SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name: Prósthesis, spinous process spacer

Device Trade Name: X STOP® Interspinous Process Decompression System ("X STOP")

Applicant's Name and Address: St. Francis Medical Technologies, Inc.
960 Atlantic Ave, Suite 102
Alameda, CA 94501

Date(s) of Panel Recommendation: August 31, 2004

Premarket Approval Application (PMA) Number: P040001

Date of Notice of Approval to Applicant: NOV 21 2005

II. INDICATIONS FOR USE

The X STOP Interspinous Process Decompression System (hereinafter called the X STOP) is indicated for treatment of patients aged 50 or older suffering from neurogenic intermittent claudication secondary to a confirmed diagnosis of lumbar spinal stenosis (with X-Ray, MRI, and/or CT evidence of thickened ligamentum flavum, narrowed lateral recess and/or central canal narrowing). The X STOP is indicated for those patients with moderately impaired physical function who experience relief in flexion from their symptoms of leg/buttock/groin pain, with or without back pain, and have undergone a regimen of at least 6 months of nonoperative treatment. The X STOP may be implanted at one or two lumbar levels in patients in whom operative treatment is indicated at no more than two levels.

III. CONTRAINDICATIONS

The X STOP is contraindicated in patients with:

- an allergy to titanium or titanium alloy;
- spinal anatomy or disease that would prevent implantation of the device or cause the device to be unstable *in situ*, such as:
  - significant instability of the lumbar spine, e.g., isthmic spondylolisthesis or degenerative spondylolisthesis greater than grade 1.0 (on a scale of 1 to 4);
  - an ankylosed segment at the affected level(s);
  - acute fracture of the spinous process or pars interarticularis
  - significant scoliosis (Cobb angle greater than 25 degrees);
- cauda equina syndrome defined as neural compression causing neurogenic bowel or bladder dysfunction;
- diagnosis of severe osteoporosis, defined as bone mineral density (from DEXA scan or some comparable study) in the spine or hip that is more than 2.5 SD below the mean of adult normals in the presence of one or more fragility fractures;
- active systemic infection or infection localized to the site of implantation.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the X STOP labeling.

V. DEVICE DESCRIPTION

The X STOP is a titanium implant that fits between the spinous processes of the lumbar spine. It is made from Ti-6AI-4V Eli titanium alloy (ISO 5832/3) and consists of two components: a spacer assembly and a wing assembly. The spacer assembly is comprised of a tissue expander, an oval spacer, and a fixed wing. The wing assembly component is comprised of an adjustable wing and locking screw.

The X STOP is available in five (5) sizes: 6mm, 8mm, 10mm, 12mm, and 14mm. The size refers to the minor diameter of the oval spacer on the spacer assembly of the X STOP.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Non-surgical alternatives include non-steroidal anti-inflammatory medications, analgesics, oral and epidural steroids, an initial period of rest, physical therapy, and bracing. Surgical alternatives include various decompressive procedures (e.g., laminectomy, hemilaminectomy, laminotomy, hemilaminotomy, laminoplasty, foraminotomy, facetectomy), with or without a concomitant fusion procedure.

VII. MARKETING HISTORY

The X STOP has been commercially available in markets outside of the United States since 2001. A listing of the countries in which the device has been commercially available is included below in **Table 1**. The X STOP has not been withdrawn from marketing in any of these markets.

Table 1: Use of X STOP in Other Countries

Australia	Netherlands
Austria	New Zealand
Czech Republic	Norway
Denmark	South Africa
Germany	Spain
Greece	Sweden
Israel	Switzerland
Italy	Turkey
Japan	United Kingdom

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The X STOP was implanted via a minimal posterior approach in 100 investigational subjects, and compared to 91 control subjects who were treated with continued non-operative therapy.

Table 2 presents adverse events that occurred perioperatively, or were thought to be causally or temporally related to treatment (as classified by the study investigator). Four patients died in each treatment group during the course of the study. In the X STOP group, 2 patients died from

cancer, 1 from pneumonia, and 1 from congestive heart failure (CHF) complications following implant surgery. In the control group, causes of death were cancer, pulmonary embolism following foot surgery, Parkinson's disease, and myocardial infarction.

Table 2: Summary of Adverse Events Related to the X STOP, Lumbar Spinal Stenosis, Surgery, or Epidural Injections

Type of Adverse Event/Complication	Surgery/ Discharge		6 Weeks		6 Months		12 Months		24 Months		Overall*	
Treatment Group (X = X STOP, C = Control)	X	C	X	C	X	C	X	C	X	C	X (%)	C (%)
# of Patients at Each Follow-up Interval	**100**	**91**	**100**	**91**	**99**	**91**	**98**	**89**	**96**	**83**	**(N = 100)**	**(N = 91)**
DEVICE-RELATED ADVERSE EVENTS												
Device migration/dislodgement			1								1 (1.0%)	-
Malpositioned implant			1								1 (1.0%)	-
Spinous process fracture							1				1 (1.0%)	-
SUBTOTAL			**2**				**1**				**3 (3.0%)**	-
ADVERSE EVENTS RELATED TO LUMBAR SPINAL STENOSIS, SURGERY OR EPIDURAL INJECTION												
Coronary episode, ischemic	1										1 (1.0%)	0
Heart attack				1							0	1 (1.1%)
Epidural injection reaction		1		2						1	0	4 (4.4%)
Epidural injection failed (aborted)		1									0	1 (1.1%)
Hematoma at surgical site			1								1 (1.0%)	0
Incisional pain			1								1 (1.0%)	0
Pain and progressive neurological deficit				1							0	1 (1.1%)
Pain worsening in low back									1		1 (1.0%)	0
Pain, stenosis (progressed to laminectomy)**		2		3	3	9	1	4	2	8	6 (6.0%)	26 (28.6%)
Pulmonary edema			1								1 (1.0%)	0
Respiratory distress	1										1 (1.0%)	0
Wound dehiscence			1								1 (1.0%)	0
Wound swelling	1										1 (1.0%)	0
SUBTOTAL	**3**	**4**	**4**	**7**	**3**	**9**	**1**	**4**	**3**	**9**	**14 (14.0%)**	**33 (36.3%)**
TOTAL # of Events	**3**	**4**	**6**	**7**	**3**	**9**	**2**	**4**	**3**	**9**	**17 (17.0%)**	**33 (36.3%)**

