SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Femoral Introducer Sheath Hemostasis Device

Device Trade Name: FISH™ Device

Applicant: MIR Corporation
907 W. Second St.
Bloomington, IN 47403

Premarket Approval (PMA) Application Number: P050043

Date of Panel Recommendation: None

Date of Notice of Approval to Applicant: August 20, 2007

II. INDICATIONS FOR USE

The Femoral Introducer Sheath and Hemostasis Device (FISH™ Device) is intended for hemostatic closure of femoral artery access sites. The system is indicated for use in reducing time to hemostasis and time to ambulation in patients who have undergone diagnostic procedures using 5, 6, or 8 French procedural sheaths.

III. CONTRAINDICATIONS

This product should not be used in patients who have a known sensitivity or allergy to porcine derived material or resorbable sutures.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions for the FISH™ device can be found in the Instructions for Use.

V. DEVICE DESCRIPTION

FISH™ is an approach to vascular closure that utilizes a patch of ExtraCellular Matrix (ECM), pre-mounted on a sheath introducer, to serve as the closure mechanism. The device is supplied in a sterile ready to use kit with access needle, guide wire and pre-dilator. The kit is packaged in a thermoform tray with a Tyvek™ covered lid.

Materials and Configuration

Small Intestinal Submucosa (SIS) Composition is a natural biomaterial, primarily composed of protein with secondary amounts of carbohydrates and lipids. SIS is obtained from porcine intestine using a process that retains the natural composition of matrix molecules such as collagen (Types I, III, VI), glycosaminoglycans (hyaluronic acid, chondroitin sulfate A and B, heparin, and heparin sulfate), proteoglycans, and glycoproteins (fibronectin), which are known to have important roles in host tissue repair and remodeling.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for attaining hemostasis at the femoral artery puncture site post-catheterization include mechanical compression, manual compression, percutaneous delivery of sutures at the femoral access site, collagen-based hemostasis devices and staples.

VII. MARKETING HISTORY

The FISH™ device has not been marketed within the United States or any place outside of the United States.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The FISH™ System was evaluated in a randomized controlled clinical investigation involving 206 diagnostic patients enrolled at 8 United States clinical sites, 139 (67%) who received the FISH™ device and 67 (33%) the control, Manual Compression (MC). Prior to enrollment of randomized patients, each site enrolled non-randomized roll-in patients for training purposes. There were a total of 19 diagnostic roll-in patients.

There was one (1) death reported during the randomized investigation, which was not device-related. This patient was randomized to the FISH™ device.

Closure method-related adverse events seen in the clinical study were:

- Hematoma
- Bleeding Requiring Transfusion
- Pseudoaneurysm Requiring Thrombin Injection

Potential complications of allergic reaction, adhesion formation, infection or abscess, foreign body reaction, wound dehiscence, or vessel occlusion were not seen.

Table 1 summarizes the adverse events reported within the randomized investigation's 30-day follow-up period. Events are summarized by percentage of randomized patients experiencing the event during the clinical investigation.

Table 1. Major and Minor Complications through 30 Days – Diagnostic Intent-To-Treat (ITT) Patients

Cumulative Major and Minor Complications - Blackwelder Test for Equivalence					
Randomized Subjects n = 206	FISH™ Device (n=139)		Manual Comp. (n=67)		p-value **
	% of Patients 95% CI *	No. of Events	% of Patients 95% CI *	No. of Events	
Combined Major Complications	0.72% (0.02%, 3.94%)	1	0% (0.0%, 5.36%)	0	<0.0001
Access-site related bleeding requiring transfusion	0.72% (0.01%, 2.88%)	1	0 (0.0%, 3.42%)	0	<0.0001
New ischemia in ipsilateral leg	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Vascular surgical repair, Ultrasound guided compression, transcatheter embolization, or stent graft	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Surgery for access-site related nerve injury	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Permanent access-site related nerve injury	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Access-site related infection requiring intravenous (IV) antibiotics and/or extended hospitalization	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Combined Minor Complications	2.88% (0.79%, 7.20%)	4	1.49% (0.04%, 8.04%)	1	0.039
Access-site related hematoma > 6cm	2.16% (0.45%, 6.18%)	3	1.49% (0.04%, 8.04%)	1	0.012
Pseudoaneurysm treated with ultrasound-guided thrombin injection	0.72% (0.13%, 3.73%)	1	0% (0.02%, 5.14%)	0	<0.0001
Pseudoaneurysm treated with ultrasound-guided fibrin adhesive injection	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Non-treated pseudoaneurysm (documented by ultrasound)	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Non-treated Arteriovenous Fistula (documented by ultrasound)	0 (0.0%, --)	0	0 (0.0%, --)	0	--
Device Success***	99% 137/139	--	-- --	--	--
Procedure Success****	100% 139/139	--	100% 67/67	--	--

