endovascular procedures utilizing a 5F, 6F or 7F procedural sheath.

C. Contraindications

There are no known contraindications to the use of Mynx.

D. Warnings and Precautions

The warnings and precautions are located in the Mynx Instructions for Use.

E. Device Description

1. Materials and Configuration

Mynx is comprised of a polyethylene glycol (PEG) synthetic sealant that is delivered extravascularly using a balloon catheter to seal femoral arterial access site punctures. Mynx is provided sterile in a sealed pouch. The device components are:

- Balloon catheter with integrated water-soluble synthetic sealant
- 10 ml locking syringe

2. Principles of Operation

At the end of a diagnostic or interventional procedure, the Mynx balloon catheter is inserted through the existing introducer sheath in the femoral artery to provide temporary hemostasis at the arteriotomy site. Upon deployment, the balloon catheter temporarily seals the arteriotomy from inside the artery. The shuttle is advanced towards the arteriotomy site and retracted to expose the freeze-dried water-soluble synthetic sealant. A tamping tube is used to localize the sealant at the arteriotomy site. The sealant rapidly swells as it is exposed to blood and other fluids, and forms a flexible sealant that provides local hemostasis. After delivery of the sealant, the balloon catheter is deflated and removed along with the introducer sheath and tamping tube. The sealant subsequently bioresorbs completely within 30 days.

F. Alternative Practices and Procedures

Alternative practices for achieving hemostasis of the femoral artery access sites post-catheterization procedures include manual or mechanical compression methods, collagen hemostasis sealing and suturing devices. Pressure dressings and sandbags are routinely used in combination with compression methods to control access site oozing.

G. Marketing History

Mynx has not been marketed in the United States or any foreign country.

H. Potential Adverse Effects of the Device on Health

Mynx was evaluated in a prospective, multi-center, non-randomized clinical trial designed to evaluate the safety and effectiveness of Mynx in sealing femoral arterial access sites. The study was conducted in Europe at 5 institutions involving 190 pivotal patients, using the control group (patients treated with standard compression) from the MATRIX Trial, conducted under IDE# G030182 as a historical control group. Of the patients enrolled in the Mynx Trial, 95 patients (50%) underwent diagnostic procedures and 95 patients (50%) underwent interventional procedures. Patients eligible for participation included candidates for early ambulation and patients who were clinically indicated for a diagnostic or an interventional procedure involving access through the femoral artery using a 5F, 6F or 7F sheath.

Table 1 provides an event-based analysis of the complications reported for the Mynx patients during the 30-day follow-up period and a comparison to the standard compression patients enrolled in the MATRIX Trial. **Tables 2 and 3** include the same information stratified by type of procedure (diagnostic and interventional).

Table 1: Major and Minor Complications (Intent-to-Treat)
All Patients

All Patients	Mynx* (n=190)	Standard Compression (n=164)	p-value†
Major Complications By Event			
Vascular Repair	0.0% (0/190)	0.0% (0/164)	N/A
Permanent Access Site-Related Nerve Injury	0.0% (0/190)	0.0% (0/164)	N/A
Surgery For Access Site-Related Nerve Injury	0.0% (0/190)	0.0% (0/164)	N/A
Access Site-Related Bleeding Requiring Transfusion	0.5% (1/190)	0.0% (0/164)	0.0021
New Ipsilateral Lower Extremity Ischemia Requiring Invasive/Non Invasive Intervention	0.0% (0/190)	0.0% (0/164)	N/A
Access Site-Related Infection - Major	0.0% (0/190)	0.0% (0/164)	N/A
Local Access Site Inflammatory Reaction - Major	0.0% (0/190)	0.0% (0/164)	N/A
Generalized Infection	0.0% (0/190)	0.0% (0/164)	N/A
Any Major Complication	**0.5% (1/190)**	**0.0% (0/164)**	**0.0021**
Minor Complications By Event			
Pseudoaneurysm – Treated With Thrombin Injection	0.5% (1/190)	0.0% (0/164)	0.0021
Pseudoaneurysm - Not Requiring Treatment ‡	2.6% (5/190)	0/0% (0/164)	0.0831
AV Fistula	0.0% (0/190)*	0.0% (0/164)	N/A
Hematoma ≥ 6 cm	3.2% (6/190)* §	0.6% (1/164)	0.0853
Access Site-Related Bleeding Requiring > 30 min to Achieve Hemostasis	0.0% (0/190)	0.6% (1/164)	0.0002
Late Access Site-Related Bleeding (Following Hospital Discharge)	0.0% (0/190)	0.0% (0/164)	N/A
Ipsilateral Lower Extremity Arterial Emboli	0.0% (0/190)	0.0% (0/164)	N/A
Transient Loss of Ipsilateral Lower Extremity Pulse	0.0% (0/190)	0.0% (0/164)	N/A
Ipsilateral Deep Vein Thrombosis	0.0% (0/190)*	0.0% (0/164)	N/A
Transient Access Site-Related Nerve Injury	0.0% (0/190)	0.0% (0/164)	N/A
Access Site-Related Vessel Laceration	0.0% (0/190)	0.0% (0/164)	N/A
Access Site Wound Dehiscence	0.0% (0/190)	0.0% (0/164)	N/A
Local Access Site Infection - Minor	0.0% (0/190)	0.0% (0/164)	N/A
Local Access Site Inflammatory Reaction - Minor	0.0% (0/190)	0.0% (0/164)	N/A
Any Minor Complication	**3.7% (7/190)**	**1.2% (2/164)**	0.0921

* Does not include non-device related events consisting of: AV Fistula (n=2), Ipsilateral Deep Vein Thrombosis (n=1), and Hematoma (n=1).