*# Events = # Patients

**The study protocol did not specify criteria for proceeding to laminectomy in either treatment group.

Note: Time intervals for this and other tables in the Summary of Safety and Effectiveness are defined as follows: 6 weeks = 1 - 42 days; 6 months = 43 - 182 days; 12 months = 183 - 365 days; 24 months ≥ 366 days.

Table 3 lists post-implantation interventions in the X STOP group and surgical procedures in the control group. One implant was removed after it dislodged subsequent to a fall. Six X STOP patients and 24 control patients underwent a laminectomy for continued stenosis symptoms, based on a determination made by the individual physician and patient. (The study protocol did not specify criteria for proceeding to laminectomy in either treatment group).

Table 3: Summary of Surgical Interventions

Type of Intervention	Surgery/ Discharge		6 Weeks		6 Months		12 Months		24 Months		Overall*	
Treatment Group (X = X STOP, C = Control)	X	C	X	C	X	C	X	C	X	C	X (%)	C (%)
# of Patients at Each Follow-up Interval	**100**	**91**	**100**	**91**	**99**	**91**	**98**	**89**	**96**	**83**	**(N = 100)**	**(N = 91)**
IMPLANT REMOVAL and/or LAMINECTOMY												
Implant removal alone			1								1 (1%)	NA
Laminectomy**				1	2	11	2	4	2	8	6 (6%)	24 (26%)
REOPERATION												
Drainage of hematoma			1								1 (1%)	-
Aspiration of wound swelling			1								1 (1%)	-
Debridement and secondary wound closure			1								1 (1%)	-
TOTAL # of Interventions	-	-	**4**	**2**	**2**	**10**	**2**	**4**	**2**	**8**	**10 (10%)**	**24 (26%)**

* # of interventions = # of patients

**All X STOP patients who underwent laminectomy had implant(s) removed at time of laminectomy

Table 4 presents "systemic" adverse events that were thought to have no relationship, either causal or temporal, to the device or study-related procedures (as classified by the study

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investigator). The most frequently reported adverse events unrelated to treatment were lower extremity disorders, lower back disorders, accidental injury, and hip disorders.

Table 4: Adverse Events Unrelated to Device or Treatment

Type of Adverse Event/Complication		Surgery		6 Weeks		6 Months		12 Months		24 Months		Overall # Events		Overall # Patients	
Treatment Group (X = X STOP; C=Control)		X	C	X	C	X	C	X	C	X	C	X	C	X	C
# of Patients at Each Follow-up Interval		100	91	100	91	99	91	98	89	96	83				
SYSTEMIC EVENTS*															
System	Code/Event														
Body as a Whole	Cancer						1	2		2		4	1	4	1
	Death			1		1	1		1	2	2	4	4	4	4
	Injury, Accidental			3		2	2	6	2	3		14	4	11	4
	Weight Gain			1								1	0	1	0
Cardiovascular	CV Disorder							2		2		4	0	4	0
Endocrine	Diabetes							1				1	0	1	0
Gastrointestinal	GI Disorder					2		1		1		4	0	3	0
Genitourinary	Chronic Renal Failure					1						1	0	1	0
	GU Infection			1								1	0	1	0
	Pain, Groin			2								2	0	2	0
Hematological	Anemia					1						1	0	1	0
Hepatobiliary	Gallstones							1				1	0	1	0
Immunological	Allergy	1										1	0	1	0
Musculoskeletal	Back, Unspecified					1		1		1		3	0	3	0
	Hip					4		4	1	5	2	13	3	11	3
	Lower Back			3		5	2	5	3	8	2	21	7	16	7
	Lower Extremity			1	2	6	1	6	2	3		16	5	13	3
	Rib									1		1	0	1	0
	Upper Back					2		1		1		4	0	4	0
	Upper Extremity				1			2		2	1	4	2	4	2
	Unspecified							1				1	0	1	0
	Pain, Groin						1	1	1			1	2	1	2
Neurological	Headache			1								1	0	1	0
	Neurological Disorder						1	1				1	1	1	1
	Neuropathy					2		2				4	0	4	0
	Stroke								1	1		1	1	1	1
Neuropsychological	NP Disorder			1		1			1	3		5	1	5	1
Peripheral Vascular	PV Disorder							1				1	0	1	0
Respiratory	Respiratory Infection			2		1						3	0	3	0
	Respiratory Disorder								1			0	1	0	1
	TOTAL # of Events	1	0	16	3	29	9	38	13	35	7	119	32		

Of note, there were 64 musculoskeletal events in 54 patients in the X STOP group that were thought to have no relationship, either causal or temporal, to the device or study-related procedures (as classified by the study investigator) as compared to 19 musculoskeletal events in 17 patients in the control group. There were no statistically significant differences between the study groups in any single category presented in Table 4 with one exception: the incidence of lower extremity disorders was significantly higher in the X STOP group ($p=0.018$). The high incidence of lower extremity and back events suggests that treatment may have been incomplete for both groups, although there is a greater incidence in the X STOP group.