* Exact 95% Confidence Interval (CI) based on Clopper-Pearson method

** Blackwelder's test with an equivalent limit of 0.05. The significance level of 0.041 was used for the interim analysis (p-value was not calculated if Adverse Event rates were 0 for both treatment groups)

***Device Success – the ability to achieve hemostasis without major adverse events or the use of mechanical compression and within the allotted time (60 minutes).

**** Procedure Success – the ability to establish hemostasis in a given subject within any time period using any method.

Table 1 shows that the overall Major Adverse Clinical Event (MACE) rates were 0.72% and 0.0% for FISH™ device and control group, respectively. The overall Minor Adverse Events rates were 2.88% and 1.5% for the FISH™ device and control group, respectively. The p-values were used for both MACE and Minor Adverse Events < 0.0001 and <0.041 respectively. The results of this statistical analysis demonstrate that the FISH™ device is non-inferior to Manual Compression in terms of safety.

IX. SUMMARY OF PRECLINICAL STUDIES

Objectives

The objectives of the preclinical studies were to test the biocompatibility, device functionality, sterilization, and shelf life of the device.

Biocompatibility

The FISH™ device was studied for compatibility with standards listed in International Organization for Standardization (ISO) 10993 Biological Evaluation of Medical Devices. The evaluation included cytotoxicity, systemic toxicity, hemolysis, sensitization, irritation and pyrogenicity. The evaluation demonstrated that the FISH™ device is non-toxic, non-hemolytic, non-irritant, and non-pyrogenic.

Table 2. Biocompatibility Test Results

Test Description	Standard Method	Category	Acceptance Criteria	Results
Cytotoxicity Study Using the ISO Elution Method, (1X Minimal Essential Media Extract)	ISO 10993-5	1	No evidence of test sample causing cell lysis or toxicity.	PASS
Murine Local Lymph Node Assay – 0.9% Sodium Chloride Extract	ISO 10993-10	1	The test samples are to be considered not sensitizing to the animal.	PASS
Murine Local Lymph Node Assay – Dimethyl Sulfoxide (DMSO) Extract	ISO 10993-10	1	The test samples are to be considered not sensitizing to the animal.	PASS
ISO Intracutaneous Study – Extract – Sesame Oil Extract	ISO 10993-10	1	No evidence of irritation from the extract injected intracutaneously into rabbits.	PASS
USP (United States Pharmacopeia) and ISO Systemic Toxicity Study – Extract – 0.9% Sodium Chloride Extract	ISO 10993-11	1	No mortality or evidence of systemic toxicity from the extract injected into mice by either an intravenous or intraperitoneal route.	PASS
USP and ISO Systemic Toxicity Study – Extract – Sodium Chloride Extract	ISO 10993-11	1	No mortality or evidence of systemic toxicity from the extract injected into mice by either an intravenous or intraperitoneal route.	PASS
In Vitro Hemolysis Study (Modified ASTM (American Society for Testing and Materials) Method) – 0.9% Sodium Chloride Extract	ISO 10993-4	1	The test samples shall be found to be nonhemolytic.	PASS

Test Description	Standard Method	Category	Acceptance Criteria	Results
Plasma Recalcification Time Coagulation Study – Plasma Extract	ISO 10993-4	1	The test samples shall not significantly decrease the coagulation time of human plasma.	PASS
ISO Intracutaneous Study – Extract – 0.9% Sodium Chloride Extract	ISO 10993-10	1	No evidence of irritation from the extract injected intracutaneously into rabbits.	PASS
Thromboresistance	ISO 10993	2	Cannot cause abnormal or significant thrombus	PASS

Functionality

Laboratory testing was conducted on the FISH™ device to evaluate the physical characteristics of the device relative to its performance and safety. Results from these physical tests provide evidence that the device performs consistently and meets currently accepted industry standards. Table 3 summarizes the results of functionality device testing.