§ Does not include 1 patient with a pre-existing hematoma prior to deployment of Mynx.
‡ In a subset of patients treated with Mynx, ultrasound assessment was performed prior to patient discharge which revealed some patients had developed small pseudoaneurysms which resolved spontaneously. The events are reported in the table above, but are not included in the overall rate of minor complications.
† p-value based on test for non-inferiority

Table 2. Major and Minor Complications (Intent-to-Treat) Diagnostic Patients

Diagnostic Patients	Mynx* (n=95)	Standard Compression (n=83)	p-value†
Major Complications By Event			
Vascular Repair	0.0% (0/95)	0.0% (0/83)	N/A
Permanent Access Site-Related Nerve Injury	0.0% (0/95)	0.0% (0/83)	N/A
Surgery For Access Site-Related Nerve Injury	0.0% (0/95)	0.0% (0/83)	N/A
Access Site-Related Bleeding Requiring Transfusion	0.0% (0/95)	0.0% (0/83)	N/A
New Ipsilateral Lower Extremity Ischemia Requiring Invasive/Non Invasive Intervention	0.0% (0/95)	0.0% (0/83)	N/A
Access Site-Related Infection - Major	0.0% (0/95)	0.0% (0/83)	N/A
Local Access Site Inflammatory Reaction - Major	0.0% (0/95)	0.0% (0/83)	N/A
Generalized Infection	0.0% (0/95)	0.0% (0/83)	N/A
Any Major Complication	**0.0% (0/95)**	**0.0% (0/83)**	N/A
Minor Complications By Event			
Pseudoaneurysm - Treated With Thrombin Injection	1.1% (1/95)	0.0% (0/83)	0.0459
Pseudoaneurysm - Not Requiring Treatment ‡	1.1% (1/95)	0.0% (0/83)	0.0459
AV Fistula	0.0% (0/95)*	0.0% (0/83)	N/A
Hematoma ≥ 6 cm	2.1% (2/95)*§	1.2% (1/83)	0.0599
Access Site-Related Bleeding Requiring > 30 min to Achieve Hemostasis	0.0% (0/95)	0.0% (0/83)	N/A
Late Access Site-Related Bleeding (Following Hospital Discharge)	0.0% (0/95)	0.0% (0/83)	N/A
Ipsilateral Lower Extremity Arterial Emboli	0.0% (0/95)	0.0% (0/83)	N/A
Transient Loss of Ipsilateral Lower Extremity Pulse	0.0% (0/95)	0.0% (0/83)	N/A
Ipsilateral Deep Vein Thrombosis	0.0% (0/95)	0.0% (0/83)	N/A
Transient Access Site-Related Nerve Injury	0.0% (0/95)	0.0% (0/83)	N/A
Access Site-Related Vessel Laceration	0.0% (0/95)	0.0% (0/83)	N/A
Access Site Wound Dehiscence	0.0% (0/95)	0.0% (0/83)	N/A
Local Access Site Infection - Minor	0.0% (0/95)	0.0% (0/83)	N/A
Local Access Site Inflammatory Reaction - Minor	0.0% (0/95)	0.0% (0/83)	N/A
Any Minor Complication	**3.2% (3/95)**	**1.2% (1/83)**	0.1458

* Excludes non-device related events consisting of: AV Fistula (n=2) and Hematoma (n=1).
§ Excludes 1 patient with pre-existing hematoma prior to deployment of Mynx.
‡ In a subset of patients treated with Mynx, ultrasound assessment prior to patient discharge was required which revealed some patients had developed pseudoaneurysms which resolved spontaneously. The event is reported in the table above, but is not included in the overall rate of minor complications.
† p-value based on test for non-inferiority.

Table 3. Major and Minor Complications (Intent-to-Treat) Interventional Patients

Interventional Patients	Mynx* (n=95)	Standard Compression (n=81)	p-value†
Major Complications By Event			
Vascular Repair	0.0% (0/95)	0.0% (0/81)	N/A
Permanent Access Site-Related Nerve Injury	0.0% (0/95)	0.0% (0/81)	N/A
Surgery For Access Site-Related Nerve Injury	0.0% (0/95)	0.0% (0/81)	N/A
Access Site-Related Bleeding Requiring Transfusion	1.1% (1/95)	0.0% (0/81)	0.0459
New Ipsilateral Lower Extremity Ischemia Requiring Invasive/Non Invasive Intervention	0.0% (0/95)	0.0% (0/81)	N/A
Access Site-Related Infection - Major	0.0% (0/95)	0.0% (0/81)	N/A
Local Access Site Inflammatory Reaction - Major	0.0% (0/95)	0.0% (0/81)	N/A
Generalized Infection	0.0% (0/95)	0.0% (0/81)	N/A
Any Major Complication	**1.1% (1/95)**	0.0% (0/81)	0.0459
Minor Complications By Event			
Pseudoaneurysm - Treated With Thrombin Injection	0.0% (0/95)	0.0% (0/81)	N/A
Pseudoaneurysm - Not Requiring Treatment**	4.2% (4/95)	0.0% (0/81)	0.4819
AV Fistula	0.0% (0/95)	0.0% (0/81)	N/A
Hematoma ≥ 6 cm	4.2% (4/95)	0.0% (0/81)	0.4819
Access Site-Related Bleeding Requiring > 30 min to Achieve Hemostasis	0.0% (0/95)	1.2% (1/81)	0.0060
Late Access Site-Related Bleeding (Following Hospital Discharge)	0.0% (0/95)	0.0% (0/81)	N/A
Ipsilateral Lower Extremity Arterial Emboli	0.0% (0/95)	0.0% (0/81)	N/A
Transient Loss of Ipsilateral Lower Extremity Pulse	0.0% (0/95)	0.0% (0/81)	N/A
Ipsilateral Deep Vein Thrombosis	0.0% (0/95)*	0.0% (0/81)	N/A
Transient Access Site-Related Nerve Injury	0.0% (0/95)	0.0% (0/81)	N/A
Access Site-Related Vessel Laceration	0.0% (0/95)	0.0% (0/81)	N/A
Access Site Wound Dehiscence	0.0% (0/95)	0.0% (0/81)	N/A
Local Access Site Infection - Minor	0.0% (0/95)	0.0% (0/81)	N/A
Local Access Site Inflammatory Reaction - Minor	0.0% (0/95)	0.0% (0/81)	N/A
Any Minor Complication	**4.2% (4/95)**	**1.2% (1/81)**	0.2950