Potential Adverse Events

The following potential adverse events (singly or in combination) could also result from implantation of the X STOP; some of these adverse events were reported in the Pivotal Clinical Trial:

X STOP Related:

- implant dislodgement/migration
- implant not positioned correctly
- fracture of the spinous process
- additional surgery, which could include removal of the X STOP implant
- foreign body reaction
- mechanical failure of the device
- failure of the device/procedure to improve symptoms and/or function

Surgery Related:

- reactions to anesthesia
- myocardial infarction
- infection
- blood vessel damage/bleeding
- deep vein thrombosis
- hematoma
- pneumonia
- neurological system compromise
- stroke
- nerve injury or spinal cord damage
- paralysis
- thrombus formation
- wound dehiscence or delayed healing
- pain/discomfort at the operative site
- death

IX. SUMMARY OF PRECLINICAL AND CLINICAL RADIOGRAPHIC STUDIES

Laboratory Studies

Biocompatibility

The X STOP is manufactured out of materials (Ti-6AI-4V Eli titanium alloy (ISO 5832/3)) whose biocompatibility has been well characterized. Therefore, no biocompatibility testing was provided.

Sterility and Shelf Life Testing

Sterility and shelf life testing was conducted to characterize the appropriate shelf life for the X STOP. The X STOP will have a 2 year shelf life and will be provided sterile. The surgical instruments used to implant the X STOP are provided non-sterile.

The objective of the mechanical testing studies was to characterize the performance of the X STOP under static and dynamic loads, and to assess its safety and mechanism of action.

Static and Dynamic Mechanical Testing

Static and dynamic fatigue tests were conducted to characterize the X STOP and determine its ultimate strength. The evaluations and results are summarized in **Table 5** for the principle tests

of the spacer (which is placed between the spinous processes, as part of the spacer assembly), the spacer assembly (which includes the spacer, the tissue expander, and the fixed wing), and the wing assembly (which consists of a universal wing and a locking screw). The following tests were performed on an unwelded version of the device. These tests were determined to be applicable to the final welded version that was tested in the pivotal clinical study.

Table 5: Mechanical Testing

Study	Conclusions
Spacer Axial Compressive Fatigue Strength: Fatigue axial compression testing was performed on six X STOP spacers (three 6mm, three 8mm) to estimate the fatigue strength.	The X STOP device achieved run out to 10 million cycles at 7117 N without failure. This fatigue load is more than eight times the mean load to failure of the L1 - L4 spinous processes due to X STOP loading during extension.
Spacer Assembly Cantilever Bending Strength -- Static and Dynamic: Cantilever bending static and fatigue tests were performed on seven X STOP spacer assemblies to estimate the bending strength and bending fatigue strength of the assembly (tissue expander, oval spacer, and fixed wing) due to loads on the wing. Strain-gauged X STOP devices implanted in six cadaver motion segments were used to measure the loads on the implants due to motion segment axial rotation.	The bending static and fatigue strength of the spacer assembly is sufficient to withstand the biomechanically modeled loads applied by the interspinous spacer during device insertion and axial rotation of the motion segment. The expected maximum load on the shaft was less than 1/6th of the endurance limit and less than 1/16th of the failure load.
Spacer Assembly Axial Torsion Strength -- Static and Dynamic: Static and dynamic axial torsion tests were performed on a total of five X STOP spacer assemblies to evaluate the strength of the assembly due to torsional loads that could be applied to the axis of the spacer as the spine is flexed and extended. Strain-gauged X STOP devices implanted in six cadaver motion segments were used to measure the loads on the implants due to flexion and extension of the motion segments.	The bending static and fatigue strength of the spacer assembly is sufficient to withstand the biomechanically modeled loads applied by the interspinous spacer during flexion and extension of the motion segment. The expected maximum load on the tissue expander shaft was 1/49th of the endurance limit and 1/142nd of the failure load.
Wing Assembly Cantilever Bending Static Strength: Cantilever bending static (n=2) and fatigue (n=7) testing was performed to estimate the bending strength and bending fatigue strength of the Universal Wing assembly component. The release torque of each Universal Wing screw was measured after each fatigue test.	The endurance limit of the modified Universal Wing was more than six times the highest expected load applied by the spinous processes during physiologic motion.
Wing Assembly Release Torque following Cantilever Bending Fatigue Strength: Release torque of each Universal Wing screw in the wing assembly was measured following the cantilever bending fatigue testing above.	After fatigue loading, the release torque of the Universal Wing screw was within specifications.

Additional mechanical testing was performed prior to the pivotal study, to validate the final welded design of the implant compared to an earlier unwelded design that was not studied in the

pivotal clinical trial. All of the results were acceptable, indicating that the modifications either had no effect on (or improved) the mechanical properties of the device.

In vitro Biomechanical Testing

A series of biomechanical tests were performed on cadaveric spine specimens to assess the safety and mechanism of action of the X STOP. The results are summarized in **Table 6**:

Table 6: Biomechanical Testing

Study	Conclusions
X STOP *In Situ* Loads and Spinous Process Failure Loads were measured during extension of the cadaveric lumbar spine specimens with strain-gauged X STOP spacers implanted. The ultimate strength of the spinous processes was also measured, using oval spacers attached to the ram of the axial testing frame.	The peak loads measured during the simulated physiologic loading of the spinous processes were below 20% of the mean load to failure of the L1 to L4 spinous processes.
X STOP Insertion Loads (n=10 lumbar motion segments) **and Lateral Spinous Process Failure Loads** (n=7 lumbar cadaveric spine specimens) were measured.	Mean lateral insertion load of the X STOP (66 ± 46 N) was significantly less than the mean spinous process failure load (317 ± 197 N). There was no significant difference between the mean failure loads of specimens loaded laterally in the cranial, middle, or caudal aspect of the spinous processes.
X STOP Stability was assessed during flexion/extension and axial rotation tests at extreme loads with the implant placed 1) at the recommended position described in the surgical technique, and 2) at a posterior position in the interspinous space.	The results of the studies confirmed that when the X STOP is placed anterior to the cranial and caudal apices of the spinous processes, it will remain stable even during extreme loading, while implants placed posterior to the apices may be unstable.
Effect of the X STOP on Canal and Foraminal Dimensions was evaluated by MRI scanning eight cadaver spines in flexion, neutral, and extension, and measuring the dimensions of the spinal canal and neural foramen at the implanted and adjacent levels.	With the X STOP present, the mean canal area significantly increased in extension and in neutral. The mean canal diameter significantly increased in extension. The mean subarticular diameter significantly increased in extension and in neutral. The mean foraminal area and width significantly increased in extension. No dimensions were statistically affected at the adjacent levels.
Effect of the X STOP on Spinal Kinematics was assessed by loading seven lumbar cadaver spines in flexion/extension, axial rotation, and lateral bending (with a superimposed compressive force), and measuring the intervertebral motion at the implanted and adjacent levels.	During flexion/extension, the mean range of motion (ROM) was significantly decreased at the implanted level. The mean flexion/ extension ROM was unaffected at the adjacent levels. During axial rotation and lateral bending, the mean ROM was unaffected at the implanted and adjacent levels.
Effect of the X STOP on Disc Pressure was measured by loading eight lumbar cadaver spines in the flexed, neutral, and extended positions, and measuring disc pressures with a pressure transducer at the implanted and adjacent levels.	The X STOP significantly decreased the mean pressures in the posterior annulus and nucleus in the extended and neutral positions at the implanted level. There was no significant effect on adjacent level pressures.

X. SUMMARY OF CLINICAL STUDIES

Preliminary Device Designs and Pilot Studies

The device design being approved is a modified version of earlier designs that were implanted in pilot studies. The first version was a single-piece design and was implanted in one (1) patient. A second version was a multi-piece design and was implanted in nine (9) additional patients in an original pilot study. A third version was another multi-piece design, in sizes up to 12mm, that was implanted in 22 patients; this second pilot study was discontinued due to adverse events related to disassembly of the device. Changes were made to the device design and manufacture, and the pivotal clinical study was initiated with a final, "welded" version of the device. The data throughout the remainder of this SUMMARY OF CLINICAL STUDIES section are all based on this final (fourth) version of the device, which is the version being approved.

Study Objectives

The objectives of the clinical study were to evaluate the safety and effectiveness of the X STOP Interspinous Process Decompression System in the treatment of neurogenic intermittent claudication secondary to mild or moderate lumbar spinal stenosis (LSS).

Study Design

A multi-center, prospective, randomized, controlled study was conducted in which 191 subjects (100 X STOP, 91 Control) were enrolled and treated at 9 centers. Patients were randomized in a one-to-one ratio to either the X STOP group (receiving implantation of the device at one or two levels via a minimal posterior approach) or the control group (continued non-operative therapy which included the use of bed rest, a lumbar corset, and a varied number of epidural steroid injections). Nonsteroidal anti-inflammatories (NSAIDs), analgesics, and physical therapy were prescribed as needed in both groups.

Safety and effectiveness was assessed using the criteria in Table 7. An individual subject was considered a study success (Overall Treatment Success) if all of these conditions were met. The Zurich Claudication Questionnaire (ZCQ), a validated outcomes instrument specific to lumbar spinal stenosis, was used as one of the clinical outcome measures.

Table 7: Components of Overall Treatment Success

Criterion	X STOP	Control
ZCQ Success: • Improvement in Physical Function (by > 0.5 pts) • Improvement in Symptom Severity (by > 0.5 pts) • "Satisfied" or "Somewhat Satisfied" (< 2.5 pts)	X	X
No additional surgery for lumbar stenosis	X	X
Maintenance of distraction	X	
No dislodgement of the implant	X	
Absence of implant-related complications	X	

Inclusion/Exclusion Criteria

To qualify for enrollment in the study, subjects met all the inclusion criteria and none of the exclusion criteria listed in the following **Table 8**:

Table 8: Inclusion and Exclusion Criteria in the pivotal clinical study

Inclusion	Exclusion
• 50 years old or older • Leg/buttock/groin pain, with or without back pain, that can be completely relieved by flexion such as when sitting in a chair. If back pain is also present, it must be partially relieved when flexed • Can sit for 50 minutes without pain • Can walk 50 feet or more • Narrowing of the lumbar spinal canal, nerve root canal or intervertebral foramen at 1 or 2 levels using CT scans and/or MRI where the area of spinal canal is 50% less when compared to segments above and below • Has completed at least 6 months of conservative therapy, which may include physical therapy, bracing, systemic or injected medications • Signed Patient Informed Consent document • Physically and mentally willing and able to comply • Lives in immediate area and has no plans to relocate to another geographic area before completion of the study, or lives outside the immediate area and will comply with the scheduled postoperative visits with a prearranged and designated physician	• Cannot sit for 50 minutes • Cannot walk more than 50 feet • Unremitting pain in any spinal position • Axial back pain only without leg/buttock/groin pain • Fixed motor deficit • Cauda equina syndrome defined as neural compression causing neurogenic bowel (rectal incontinence) or bladder (bladder retention or incontinence) dysfunction • Severe symptomatic lumbar spinal stenosis at > 2 levels • Significant instability of the lumbar spine • Has had any surgery of the lumbar spine • Significant peripheral neuropathy by nerve conduction velocity tests (peroneal and sural nerves) • Acute denervation secondary to radiculopathy, as shown by EMG • Significant scoliosis (Cobb angle > 25 degrees) • Significant peripheral vascular disease (diminished dorsalis pedus or tibial pulses) • Spondylolisthesis >Grade I at affected level • Sustained pathologic fractures of the vertebrae or multiple fractures of the vertebrae and/or hips • Severe osteoporosis of the spine or hip (DEXA and NOF definition; BMD <2.5 SD below mean in the presence of one or more fragility fractures) • Obesity (BMI >40kg/m2) • Active systemic disease such as AIDS, HIV, hepatitis, etc • Active infection • Angina, active rheumatoid arthritis, advanced diabetes or any other systemic disease that would affect the subject's welfare or outcome of the study • Paget's disease at involved segment or metastasis to the vertebrae • History of narcotic abuse • Allergy to any component of the device such as titanium • Immunologically suppressed, or has received steroids at any dose daily for >1 month within last 12 months • Involved in study of another investigational product that may affect outcome • Pregnant or planning to become pregnant during study period