Table 3. FISH™ Device Mechanical Testing

Test	Acceptance Criteria	Results
Packaging (n=6)		
No Entrapment	No entrapment of suture, guidewire holder, guidewire	PASS
No Breach	No breach of packaging	PASS
No visible channels	No channel shall appear across the seal	PASS
No lengthwise warp/curl	No lengthwise warp/curl greater than 0.25"	PASS
Packaging Burst Test (n=6)		
Burst Pressure	No seal burst below 2.5 PSI (Pounds-force per Square Inch)	PASS
Dilator Tip Insertion (n=9)		
Ease of Insertion	No visual sign of tip distortion	PASS
Kinking of tubing	No dilator shall kink during insertion	PASS
Sheath Tip Insertion (n=9)		
Ease of Insertion	No visual sign of tip distortion	PASS
Kinking of tubing	No sheath shall kink during insertion	PASS
SIS Sleeve Insertion (n=9)		
Ease of Insertion	All patches shall enter the in vitro model	PASS
Note condition of SIS patch	No patch shall tear, suture break or sheath damage occur during insertion	PASS
Remove Release Wire (n=9)		
Ease of removal	All release wires need to release without difficulty	PASS
Advancement of Sheath (n=8)		
SIS patch resistance	Sheath shall move without moving patch	PASS
Dilator Hub, Valve Cap Snap Fit (n=8)		
Ease of Removal	All dilator hubs must be removable from the sheath hubs	PASS
Leak Test (n=8)		
Valve Cap	No leaks allowed	PASS
Valve – Dilator	No leaks allowed	PASS
Valve – Release Wire	No leaks allowed	PASS

Test	Acceptance Criteria	Results
Handle		
Barb and Flush Tube	No leaks allowed	PASS
Insertion Site	No leaks allowed	PASS
Device Compatibility (n=8)		
Ease of Introduction	All devices must easily enter the hub and tubing of the sheath	PASS
Resistance of advancing device	No device shall experience "hang up" or high resistance	PASS
Leak Test – Hemostatic Valve (n=8)		
With catheter installed	No leaks shall develop with catheter in place in the sheath hub	PASS
After catheter removed	No leaks shall develop when catheter is removed from sheath hub	PASS
Device Compatibility (n=8)		
Removal of device	No device shall have difficulty being removed	PASS
Removal of Sheath (n=8)		
Movement of SIS	SIS patch must stay in position and create a hydrostatic seal after sheath removal	PASS
Centimeter markings (n=8)		
Adherence	At least 75% of marking shall remain after use	PASS
Compression Mechanism (n=8)		
Pass/Fail	Compression suture shall deploy with minimal effort and not fail	PASS
Release Wire Assembly (n=8)		
Retention Strength (lbs)	Assembly must equal or exceed 3.5lbs.	PASS
Flushtube/Barb Assembly (n=9)		
Retention Strength (lbs)	Assembly must equal or exceed 4lbs.	PASS
Suture Tab Assembly (n=6)		
Retention Strength (lbs)	Retention strength must exceed 2lbs or suture must break.	PASS

Various ISO and ASTM Standard were used in developing the protocols used in the test listed in the table above.

Sterilization and Shelf Life

The FISH™ device is packaged in a Tyvek™ covered polyethylene glycol (PEG) tray, which is heat sealed. All of the components are manufactured in a clean-room environment and the final product is sterilized using Ethylene Oxide (EtO) sterilization. The Sterilization process was validated with a modified Method "C" (Overkill Method) as referenced in Section B.4.3 of the International Standard document ANSI/AAMI/ISO 11135:1994. The successful execution of this demonstrated a theoretical 10^{-6} level of sterility or the probability of one non-sterile unit in one million. The product has passed 12 month shelf life testing included non-accelerated aging for both the device and packaging as well as meeting ASTM and ISO standards for drop testing, low pressure hazards, vehicle stacking and vehicle vibration.

Table 4. Results from sterilization testing

Acceptance Criteria	Results
Residue Testing: <20 mg/device for EtO	PASS
Residue Testing: <12 ethylene chlorohydrin	PASS
Product Sterility: Negative for growth for the half-cycle	PASS
Bacteriostasis/Fungistasis: No evidence of bacteriostatic or fungistatic effects on product	PASS
Biological Indicators - Internal Process Challenge Devices and External Process Challenge Devices: negative for growth	PASS

Animal Studies

Animal testing was conducted to assess the safety and effectiveness of the FISH™ device. The animal testing was performed in 12 canines and 8 swine with one device per animal. Six animals were evaluated acutely (24 hours) and 14 were evaluated with chronic follow-up (2-50 days). The results provided preliminary evidence of device safety and effectiveness when the device is used as directed.