* Excludes non-device related events consisting of: Ipsilateral Deep Vein Thrombosis (n=1).
**In a subset of patients treated with Mynx, ultrasound assessment prior to patient discharge was required which revealed some patients had developed pseudoaneurysms which resolved spontaneously. The events are reported in the table above but are not included in the overall rate of minor complications.
† p-value based on test for non-inferiority.

The combined rate of major complications was the primary safety endpoint of the trial. A major complication was defined as vascular repair, surgically treated or permanent nerve injury at the access site, access site-related transfusion, any new ipsilateral lower extremity ischemia, access site-related infection treated with intravenous (IV) antibiotics or re-hospitalization, inflammatory reaction treated with IV antibiotics, surgical intervention or extended hospitalization and generalized infection or septicemia treated with IV antibiotics. The major complication rate for all patients in

the Mynx group was 0.5% (1/190) compared to 0.0% (0/164) in the standard compression group.

The combined rate of minor complications was the secondary safety endpoint. A minor complication was defined as pseudoaneurysm treated with thrombin injection, AV fistula, hematoma ≥ 6 cm, access site-related bleeding requiring > 30 minutes to re-achieve hemostasis, late access site-related bleeding, ipsilateral lower extremity arterial emboli, transient loss of ipsilateral lower extremity pulse, ipsilateral deep vein thrombosis, transient access site-related nerve injury, access site-related vessel laceration, access site wound dehiscence, access site infection treated with intramuscular or oral antibiotics, and access site inflammation treated with oral antibiotics. The minor complication rate for all patients in the Mynx group was 3.7% (7/190) compared to 1.2% (2/164) in the standard compression group. The study was not designed to test any formal hypotheses for the secondary endpoints. The rate of any complication (major or minor) for all patients was 4.2% for Mynx and 1.2% for standard compression.

None of the complications in the Mynx Trial were considered unanticipated events. The observed complication rates support the trial hypotheses that the combined rate of major complications for the Mynx arm are non-inferior to those of the historical control group. There were no deaths during the study.

Potential complications of allergic reaction, foreign body reaction, inflammation, infection, or vessel laceration were not observed during this study.

I. Summary of Preclinical Studies

1. *In Vitro* Product Bench Testing

A series of *in vitro* tests were conducted to verify the performance of Mynx. Mynx devices were tested in accordance with the acceptance criteria defined in the Mynx product specification (PS1483) or as specified in the design verification test protocol (TPR2045-01). All of the test results met or exceeded the specified requirements in the product specification and test protocols. Device testing included the following:

- Environmental conditioning test
- Altitude and simulated transportation test
- Packaging integrity—leak test, seal strength integrity, sterility
- Catheter functional testing—balloon diameter, balloon length, distal necked shaft profile, delivery cartridge outer diameter, pusher engagement marker length, balloon crossing profile, sealant position, catheter length, balloon inflation time, balloon deflation time, catheter fatigue, catheter fixed weight, pressure relief, catheter/balloon rupture strength, catheter tensile strength, catheter removal force, unsheathing force
- Sealant testing – sealant swelling, sealant thickness, sealant disappearance
- Bacterial endotoxin testing (Limulus Amebocyte Lysate)

2. Biocompatibility Testing

Biocompatibility testing of Mynx was conducted in accordance with the FDA guidance document entitled, "Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices, May 1, 1995 (G95-1)" and International Organization for Standards 10993: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing, Third Edition 2003-08-01." Due to the similarities in materials between Mynx and MATRIX, the biocompatibility test results for MATRIX were used to support the biocompatibility of Mynx. Additional confirmatory testing was performed on Mynx devices to support the biocompatibility of new materials and changes in sealant processing.

The following tests were conducted on MATRIX devices: cytotoxicity, sensitization, intracutaneous reactivity, systemic toxicity, genotoxicity, implantation, hemolysis and pyrogen. As confirmatory testing, Mynx devices successfully completed hemolysis, cytotoxicity, intracutaneous reactivity, and two and four week implantation studies.