Patient Assessments

Primary effectiveness data were collected prior to the initial treatment, and at 6 weeks, 6 months, 12 months, and 24 months following the initial treatment. Complications and adverse events, device-related or not, were evaluated over the course of the clinical study. Overall success was determined from data collected during the initial 24 months of follow-up. Primary outcome

parameters were evaluated for all treated subjects and included ZCQ success and additional surgery for lumbar stenosis in both treatment groups as well as maintenance of distraction (based on radiographic measurements of each level treated), implant dislodgement, and implant-related complications in the X STOP group only. The ZCQ captures data in three distinct domains: Symptom Severity (SS), Physical Function (PF), and post-treatment Patient Satisfaction (PS). In each domain, a lower score represents a better outcome/condition. As noted in Table 7, ZCQ success was achieved if the patient was at least "somewhat satisfied" (PS score < 2.5), and experienced clinically significant improvement (by at least 0.5 points) in both the SS and PF domains. Safety information was assessed in all patients by an analysis of reported adverse events and additional surgeries.

Back and leg pain assessments, analgesic use, radiographic parameters, and a general health index, the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), were secondary outcome measures.

Demographic Data and Patient Accounting

The sponsor enrolled 229 patients at 9 centers. Of these 229 patients, 191 were treated (100 X STOP and 91 control); 14 X STOP and 24 control patients withdrew or were excluded before treatment. As previously noted, four patients died in each treatment group during the course of the study. Therefore, 183 patients (96 X STOP, 87 control) were considered "evaluable" at the 24 month postoperative follow-up. Demographic information on the treated population is presented in **Table 9**, and patient accounting data are summarized below in **Table 10**.

Table 9: Demographic Information – Treated Population

Variable	X STOP	Control	p-value
Age (yr.) Mean [Range]	70.0 [50-94]	69.1 [50-88]	0.513
Weight (lbs.) Mean [Range]	177.1 [105-265]	180.2 [98-293]	0.569
Height (in.) Mean [Range]	67.3 [56-74]	66.3 [56-75]	0.117
Gender: Male Female	57 (57.0%) 43 (43.0%)	46 (50.5%) 45 (49.5%)	0.387
Spondylolisthesis Present	35 (35.0%)	24 (26.7%)	0.272
ZCQ Symptom Severity	3.14	3.10	
ZCQ Physical Function	2.48	2.48	
SF-36 PCS	27.8	28.9	
SF-36 MCS	51.5	50.6	
Back Pain Score (mean) frequency/severity Sitting Standing Walking	 0.5/0.49 1.79/1.74 1.85/1.78	 0.69/0.67 1.99/1.93 2.11/2.14	
Leg Pain Score (mean) frequency/severity Sitting Standing Walking	 0.39/0.38 2.34/2.27 2.58/2.53	 0.36/0.37 2.24/2.24 2.57/2.59	

Table 10: Patient Accounting

	Preop		Intraop		6 Weeks		6 months		12 months		24 months	
Group X=device; C=Control	X	C	X	C	X	C	X	C	X	C	X	C
Theoretical[1]	114	115	100	91	100	91	100	91	100	91	100	91
Deaths, (cumulative)					1 (1)		1 (2)	1 (1)	0 (2)	1 (2)	2 (4)	2 (4)[4]
Failures[2], **(cumulative)**				1 (1)	1 (1)	1 (2)	2 (3)	11 (13)	2 (5)	4 (17)	2 (7)	8 (25)[4]
Expected[3]			100	90	98	89	95	77	93	72	89	63[4]
Evaluated*			100	90	94	70	88	64	88	69	88	58
Lost	14**	24**	0	0	4	19	7	13	5	3	1	5
Actual % Follow-up*	88%	79%			96%	79%	93%	83%	95%	96%	99%	92%

1 Theoretical = Patients enrolled in the study
2 For example, device removals, replacement, laminectomy
3 Expected = Theoretical – (Deaths + Failures)
4 One control patient underwent a laminectomy on day 56 (study failure at 6 month follow-up window) and subsequently died on day 660 (death at 24 month follow-up window); for the purposes of calculating the "expected" number of patients at the 24 month follow-up window, this patient was counted only once.
* This number includes those patients who were evaluated outside the prescribed follow-up windows
** These patients were enrolled but not treated

Treatment Information

Within the X STOP group of treated patients, the number and locations of spinal levels implanted are shown in **Table 11**.

Table 11: Involved Levels in the X STOP Treated Population

Variable	X STOP	
	n/N	%
Number of levels:		
1	64/100	64.0%
2	36/100	36.0%
Operated levels:		
L1-L2	0/136	0.0%
L2-L3	3/136	2.2%
L3-L4	43/136	31.6%
L4-L5	89/136	65.4%
L5-S1	1/136	0.7%

Within the control group, the numbers of epidural injections given are shown in Table 12.