X. SUMMARY OF CLINICAL STUDIES

Objectives

The objectives of the clinical studies were to assess the safety and effectiveness of the FISH™ device in the treatment of bleeding that occurs during femoral artery catheterization.

Study Design

The FISH™ closure device was studied in an open-label, randomized, multi-center clinical trial which enrolled 297 diagnostic and interventional patients. This United States based trial compared the FISH™ device to manual compression. The study included both diagnostic (N=206) and interventional (N=91) patients requiring a procedure with an 8 Fr or smaller sheath size. The study of interventional patients with the FISH™ device is currently ongoing. Data from the interventional study is not discussed here. Each investigator had the opportunity to enroll up to 2 roll-in patients which were non-randomized patients. There were a total of 28 roll-in (diagnostic and interventional) patients in the study. The patients were randomized using a 2:1 randomization scheme (FISH™ device vs. Manual Compression). Of the 206 diagnostic patients enrolled in the study, 139 received the FISH™ device and 67 received manual compression.

This study included 8 U.S. sites and enrolled patients between January 2004 and June 2006. There were a total of 40 investigators who enrolled patients for the study. The endpoints for the study were safety where the study device was required to show equivalence to the control and effectiveness where the device was required to demonstrate superiority in reduced time hemostasis, ambulation, eligible discharge and discharge.

All patients enrolled in the study provided a signed written informed consent and agreed to return for a follow-up evaluation at 30±5 days. The study included patients who were undergoing diagnostic or therapeutic coronary or peripheral procedure performed percutaneously via the common femoral artery. The candidates were required to meet general inclusion and exclusion criteria. The patients did not require a femoral artery angiogram prior to placement of the FISH™ device.

Inclusion Criteria

Patients were enrolled in the study if they met all of the following inclusion criteria:

1. Candidate for a diagnostic or therapeutic coronary or peripheral procedure performed percutaneously via the common femoral artery
2. Patient age > 18 years old and < 80 years old
3. Patient agrees to return for a follow-up evaluation at 30 ± 5 days
4. Patient provides a signed written informed consent

Exclusion Criteria

Patients were not enrolled in the study if any of the following exclusion criteria were present:

1. Known significant bleeding or platelet disorder
2. Von Willebrand's disease
3. Anemia (Hgb (Hemoglobin) < 10 grams per deciliter, Hct (Hematocrit) < 30%)
4. Thrombasthenia
5. Systemic Hypertension (> 180 mm Hg systolic) unresponsive to treatment
6. Pregnant or lactating
7. ACT (Activated Clotting Time) > 400 seconds at time of sheath removal
8. A known allergic reaction to pork products or any other materials used in the device
9. Preexisting immune deficiency
10. Needing a procedure requiring an introducer sheath size of > 8 French
11. Arterial closure site depth > 7.5 centimeters
12. Ipsilateral arterial site closure with manual compression ≤ 6 weeks before the catheterization procedure
13. Closure with another closure device ≤ 180 days before the catheterization procedure.
14. Known hypercoagulable – repeated problems with clotting
15. Patient has unilateral or bilateral lower extremity amputation(s)
16. Patient is unable to routinely walk at least 20 feet without assistance
17. Patient has active systemic or cutaneous infection or inflammation
18. Patient has a pre-existing severe noncardiac systemic disease or illness that results in an expected life expectancy of < 30 days
19. Patient is participating in the study of another investigational device or drug in which follow-up is ongoing
20. Systemic fibrinolytic agents have been used ≤ 24 hours prior to or during the catheterization procedure such that the fibrinogen level is < 100 mg/dl (milligrams per deciliter)