The results of the Mynx testing confirmed that Mynx is non-cytotoxic, non-hemolytic, and the Mynx sealant is a non-irritant as demonstrated in the intracutaneous reactivity study. In addition, the subcutaneous implantation study demonstrated that the sealant is a non-irritant macroscopically and microscopically at four weeks. These results are equivalent to the MATRIX biocompatibility testing results that also demonstrated the water-soluble synthetic sealant was a non-irritant macroscopically and microscopically at four weeks.

3. Sterilization Validation Testing

Mynx devices are sterilized using electron beam (e-beam) irradiation. Sterilization validation testing was performed on three consecutive lots to provide a high degree of assurance that e-beam irradiation was effective in routinely and reliably achieving sterility of Mynx at a sterility assurance level (SAL) of 10^{-6}.

The Mynx sterilization validation testing demonstrated that the e-beam sterilization process will routinely and reliably:

- Produce a sterility assurance level that meets or exceeds a probability of a single microbial survivor of one in one million (SAL = 10^{-6})
- Demonstrate that the intended sterilization process is reliable, reproducible and can consistently meet the process specifications
- Substantiate the target sterilization dose for Mynx

4. Shelf Life Testing

Shelf life testing was previously performed on Matrix (Model #MX-100). The results of the shelf life testing supporting a shelf life of 9 months were reported in the Matrix

PMA (#P040044) for Matrix. Data from the shelf life testing of Matrix remain applicable to Mynx since the materials used in the manufacture of both devices are very similar, if not identical, with the exception of two new materials (a fluorinated ether oil lubricant and a cyanoacrylate activator) that were introduced in Mynx. Neither of the two new materials is intended for patient contact.

Additional 15-month real time aging was performed on Matrix devices and subsequent testing demonstrated that the devices met the requirements defined in the product specification. The data therefore support a shelf life of 12 months.

5. Animal Studies

Acute and chronic animal studies were performed to confirm the safety and performance of Mynx. In an acute study, a total of 8 femoral puncture sites in two sheep were evaluated, including 6 sites treated with Mynx devices and 2 control puncture sites treated with manual compression. All Mynx devices were successfully deployed according to the Instructions for Use. The mean time to hemostasis for sites treated with Mynx was 1.5 minutes, compared to 7.5 minutes for the manual compression control. All vessels were evaluated with Doppler ultrasound and determined to be patent with normal hemodynamics and no evidence of obstruction or embolization and no remarkable difference from the baseline evaluation. One small hematoma was reported above the artery for one of the control puncture sites. No other adverse events were reported.

In a chronic study, four female pigs were used. Two of the animals received Matrix in the ipsilateral femoral artery and Mynx at the contralateral femoral artery. The remaining two animals were treated with Mynx on both the ipsilateral and contralateral sides. Each of the 6 Mynx deployments was successful in achieving hemostasis within 30 seconds following device deployment and removal. The Matrix devices were successful in achieving access site hemostasis within two minutes of the procedure. Acute success following each deployment was verified via direct visual observation of the groin site.

Two hours post-procedure, ultrasound findings for each of the treated access sites confirmed that there were no signs of post procedure extravasation or impeded flow at or distal to the access site.

Each animal was monitored for 29 days at least once daily and observed for groin site abnormalities. The animals were also graded with respect to ambulation. At day 29, a final visual assessment was performed to assess wound site healing followed by angiographic follow-up to assess the treated vessels for patency and to look for any intra-arterial disturbances or abnormalities that may be related to Mynx or Matrix. Visual observation showed the access sites were completely healed. Upon angiographic visualization, vessel patency was noted in all Mynx and Matrix access (treatment) sites showing strong arterial flow and patent vessels with no narrowing or other abnormalities.

Upon sacrifice of each animal, an animal autopsy was performed. At this time, the pathologist performed gross pathology of the liver, spleen, lungs, kidneys and other vital organs and confirmed all to be in pristine condition for each animal. In addition, it was noted at all treatment sites that the sealant had fully degraded and there was a minimal presence of fibrous tissue (secondary to trauma resulting from the initial puncture and procedural sheath placement).

Histological findings were consistent with minimal foreign body reaction to a substance of this nature. The implanted synthetic sealant did not elicit any reactions that were uncharacteristic or unexpected. The substance in its solid and liquid form promoted complete healing at the arteriotomy site and the cellular response was completely normal. Despite ongoing cellular activity, neither Matrix nor Mynx was grossly or microscopically detectable at 29 days.

Acute and chronic studies confirmed that Mynx and Matrix were successful in obtaining rapid hemostasis. No acute or chronic complications were reported. Chronic safety of Mynx was demonstrated throughout the observation period of the animals for 29 days followed by angiographic follow up, gross pathology and histology. All tests demonstrated that Mynx is a safe and effective means for achieving arterial access site hemostasis in the animal model. An analysis of histological findings demonstrated that Mynx was equivalent or better than Matrix.

6. Mechanism of Closure

Theoretical analyses and *in vitro* tests were conducted to characterize the Mynx and Matrix mechanisms of closure, including the following:

- Theoretical Analyses of mechanism of closure (Mynx versus Matrix)
- Preclinical *In Vitro* Clinical Simulation

These analyses provide rationales and data that demonstrate how the hydrated Mynx sealant produces durable hemostasis outcomes comparable to that of the Matrix sealant in spite of the substantial difference in hydrated volume.