Table 12: Number of Epidural Injections in the Control Group

# of Injections per Patient	Number of Patients		# Patients who went on to laminectomy	Mean # of Days to Surgery (Range)
	(n/N)	%		
1 Injection Only (Initial Treatment)	32/91	35%	10	189 (56-541)
# of Additional Injections				
1	22/91	24%	9	264 (103 – 507)
2	21/91	23%	3	386 (123 – 465)
3	8/91	9%	0	N/A
4 or more	8/91	9%	2	631 (586 – 676)

Twenty-two patients in the control group received 1 additional injection following the initial treatment, 9 of whom went on to a laminectomy. The mean time to secondary surgery in this group was 264 days. With increasing numbers of injections per patient, the average time to secondary surgery increased, to 631 days for patients who received 4 or more injections.

Those patients who responded positively to initial injections received additional injections when symptoms warranted treatment, thereby extending the course of their conservative therapy. Patients who did not obtain adequate symptom relief from injections received fewer total injections and proceeded to laminectomy surgery more rapidly.

Of the 91 patients, 59 patients had $\geq$2 injections; 32 patients had only one injection. Second injections were left to the discretion of the investigator. The protocol did not stipulate what criteria qualified patients for additional injections.

Data Analysis and Results

The primary effectiveness endpoint was the percentage of patients with overall treatment success in the evaluable population of each treatment group at the 24 month follow-up. Patients reaching a defined endpoint (e.g., laminectomy) before completing the study were included as failures in the computation of success rates.

Secondary efficacy variables, safety variables, and demographic and baseline variables were similarly analyzed except that missing data were not imputed. Categorical variables were analyzed using the Fisher exact test. Continuous variables were analyzed using analysis of variance (ANOVA). Two-tailed p-values were calculated and considered to be statistically significant when $p < 0.05$.

Clinical effectiveness

The primary effectiveness endpoint of this study was the difference in the proportion of overall treatment success between the two study groups at 24 months follow-up. Success rates were variable across the nine investigational sites, with one site showing a significantly higher percentage of patients who had overall treatment success. The X STOP success rates were greater than the control success rates at all nine centers that participated in the clinical trial. **Table 13** shows success rates calculated in two ways—for all sites, and excluding the investigational site with the highest success rates (Site 01/04). These results are shown for the "evaluable population," defined as all patients who survived through 24 month follow-up.

Table 13: Treatment Success at 24 Month Follow-Up – Evaluable Population†

Outcome Parameter	All Sites			All Sites Excluding Site 01/04		
	X STOP n/N (%)	Control n/N (%)	p-value	X STOP n/N (%)	Control n/N (%)	p-value
ZCQ Success	45/96 (47%)	4/87 (5%)	<0.001*	28/76 (37%)	2/70 (3%)	<0.001*
No additional surgery for lumbar stenosis[a]	86/96 (90%)	57/87 (66%)	<0.001*	66/76 (87%)	44/70 (63%)	<0.001*
Maintained distraction[b]	81/96 (84%)	NA	NA	61/76 (80%)	NA	NA
No dislodgement[c]	92/96 (96%)	NA	NA	72/76 (95%)	NA	NA
Absence of implant-related complications[d]	90/96 (94%)	NA	NA	71/76 (93%)	NA	NA
Overall Treatment Success[e]	**41/94 (44%)**	**4/87 (5%)**	**<0.001***	**26/76 (34%)**	**2/70 (3%)**	**<0.001***

†Evaluable population was defined as all treated patients who survived through 24 month follow-up

* Indicating a level of significance < 0.05; P-values determined using Fisher exact test

[a]The X STOP group includes 6 patients who underwent device removal and laminectomy; 1 patient who underwent device removal only; and 3 patients who did not have 24 month outcome data available and were therefore classified as device failures in this category.

[b]The X STOP group includes 4 patients who failed to maintain distraction; and 11 patients who had insufficient data at 24 months to determine maintenance of distraction and were therefore classified as failures in this category; among the 85 patients for whom sufficient data were available, distraction was maintained at 96% of the levels measured (i.e., 109 of 113 implanted levels)

[c]The X STOP group includes 1 patient in whom the implant dislodged after a fall; and 3 patients who did not have 24 month outcome data available and were therefore classified as device failures in this category.

[d]The X STOP group includes 1 patient with device dislodgement; 1 patient with an asymptomatic spinous process fracture; 1 patient with malpositioned implants; and 3 patients who did not have 24 month outcome data available and were therefore classified as device failures in this category.

[e]Two X STOP patients were removed from the overall treatment success analysis because they received post-operative epidural injections following motor vehicle accidents.

Within the evaluable population, the subset of patients most likely to benefit from the X STOP device was identified (via post-hoc analysis) as those with moderately impaired physical function at baseline (defined as patients having baseline ZCQ PF scores > 2.0). **Table 14** shows success rates in this indicated population calculated in two ways—for all sites, and excluding the investigational site with the highest success rates (Site 01/04).

Table 14: Treatment Success at 24 Month Follow-Up – Indicated Population†

Outcome Parameter	All Sites			All Sites Excluding Site 01/04		
	X STOP	Control	p-value	X STOP	Control	p-value
	n/N (%)	n/N (%)		n/N (%)	n/N (%)	
ZCQ Success	41/73 (56%)	4/66 (6%)	<0.001*	25/54 (46%)	2/53 (4%)	<0.001*
• *Physical Function*	*47/73 (64%)*	*11/66 (17%)*	*<0.001**	*32/54 (59%)*	*6/53 (11%)*	*<0.001**
• *Symptom Severity*	*53/73 (73%)*	*16/66 (24%)*	*<0.001**	*30/54 (56%)*	*7/53 (13%)*	*<0.001**
• *Patient Satisfaction*	*48/73 (66%)*	*11/66 (17%)*	*<0.001**	*35/54 (65%)*	*9/53 (17%)*	*<0.001**
No additional surgery for lumbar stenosis[a]	66/73 (90%)	37/66 (56%)	<0.001*	48/54 (89%)	28/53 (53%)	<0.001*
Maintained distraction[b]	64/73 (88%)	NA	NA	45/54 (83%)	NA	NA
No dislodgement[c]	70/73 (96%)	NA	NA	51/54 (94%)	NA	NA
Absence of implant-related complications[d]	69/73 (95%)	NA	NA	50/54 (93%)	NA	NA
Overall Treatment Success[e]	**38/71 (54%)**	**4/66 (6%)**	**<0.001***	**22/52 (42%)**	**2/53 (4%)**	**<0.001***

†Target population was defined as patients with moderately impaired physical function at baseline (baseline PF score > 2.0)

*Indicating a level of significance < 0.05; P-values determined using Fisher exact test

[a]The X STOP group includes 4 patients who underwent device removal and laminectomy; 1 patient who underwent device removal only; and 2 patients who did not have 24 month outcome data available and were therefore classified as device failures.