21. There is indication that puncture has been made in the profunda femoris artery, superficial femoral artery, or at the bifurcation of the arteries
22. Patient has had prior ipsilateral femoral vascular surgery or prior stent placement in the vicinity of the puncture site
23. The puncture site is through a vascular graft
24. There has been use of an intra-aortic balloon pump through the arterial puncture site.
25. Patient has an ipsilateral venous sheath
26. Pseudoaneurysm, arteriovenous (AV) fistula, intraluminal thrombus, or arterial dissection are present in the ipsilateral femoral artery prior to arterial closure
27. Patient has intra-procedural bleeding around the access site
28. Patient has a palpable ipsilateral hematoma of any size observed during the catheterization procedure
29. Patient develops absent pedal pulses in the ipsilateral lower extremity during the catheterization procedure
30. Systolic blood pressure is < 90 mm Hg after the catheterization procedure and before device deployment
31. There was difficultly attaining arterial access, multiple punctures were required for arterial access, or the posterior wall of the femoral artery was thought to have been punctured during arterial access
32. There was difficulty inserting the introducer sheath at the start of the catheterization procedure due to vessel scarring or tortuosity
33. Patient is determined to require a procedure that will extend his/her hospitalization (e.g., patient is undergoing Coronary Artery Bypass Graft (CABG) surgery)
34. Patient has already participated in this study

Effectiveness Endpoints

The study was designed to demonstrate that time to hemostasis (TTH) is superior as compared to the control therapy. TTH was measured from the time of sheath pull to the time the patient achieved hemostasis. For this study, the time of hemostasis was defined as "absence of oozing blood that is readily treated by light compression methods (e.g., sandbags, pressure dressing, light manual pressure)."

The study was also designed to demonstrate time to ambulation (TTA) as superior compared to the control therapy. TTA was measured from the time of sheath removal to the time when the patient stood at the bedside and walked at least 20 feet without evidence of re-bleeding.

Secondary endpoints included the measure of time to eligible discharge (TTED), time to discharge (TTD), procedure success rate, and patient discomfort.

Safety Endpoints

The null hypothesis for safety was that the experimental device had a major adverse event rate that exceeded that of the control by a delta of 5%. The alternative hypothesis was that the experimental device has a primary safety endpoint rate less than that of the control or exceeding that of the control by no more than the delta 5%.

Null Hypothesis

FISH™ (%MACE) > Manual Compression (%MACE) + 5% delta

Alternative Hypothesis

FISH™ (%MACE) < Manual Compression (%MACE) + 5% delta

Patient Assessments

All patients were required to return for a follow-up examination at 30±5 days. All adverse events were recorded and physical examinations of the sites were conducted. In addition, 150 patients received femoral ultrasound evaluations of the puncture site for evidence of vascular compromise, arterio-venous fistulae or pseudoaneurysms; at 30 days, no significant findings were identified.

Demographics

The average patient age was 60 years, the average activated clotting time (ACT) at the time of sheath pull was 129 seconds and 62% of the patients were diagnosed with hypertension.

Effectiveness Results

For all effectiveness endpoints the FISH™ device proved superior in diagnostic patients compared to the control manual compression. The median times for hemostasis in the FISH™ patients were 6 minutes versus 17 minutes for the control group manual compression. The median times for ambulation for the FISH™ device were 2.0 hours for the FISH™ group versus 4.2 hours for the control. The median time to eligible discharge was 2.3 hours versus 4.5 hours for the control manual compression. The median time to discharge was 3.0 hours for the FISH™ patients versus 4.9 hours for the control group manual compression.

Figure 1. Histogram of Percentage of Patients vs. Time to Hemostasis (in minutes)

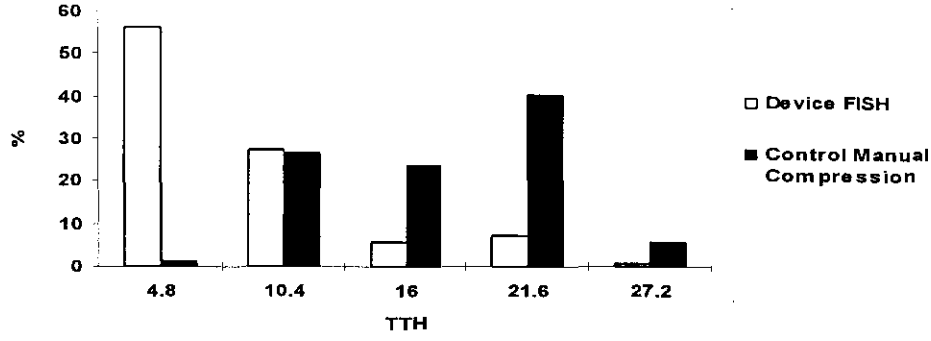


Figure 2. Histogram of Percentage of Patients vs. Time to Ambulation (in minutes)