J. Summary of Clinical Studies

The Mynx Trial—A Multi-Center European Study

The Mynx Trial was a prospective, multi-center, non-randomized clinical investigation to evaluate the safety and effectiveness of Mynx to achieve hemostasis in femoral arterial access sites in patients undergoing percutaneous diagnostic or interventional procedures using a 5F, 6F or 7F sheath. The objective for the safety endpoints of the study was to demonstrate non-inferiority to a historical control group, and the objective for the effectiveness endpoints of the study was to demonstrate superiority to the historical control group. The historical control group consisted of patients treated with standard compression who were enrolled in the control arm of the Matrix Trial conducted under IDE# G030182. Patient enrollment was monitored to ensure that 50% of the patients underwent diagnostic procedures and 50% underwent interventional

procedures. Enrollment at 5 investigational sites was initiated in July, 2005 and the final patient was enrolled in January, 2006. The primary safety endpoint was the combined rate of major complications within 30 days (± 7) and the primary effectiveness endpoints included time to hemostasis and ambulation. Secondary endpoints included hospital discharge and combined rate of minor complications within 30 days (± 7).

Patients were required to be at least 18 years of age, to have signed an Informed Consent Form and to have undergone a catheterization procedure through the femoral artery. Patients were excluded if they presented with clinically significant peripheral vascular disease, prior procedure in the ipsilateral common femoral artery ≤ 30 days before the Mynx Trial catheterization procedure, ipsilateral closure device, known allergy to contrast medium or device materials, a myocardial infarction with elevated ST segment ≤ 24 hours prior to procedure, uncontrolled hypertension, existing bleeding disorder, evidence of infection or local inflammation, chronic cortesteroid therapy ≥ 1 month duration, common femoral artery diameter < 5 mm, pre-existing bleeding around the procedural sheath, pre-existing hematoma, intraluminal thrombus, pseudoaneurysm, AV fistula, any type of dissection, fibrotic, calcified, or > 50% stenotic femoral artery, arterial puncture outside the common femoral artery, ipsilateral venous sheath, multiple arterial sticks, suspected posterior femoral arterial wall puncture, antegrade puncture, intra-aortic balloon pump, or planned extended hospitalization.

Demographics

Baseline patient demographic data, patient risk factors, concomitant therapy, and procedural variables for patients enrolled in the Mynx Trial and the standard compression group are presented in **Table 4**. Patients enrolled in the Mynx Trial and the historical control groups are very similar. The two patient cohorts are both representative of the patient population undergoing diagnostic or interventional procedures.

Table 4. Patient Demographics

All Patients	Mynx	Standard Compression	p-value†
Male	70.0% (133/190)	73.8% (121/164)	0.4781
Age (years)			
mean +/- standard deviation	66.2 +/- 10.5 (190)	64.0 +/- 13.2 (164)	0.0850
median (Q1, Q3)	66.4 (59.1, 74.0) (190)	64.4 (53.8, 75.0) (164)	0.1113
range (min, max)	(40.0, 85.6)	(33.1, 87.8)	
Body Mass Index (BMI kg/m²) mean +/- SD	27.5+/- 4.0 (190)	29.3 +/- 4.8 (164)	0.0002
Diabetes	26.8% (51/190)	18.3% (30/164)	0.0584
Tobacco Use Within Last 6 Months	18.9% (36/190)	17.1% (28/164)	0.6797
History of CHF	13.2% (25/190)	6.7% (11/164)	0.0527
History of CVA/TIA	18.9% (36/190)	6.1% (10/164)	0.0004
History of Cardiovascular Disease	50.5% (96/190)	56.1% (92/164)	0.3366
History of Renal Failure	12.6% (24/190)	2.4% (4/164)	0.0003
Hypertension Requiring Medication	78.4% (149/190)	70.1% (115/164)	0.0866
Blood Pressure – Systolic (mm Hg)			
mean +/- standard deviation	138.6 +/- 18.1 (190)	137.5 +/- 21.2 (164)	0.6099
median (Q1, Q3)	140.0 (120.0, 150.0) (190)	137.0 (122.0, 150.0) (164)	0.4961
range (min, max)	(100.0, 180.0)	(90.0, 195.0)	
Blood Pressure – Diastolic (mm Hg)			
mean +/- standard deviation	77.3 +/- 10.5 (190)	77.0 +/- 12.1 (164)	0.7971
median (Q1, Q3)	80.0 (70.0, 80.0) (190)	76.0 (68.5, 86.0) (164)	0.5945
range (min, max)	(50.0, 110.0)	(42.0, 108.0)	
Femoral Bruit	4.2% (8/190)	1.2% (2/163)	0.1147
Ipsilateral Femoral Artery Catheterization	38.9% (74/190)	42.7% (70/164)	0.5156
Prior Ipsilateral Placement of Closure Device	0.5% (1/190)	12.8% (21/164)	<.0001
Groin Site Abnormalities	2.1% (4/190)	0.0% (0/164)	0.1269
Left Femoral Artery Access Site	22.6% (43/190)	10.4% (17/164)	0.0027
Right Femoral Artery Access Site	77.4% (147/190)	89.6% (147/164)	0.0027
ACT at End of Procedure			
mean +/- standard deviation	221.4 +/- 84.0 (69)	237.5 +/- 77.5 (102)	0.2054
median (Q1, Q3)	208.0 (170.0, 240.0) (69)	245.5 (172.0, 299.0) (102)	0.0407
range (min, max)	(108.0, 634.0)	(73.0, 358.0)	
Sheath Size – 5F	0.5% (1/190)	12.8% (21/164)	<.0001
Sheath Size – 6F	94.2% (179/190)	76.2% (125/164)	<.0001
Sheath Size – 7F	5.3% (10/190)	11.0% (18/164)	0.0507

Note: ABI not measured in the Mynx Trial (not standard of care at European sites).
† p-value based on test for superiority.