[b]The X STOP group includes 2 patients who failed to maintain distraction; and 7 patients who had insufficient data at 24 months to determine maintenance of distraction; among the 66 patients for whom sufficient data were available, distraction was maintained at 98% of the levels measured (i.e., 87 of 89 implanted levels)

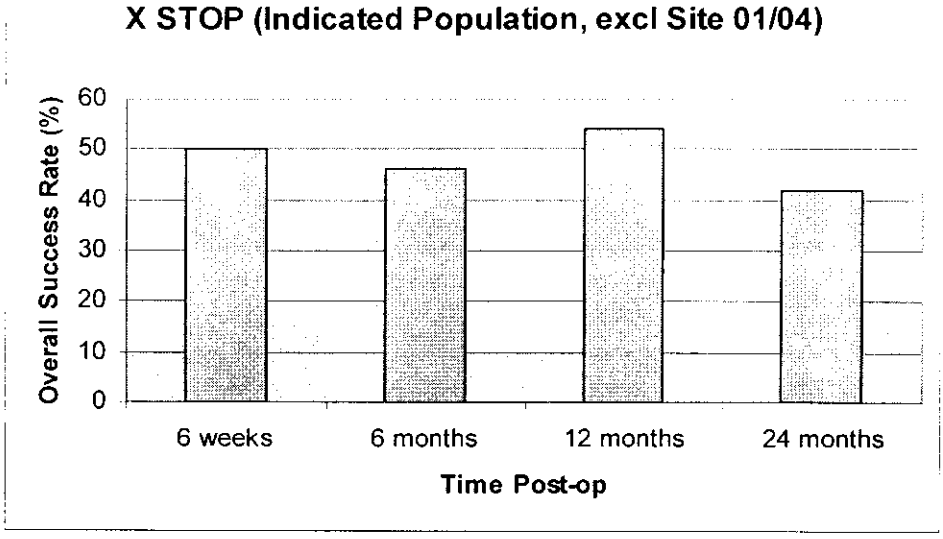
[c]The X STOP group includes 1 patient in whom the implant dislodged after a fall; and 2 patients who did not have 24 month outcome data available and were therefore classified as device failures.

[d]The X STOP group includes 1 patient with device dislodgement; 1 patient with an asymptomatic spinous process fracture; and 2 patients who did not have 24 month outcome data available and were therefore classified as device failures.

[e]Two X STOP patients were removed from the overall treatment success analysis because they received post-operative epidural injections following motor vehicle accidents.

Figure 1 below illustrates overall treatment success rates for the indicated (post hoc) population (excluding Site 01/04) at each of the post-operative follow-up intervals -- 6 weeks, 6 months, 12 months, and 24 months. Effectiveness of the device beyond 24 months post-implantation has not been demonstrated.

Figure 1. Overall success rates for the indicated population (excluding Site 01/04) at each post-operative interval



Secondary Endpoint

SF-36

Results of Quality of Life assessments (SF-36) were used to assess physical and mental well-being. The SF-36 Physical Component Summary (PCS) score is a composite of four scales that has been shown to be valid as a physical health measure. The SF-36 Mental Component Summary (MCS) is also a composite of four scales, and is less appropriate as an outcome measurement in surgical studies.

SF-36 domain scores were compared between the X STOP and control groups using an ANOVA ($p<0.05$). The mean scores for the PCS and MCS for the X STOP and control patients comprising the indicated population, at baseline and 24 month follow-up, are shown in **Table 15.** There were no statistically significant differences in mean baseline SF-36 domain scores between the X STOP and control groups. The mean change score for the PCS at the 24 month follow-up was statistically significantly higher in the X STOP group compared to the control group.

Table 15: SF-36 Domain Scores at Baseline and 24 Month Follow-up – Indicated Population

Domain	X STOP		Control	
	Preop	24 mo	Preop	24 mo
Physical Component Summary (PCS)	26.9	39.6	26.9	29.1
Mental Component Summary (MCS)	49.6	53.9	48.9	52.5

Back and Leg Pain

Back and leg pain frequency and severity scores were compared between the X STOP and control groups using the Fisher exact test ($p<0.05$). At 24 months mean back and leg pain scores were significantly less frequent and less severe in the X STOP group as compared to the control group while sitting, standing or walking. When looking at actual mean improvement the X STOP group had significantly greater improvement than the control group in frequency and severity of back pain while standing and walking, while there was no significant difference in improvement scores for back pain while sitting. The X STOP group had a significantly greater

improvement than the control group in the frequency and severity of leg pain while sitting, standing or walking at 24 months.

Analgesic Use
Analgesic use was collected throughout the study. There was no statistical difference in use between the two groups at 24 months.

Comparison to Laminectomy Outcomes

The sponsor also provided an unpublished analysis of 197 patients who underwent laminectomy by one surgeon, as an historical control for patients needing a laminectomy for lumbar stenosis symptoms. The analysis used the ZCQ assessment scale and the same definition of individual patient success employed in the X STOP pivotal trial. The patients in the laminectomy analysis were worse at baseline than those in the X STOP clinical trial. The results indicated that 47.4% of the historical laminectomy patients had a successful outcome; this compares with a 44% overall treatment success rate for evaluable X STOP patients.