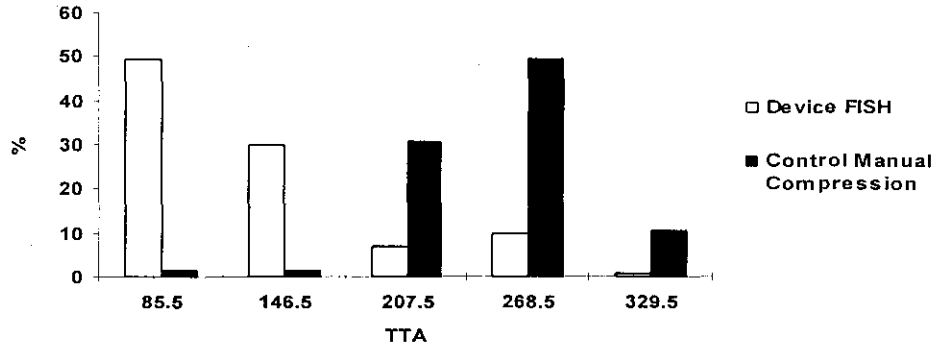


Table 5. Diagnostic Procedures: Effectiveness Endpoint Results for ITT Patients[+]

Primary Effectiveness			
Time to Hemostasis (Minutes)	FISH™	Manual Compression	p-value
N*	139	67	< 0.0001
Mean (Standard Deviation)	9.4 (8.7)	17.2 (6.7)	
Median	6	17	
Min – Max	2 - 75	7 – 55	
Time to Ambulation (Hours)	FISH™	Manual Compression	p-value
N*	131	65	<0.0001
Mean (Standard Deviation)	2.6 (2.5)	4.3 (1.0)	
Median	2.0	4.2	
Min – Max	0.9 – 19.6	1.3 – 7.3	
Secondary Effectiveness			
Time to Eligible Discharge (Hours)	FISH™	Manual Compression	p-value
N*	130	65	<0.0001
Mean (Standard Deviation)	3.1 (3.3)	5.5 (4.0)	
Median	2.3	4.5	
Min – Max	1 – 22.4	1.5 - 24.2	
Time to Discharge (Hours)	FISH™	Manual Compression	p-value
N*	127	65	<0.0001
Mean (Standard Deviation)	16.2 (43.1)	24.9 (53.1)	
Median	3.0	4.9	
Min – Max	1.5 - 263	3.4 – 217.9	
Equivalence Study At 30 Days			
Discomfort (Subjective Scale 0-10)	FISH™	Manual Compression	p-value
N*	138	67	--
Mean (Standard Deviation)	0.51 (1.5)	0.21 (1.0)	
Median	0	0	
Min – Max	0 - 8	0 – 6	

[+]The effectiveness calculations were based on the Wilcoxon Two-Sample Test using a normal approximation and two-sided criteria (Pr > Z <.0001).

*Note: Differences in sample sizes between variables were due to missing data points or delays due to subsequent procedures.

The results of the above statistical analyses demonstrate that the FISH™ device is superior to Manual Compression in terms of effectiveness measures for vascular hemostasis and equivalent relative to discomfort subjectively measured at 30 days post-procedure.