Safety Data

In this clinical study, the safety of Mynx was evaluated through a comparison of various safety endpoints between patients treated with Mynx and the historical standard compression group. The combined rate of major complications was the primary safety endpoint. The combined rate of minor complications was the secondary safety endpoint. Additionally, other adverse events and effectiveness measures were also evaluated during the Mynx Trial. An independent Clinical Events Committee (CEC) adjudicated all reported complications. **Table 1** displays the combined rate of major complications and the combined rate of minor complications for Mynx and standard compression patients. **Table 2** and **Table 3** include the complication data for diagnostic and interventional patients, respectively.

Overall, the primary safety endpoint hypothesis for this study was tested by placing a one-sided 95% upper confidence bound on the observed difference in the combined rate of major complications (Mynx rate minus the standard compression rate) using exact methods. An upper confidence bound of less than 5.0% supported the hypothesis that the major complication rate for Mynx was non-inferior to that of standard compression. In the Mynx Trial, the major complication rate was 0.5% compared to 0.0% in the historical control group. The minor complication rate was 3.7% for Mynx compared to 1.2% in the historical control group, resulting in a difference of 2.5%. The rate of either a major or a minor complication was 4.2% for Mynx versus 1.2% for standard compression, demonstrating similar results for the two groups.

The results reported in the Mynx Trial demonstrated that the Mynx treatment group is non-inferior to standard compression with respect to the rate of major complications. The observed complication rates reported in the study were within the expected range and the primary safety endpoint in the study was met.

Effectiveness Data

Effectiveness measures are summarized in **Table 5** for all patients. These effectiveness measures are stratified by type of procedure (diagnostic and interventional) in **Table 6** and **Table 7**. Time to hemostasis and time to ambulation were the primary effectiveness endpoints of the Mynx Trial. Time to hemostasis was defined as the time from tamping tube removal (i.e., device removal) to when hemostasis was first observed. The mean time to hemostasis was 1.3 ± 2.3 minutes for the Mynx group compared to 25.4 ± 16.2 minutes for the standard compression group ($p<0.0001$). The difference in mean time to hemostasis was -24.1 minutes between the two groups.

Table 5. Effectiveness Endpoints
All Patients

All Patients*	Mynx	Standard Compression	p-value†
Time to Hemostasis (minutes)			
mean ± standard deviation (n)	1.3 +/- 2.3 (183)	25.4 +/- 16.2 (161)	<0.0001
median (Q1, Q3) (n)	0.5 (0.0, 2.0) (183)	20.0 (15.0, 30.0) (161)	<0.0001
range (min, max)	(0.0, 22.5)	(6.0, 120.0)	
Time to Ambulation (hours)			
mean ± standard deviation (n)	2.6 +/- 2.6 (181)	7.4 +/- 4.8 (160)	<0.0001
median (Q1, Q3) (n)	2.0 (1.8, 2.2) (181)	6.0 (4.5, 7.4) (160)	<0.0001
range (min, max)	(1.3, 20.0)	(1.6, 26.9)	
Time to Discharge (hours) Actual			
mean ± standard deviation (n)	32.3 +/- 55.6 (153)	20.1 +/- 36.1 (160)	0.0228
median (Q1, Q3) (n)	21.5 (15.8, 26.4) (153)	14.8 (6.3, 22.0) (160)	<0.0001
range (min, max)	(2.5, 553.8)	(2.6, 404.8)	

*The number of patients used to calculate effectiveness measures differ from overall study sample size due to missing values.
† p-value based on test for superiority.

Table 6. Effectiveness Endpoints
Diagnostic Patients

Diagnostic Patients*	Mynx	Standard Compression	p-value†
Time to Hemostasis (minutes)			
mean ± standard deviation (n)	1.0 +/- 1.3 (92)	23.6 +/- 17.1 (83)	<0.0001
median (Q1, Q3) (n)	0.5 (0.0, 1.6) (92)	19.0 (14.0, 25.0) (83)	<0.0001
range (min, max)	(0.0, 6.0)	(6.0, 120.0)	
Time to Ambulation (hours)			
mean ± standard deviation (n)	2.5 +/- 2.1 (91)	5.4 +/- 2.7 (82)	<0.0001
median (Q1, Q3) (n)	2.0 (1.9, 2.3) (91)	5.2 (4.3, 6.1) (82)	<0.0001
range (min, max)	(1.4, 19.6)	(1.6, 26.9)	
Time to Discharge (hours) Actual			
mean ± standard deviation (n)	35.3 +/- 71.4 (79)	17.3 +/- 47.6 (82)	0.0621
median (Q1, Q3) (n)	21.5 (7.4, 26.3) (79)	6.3 (5.4, 7.3) (82)	<0.0001
range (min, max)	(2.5, 553.8)	(2.6, 404.8)	

*The number of patients used to calculate effectiveness measures differ from overall study sample size due to missing values.
† p-value based on test for superiority.