Table 6. Diagnostic Procedures: Patient Distribution for TTH, TTA, TTED, TTD

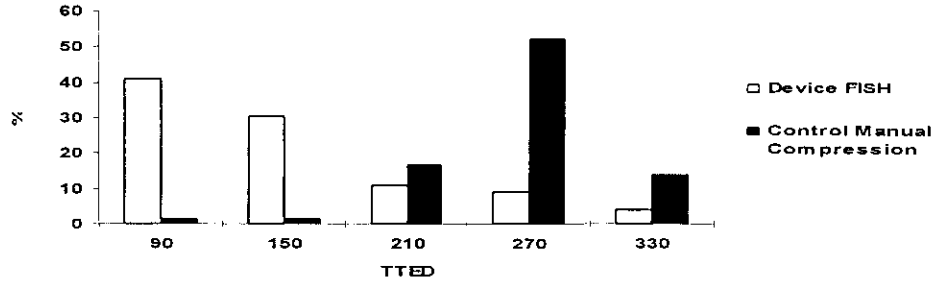
Variable	FISH™	Control Manual Compression
Time to Hemostasis		
≤ 6min	50.72% (70/138)*	0.00% (0/67)
≤ 12min	83.33% (115/138)	22.39% (15/67)
≤ 18min	89.86% (124/138)	52.24% (35/67)
≤ 24min	97.10% (134/138)	92.54% (62/67)
≤ 30min	97.83% (135/138)	98.51% (66/67)
Time to Ambulation		
≤ 2 hours	50.77% (66/130)*	1.54% (1/65)
≤ 3 hours	79.23% (103/130)	6.15% (4/65)
≤ 5 hours	96.15% (125/130)	83.08% (54/65)
≤ 7 hours	97.69% (127/130)	96.92% (63/65)
≤ 10 hours	98.46% (128/130)	100.00% (65/65)
Time to Eligible Discharge		
≤ 2 hours	41.86% (54/129)*	1.54% (1/65)
≤ 3 hours	72.87% (94/129)	3.08% (2/65)
≤ 5 hours	91.47% (118/129)	72.31% (47/65)
≤ 7 hours	96.12% (124/129)	92.31% (60/65)
≤ 10 hours	97.67% (126/129)	93.85% (61/65)
Time to Discharge		
≤ 2 hours	15.08% (19/126)*	0.00% (0/65)
≤ 3 hours	50.00% (63/126)	0.00% (0/65)
≤ 5 hours	76.98% (97/126)	58.46% (38/65)
≤ 10 hours	82.54% (104/126)	80.00% (52/65)
≤ 24 hours	88.10% (111/126)	86.15% (56/65)
≤ 48 hours	92.86% (117/126)	87.69% (57/65)

*Note: Differences in total number of patients between variables were due to missing data points or delays due to subsequent procedures.

Secondary Effectiveness Endpoints

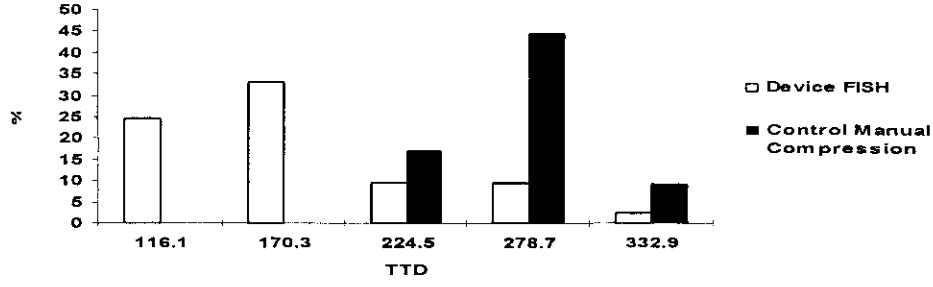
- Time to Eligible Discharge (TTED) – this was measured from the time of sheath pull to the time when the patient was deemed eligible for discharge from the hospital based only on the condition of the access site. The study demonstrated TTED superiority of the FISH™ device as compared to the control therapy.

Figure 3. Histogram of Percentage of Patients vs. Time to Eligible Discharge (in minutes)



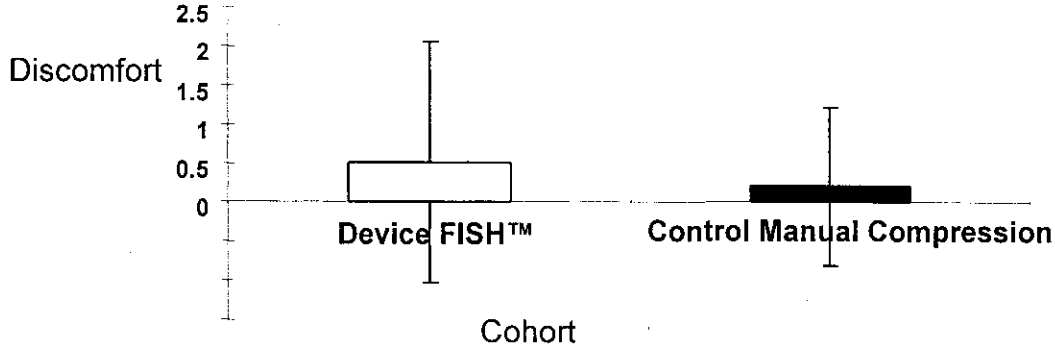
- Time to Discharge (TTD) – this was measured from time of sheath removal to the time the patient was discharged. The study demonstrated TTD superiority of the FISH™ device as compared to the control therapy.