Table 7. Effectiveness Endpoints
Interventional Patients

Interventional Patients*	Mynx	Standard Compression	p-value†
Time to Hemostasis (minutes)			
mean ± standard deviation (n)	1.5 +/- 2.9 (91)	27.3 +/- 15.2 (78)	<0.0001
median (Q1, Q3) (n)	0.6 (0.0, 2.0) (91)	25.0 (19.0, 30.0) (78)	<0.0001
range (min, max)	(0.0, 22.5)	(10.0, 120.0)	
Time to Ambulation (hours)			
mean ± standard deviation (n)	2.8 +/- 3.0 (90)	9.4 +/- 5.6 (78)	<0.0001
median (Q1, Q3) (n)	1.9 (1.8, 2.2) (90)	7.1 (5.5, 11.8) (78)	<0.0001
range (min, max)	(1.3, 20.0)	(2.5, 22.3)	
Time to Discharge (hours) Actual			
mean ± standard deviation (n)	29.0 +/- 31.1 (74)	23.0 +/- 16.9 (78)	0.1466
median (Q1, Q3) (n)	21.5 (16.8, 26.7) (74)	20.6 (17.0, 23.4) (78)	0.2876
range (min, max)	(2.9, 185.3)	(3.0, 140.0)	

*The number of patients used to calculate effectiveness measures differ from overall study sample size due to missing values.
† p-value based on test for superiority.

Time to ambulation was defined as the time from tamping tube removal to the time a patient walks at least 20 feet (or 6 meters). The mean time to ambulation was 2.6 ± 2.6 hours for the Mynx group compared to 7.4 ± 4.8 hours for the standard compression group ($p<0.0001$). The difference in mean time to ambulation was -4.8 hours between the two groups.

These results demonstrate that both primary effectiveness endpoints for the Mynx Trial were met. Mynx was shown to be significantly better than standard compression with respect to the time to hemostasis and ambulation.

Time to discharge was defined as the time from tamping tube removal to the time a patient is discharged from the hospital. The mean time to discharge was 32.3 ± 55.6 hours for the Mynx group compared to 20.1 ± 36.1 hours for the standard compression group ($p=0.02$). The difference in mean time to ambulation was 12.2 hours between the two groups. This difference may be due to the differences in the standard of care for patients treated in Europe (in the Mynx Trial) compared to patients treated in the United States (in the Matrix Study).

Table 8 includes the cumulative time to hemostasis for Mynx patients and standard compression patients.

Table 8. Cumulative Time to Hemostasis*

Time to Hemostasis (minutes)	Mynx (n=183)	Standard Compression (n=161)	Mynx Diagnostic (n=92)	Standard Compression Diagnostic (n=83)	Mynx Interventional (n=91)	Standard Compression Interventional (n=78)
1	59.0% (108)	0.0% (0)	65.2% (60)	0.0% (0)	52.7% (48)	0.0% (0)
2	83.6% (153)	0.0% (0)	88.0% (81)	0.0% (0)	79.1% (72)	0.0% (0)
3	91.8% (168)	0.0% (0)	92.4% (85)	0.0% (0)	91.2% (83)	0.0% (0)
4	94.5% (173)	0.0% (0)	94.6% (87)	0.0% (0)	94.5% (86)	0.0% (0)
5	96.2% (176)	0.0% (0)	97.8% (90)	1.2% (1)	94.5% (86)	0.0% (0)
10	98.9% (181)	5.0% (8)	**100% (92)**	7.2% (6)	97.8% (89)	2.6% (2)
15	99.4% (182)	26.7% (43)	**100% (92)**	36.1% (30)	98.9% (90)	16.7% (13)
20	99.4% (182)	53.4% (86)	**100% (92)**	66.2% (55)	98.9% (90)	39.7% (31)
25	**100%**(183)	64.6%(104)	**100% (92)**	75.9% (63)	**100% (91)**	52.6% (41)
>30	**100%(183)**	**100% (161)**	**100% (92)**	**100%(83)**	**100% (91)**	**100% (78)**

*The number of patients differs from overall study sample size due to missing values.

Table 9 includes the cumulative time to ambulation for Mynx patients and standard compression patients.

Table 9. Cumulative Time to Ambulation*

Time to Ambulation (hours)	Mynx (n=181)	Standard Compression (n=160)	Mynx Diagnostic (n=91)	Standard Compression Diagnostic (n=82)	Mynx Interventional (n=90)	Standard Compression Interventional (n=78)
2	50.8% (92)	1.3% (2)	42.9% (39)	2.4% (2)	58.9% (53)	0.0% (0)
3	90.0% (163)	3.8% (6)	90.1% (82)	4.9% (4)	90.0% (81)	2.6% (2)
4	92.3% (167)	12.5% (20)	92.3% (84)	17.1% (14)	92.2% (83)	7.7% (6)
5	93.9% (170)	35.6% (57)	95.6% (87)	47.6% (39)	92.2% (83)	23.1% (18)
10	97.2% (176)	83.8% (134)	97.8% (89)	98.8% (81)	96.7% (87)	67.9% (53)
15	98.3%(178)	89.4% (143)	98.9%(90)	98.8% (81)	97.8% (88)	79.5% (62)
20	**100%** (181)	95.6% (153)	**100% (91)**	98.8% (81)	**100% (90)**	92.3% (72)
25	**100%** (181)	99.4% (159)	**100% (91)**	98.8% (81)	**100% (90)**	**100% (78)**
>30	**100%** (181)	**100% (160)**	**100% (91)**	**100% (82)**	**100% (90)**	**100% (78)**

*The number of patients differs from overall study sample size due to missing values

Table 10 includes the cumulative time to discharge for Mynx patients and standard compression patients.

Table 10. Cumulative Time to Discharge*

Time to Discharge (hours)	Mynx All Patients (n=153)	Standard Compression All Patients (n=160)	Mynx Diagnostic (n=79)	Standard Compression Diagnostic (n=82)	Mynx Interventional (n=74)	Standard Compression Interventional (n=78)
2	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
3	2.0% (3)	1.3% (2)	2.5% (2)	1.2% (1)	1.4% (1)	1.3% (1)
4	9.8% (15)	3.1% (5)	16.5% (13)	4.9% (4)	2.7% (2)	1.3% (1)
5	11.1% (17)	11.3% (18)	19.0% (15)	18.3% (15)	2.7% (2)	3.8% (3)
10	18.3% (28)	44.4% (71)	25.3% (20)	81.7% (67)	10.8% (8)	5.1% (4)
15	24.8% (38)	50.6% (81)	29.1% (23)	82.9% (68)	20.3% (15)	16.7% (13)
20	39.9% (61)	65.6% (105)	38.0% (30)	84.1% (69)	41.9% (31)	46.2% (36)
25	66.7% (102)	85.6% (137)	67.1% (53)	89.0% (73)	66.2% (49)	82.1% (64)
30	81.7% (125)	90.6% (145)	82.3% (65)	91.5% (75)	81.1% (60)	89.7% (70)
> 30	**100% (153)**	**100% (160)**	**100% (79)**	**100% (82)**	**100%(74)**	**100% (78)**

*The number of patients differs from overall study sample size due to missing values

Procedure success was defined as successfully achieving hemostasis using any method with freedom from major complications. As shown in **Table 11**, the procedure success rate for the Mynx treatment group was 99.5% compared to 100.0% for the standard compression group.

Table 11. Procedure Success by Treatment Group

	Mynx	Standard Compression	p-value†
All Patients	99.5% (189/190)	100% (164/164)	1.0000
Diagnostic Patients	100% (95/95)	100% (83/83)	N/A
Interventional Patients	98.9% (94/95)	100% (81/81)	1.0000

† p-value based on test for superiority.

Device success was defined as the ability to deploy the delivery system, deliver the sealant, and achieve hemostasis with Mynx at the femoral artery puncture site. As shown in **Table 12**, the device success rate for the Mynx treatment group was 93.2%.

Table 12. Device Success by Treatment Group

	Mynx	Standard Compression	p-value
All Patients	93.2% (177/190)	NA	NA
Diagnostic Patients	93.7% (89/95)	NA	NA
Interventional Patients	92.6% (88/95)	NA	NA

The results from this clinical trial demonstrate that the time to hemostasis and time to ambulation for patients treated with Mynx are superior to patients treated with standard compression. Patients who have undergone diagnostic or interventional procedures and have received treatment with Mynx can safely and effectively ambulate in 2 hours. In addition, the procedure success rate for patients treated with Mynx are equivalent to patients treated with standard compression.

Gender Bias Analysis
A higher number of male patients were enrolled in the Mynx Trial, 70% male versus 30% female, which is a reflection of the general referral pattern for patients undergoing interventional and diagnostic procedures. There was no statistically significant difference in the rate of major or minor complications for either gender. In addition, there was no statistically significant difference in time to hemostasis or ambulation for either gender.

Summary of Clinical Study Results
In the Mynx Trial, the major complication rate was 0.5% compared to 0.0% in the standard compression group (Matrix Trial). The primary safety endpoint for the study was met, and Mynx was determined to be non-inferior to standard compression.

The mean time to hemostasis was 1.3 ± 2.3 minutes for the Mynx group compared to 25.4 ± 16.2 minutes for the standard compression group ($p<0.0001$). The difference in mean time to hemostasis was -24.1 minutes between the two groups. Mynx was shown to be superior to standard compression with respect to time to hemostasis.

The mean time to ambulation was 2.6 ± 2.6 hours for the Mynx group compared to 7.4 ± 4.8 hours for the standard compression group ($p<0.0001$). The difference in mean time to ambulation was -4.8 hours between the two groups. Mynx was shown to be superior to standard compression with respect to time to ambulation. As a result, all primary safety and effectiveness endpoints in the study were achieved.

With respect to secondary endpoints, the minor complication rate for Mynx was similar to standard compression, and the rate of any major or minor complication was 4.2% for Mynx and 1.2% for standard compression. The procedure success rate for Mynx was 99.5% and the device success rate was 93.2%.

K. Panel Recommendations

In accordance with the provisions of section 515(c)(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, and FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by the panel.

L. CDRH Decision

Results of the *in vitro* bench testing, preclinical *in vitro* simulation testing, biocompatibility testing, sterilization validation, animal studies, and clinical investigation provide valid scientific evidence and reasonable assurance that Mynx is safe and effective when used in accordance with its Instructions for Use. The safety of the device has been demonstrated by the fact that the incidence of major complications in the clinical investigation was equivalent to the historical control group treated with standard compression. The effectiveness of Mynx was demonstrated by showing that the time to hemostasis and ambulation was superior to patients treated with standard compression. Thus, valid scientific evidence demonstrates that Mynx is safe and effective for achievement of hemostasis at the femoral access site post diagnostic and interventional catheterization procedures performed in accordance with device labeling on patients with a 5F, 6F or 7F sheath.

CDRH performed an inspection of the manufacturing facilities and found the applicant in compliance with the Quality System Regulation (21 CFR Part 820).

CDRH issued a PMA approval letter to Access Closure, Inc. on May 16, 2007.

M. Approval Specification

1. Instructions for Use: See the device labeling.

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

3. Post-Approval Requirements and Restrictions: See approval order.