Figure 4. Histogram of Percentage of Patients vs. Time to Discharge (in minutes)



- Patient Discomfort – All patients were subjectively asked at the 30 day follow-up to rate their site-related discomfort from 0 to 10, with 0 being no pain and 10 being the worst pain imaginable. The results from this subjective study showed the device to be equal to the control.

Figure 5. Average and Standard Deviation of Patients Discomfort at 30 Days (Subjective Scale 0-10)



- Procedure Success Rate (defined as the number of patients in which hemostasis was achieved with freedom from major complications vs. the number attempted). This includes hemostasis which was achieved using adjunctive compression (such adjunctive compression is typically used for ≤ 5 minutes).

Device Failures

Device failure was defined as an instance in which hemostasis could not be achieved using the FISH™ device within an allotted time (60 minutes) or with Manual Compression (Control), meaning when additional means such as a fem-stop or a mechanical compression clamp were required to achieve hemostasis. Only one case of device failure was noted in the diagnostic patients.

Gender Differences

According to one study, approximately 36% of patients receiving catheterization are female.[1] Of the study population for this trial, 38% of the patient population were female. There was one report of a major adverse event (n=1) in the treatment group which was of a female patient. There were four total reports of combined major and minor adverse events. Three of these events occurred in women. Other endpoints did not show a statistically significant difference. Differences in the time to discharge endpoints are shown below.

Table 7. Time to discharge – gender differences

Procedure	Randomization	Gender	Ave TTH	Ave TTA	Ave TTED	Ave TTD
Diagnostic	Manual Compression	Female	17.06	251.2	356.1	1231.2
		Male	17.4	268.8	302.8	1786.6
		p-value	*0.828*	*0.263*	*0.371*	*0.487*
	Device FISH™	Female	8.12	123.0	158	310.9
		Male	9.4	162.3	195.5	1252.2
		p-value	*0.288*	*0.085*	*0.267*	*0.029*

Time to Discharge (TTD) was one effectiveness category that showed a statistically significant correlation with patient gender. This endpoint was often controlled by other parameters outside the influence of the type of closure method. This included patients who were going to have subsequent procedures based on the diagnostic procedure performed. These subsequent procedures could add significantly to the average TTD even if only a small subgroup of patients went on to follow-up procedures as seen in the chart.

Safety Results

For the diagnostic patients, the FISH™ device demonstrated safety with a total adverse event rate of 0.7% (1/139) versus the control 0.0% (0/67). The one event for the FISH™ device was a site-related bleeding requiring transfusion. These rates for MACE in the diagnostic patients were found to be equivalent ($p < 0.0001$) under the experimental conditions outlined prospectively in the investigational plan.

The minor adverse event rate was low for both the FISH™ device (2.9%) and the control (1.5%); the tests for equivalence showed these to be equal (p=0.039). The events for the device include 3 hematomas > 6 cm and 1 pseudoaneurysm. For the control there was one hematoma > 6 cm. During the course of this clinical trial there was one patient death (1 FISH™, 0 Manual Compression). The death was not related to the use of the device.

There were no Unanticipated Site-Related Adverse Events. Please see Table 1 for major and minor complications through 30 days.

XI. CONCLUSIONS DRAWN FROM STUDIES

Based on the results from the clinical, *in vivo* and *in vitro* studies there is valid scientific evidence and reasonable assurance that the FISH™ device is safe and effective when used in accordance with the instructions for use.

The FISH™ device has demonstrated safety through its low incidence of complications in diagnostic patients when compared to manual compression. The FISH™ device has demonstrated effectiveness by achieving hemostasis and ambulation earlier than the control group using manual compression.

XII. PANEL RECOMMENDATION

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 Support Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

FDA issued an approval order on August 20, 2007. The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. 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.

Postapproval Requirements and Restrictions: See approval order.

XV. REFERENCES

1. Saif S. Rathore, MPH; Yongfei Wang, MS; Martha J. Radford, MD; Diana L. Ordin, MD, MPH; and Harlan M. Krumholz, MD, SM. Sex Differences in Cardiac Catheterization after Acute Myocardial Infarction: The Role of Procedure Appropriateness. Volume 137, Issue 6; pp. 487-493:2002.