The sponsor also provided comparisons to unpublished laminectomy results reported by another surgeon for 58 patients, again using the same domain thresholds for individual patient success as employed in the X STOP pivotal trial. However, these patients also had more extensive/severe stenosis than the mild or moderate LSS patients in the X STOP trial, and the follow-up duration was variable. For the subset of 20 laminectomy patients treated at one or two levels, overall success was 55%.

In vivo Clinical Radiographic Study
Flexion-extension range of motion (ROM), foramen area, or canal area measurements were not made in the pivotal clinical study. However, following the pivotal clinical trial, a prospective, nonrandomized clinical radiographic study was undertaken to evaluate the pre- and postoperative changes in the dimensions of the spinal canal and neural foramen during flexion and extension in LSS patients who received the X STOP implant at a single European clinical site.

Measurements were made from 37 levels in 26 patients. Fifteen patients were implanted at a single level and 11 patients were implanted at two levels. The mean age was 71.3 years (range 56.1 to 94.0). MRI scans were acquired preoperatively and 6 months following X STOP surgery. Each patient was scanned prior to treatment and at 6 months after treatment while sitting in a 0.6 Tesla positional MRI scanner (Fonar, Melville, NY) in the flexed and extended positions. The intervertebral angle, foramen area, and canal area were digitally measured from each scan using image analysis software (OSIRIS 4, University Hospital of Geneva, Switzerland).

Pre- and postoperative radiographic changes, measured on an individual patient basis, are described below:

- *Flexion-Extension Range of Motion (ROM)*: Ten of the 26 patients (38%) exhibited a decreased ROM at all implanted levels following X STOP implantation; these 10 patients included three who were treated at two levels. Seven of the 11 patients (64%) treated at two levels exhibited decreased ROM at one treated level, and either no change or an

increased ROM at the other level. In total, 20 of the 37 implanted levels (54%) exhibited a decreased ROM.

- *Foramen Area*: Twenty of the 26 patients (77%) exhibited an increased foramen area at all implanted levels following X STOP implantation. An additional three patients who were treated at two levels exhibited an increased foramen area at one of the two implanted levels. In total, 31 of the 37 implanted levels (84%) exhibited an increased foramen area.
- *Canal Area*: Canal area measurements were available for 24 of the 26 patients and 35 of the 37 levels. Fifteen of the 24 patients (63%) exhibited an increased canal area at all implanted levels following X STOP implantation. One patient who was treated at two levels exhibited an increased canal area at one level, but complete canal area measurements were not available for the other level (which showed decreased foramen area). In total, 26 of the 35 implanted levels (74%) exhibited an increased canal area.

Clinical outcomes data at 6 months follow-up were available for 24 of the 26 patients. Of these 24 patients, 11 satisfied the criteria for patient success (11/24; 46.0%) where success was defined as clinically significant improvement in Physical Function and Symptom Severity scores compared to baseline ($\geq$ 0.5 point change) in patients who were "satisfied" or "very satisfied" as self-reported using the Zurich Claudication Questionnaire (ZCQ). A correlation between these radiographic changes and clinical outcomes was not demonstrated at six months post-implantation.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The data presented in the preceding sections provide reasonable assurance that the X STOP is safe and effective in the treatment of patients aged 50 or older suffering from neurogenic intermittent claudication secondary to a confirmed diagnosis of lumbar spinal stenosis (with X-Ray, MRI, and/or CT evidence of thickened ligamentum flavum, narrowed lateral recess and/or central canal narrowing). The X STOP is indicated for those patients with moderately impaired physical function who experience relief in flexion from their symptoms of leg/buttock/groin pain, with or without back pain, and have undergone a regimen of at least 6 months of nonoperative treatment. A significantly greater proportion of X STOP patients achieved overall treatment success, compared to control patients.

Risk - Benefit Analysis

The X STOP device met the primary clinical study endpoint for success, exceeding the success rate of the control in every statistical analysis. The implant resulted in a low percentage of complications, each of which resolved without significant clinical sequelae and no neurological or vascular injuries. The X STOP implantation procedure is a much less invasive procedure than other surgical decompressive procedures such as laminectomy, and can often be performed under local anesthesia. The procedure preserves local anatomy so that, should device removal become necessary, additional surgical options such as laminectomy are not precluded.

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

XII. PANEL RECOMMENDATIONS

The PMA for the X STOP was reviewed at the Orthopaedic and Rehabilitation Devices Advisory Panel meeting held on August 31, 2004. The Panel recommended to the FDA, by a vote of 5-3, that the PMA be found not approvable, citing concern with the need to identify the patient population that is most likely to benefit from the device, noting the relatively low overall effectiveness in the clinical study population. The Panel also cited concerns with the need for radiographic or other objective evidence of the device's mechanism of effect on the spine in patients, and with the longer term effectiveness of the device (beyond two years).

XIII. CDRH DECISION

FDA concurred with the Panel's recommendation of August 31, 2004, and issued a letter to St. Francis Medical Technologies requesting that the applicant: (1) provide an analysis of the study results in order to determine whether any subgroup characteristics may be predictive of successful outcomes; (2) provide the more comprehensive interpretation and summary of comparative analyses that were included in its Panel presentation; and (3) provide an analysis of a representative sample of radiographic outcomes in patients implanted at one and two levels, in order to support the claims that the device limits extension and increases canal/foraminal dimensions. In amendments received by FDA on December 27, 2004 and June 22, 2005, the applicant submitted the required data. This information was reviewed and found to be adequate. The Indications for Use have been revised to specify that the device is indicated only in patients with moderately impaired physical function. Labeling information related to device mechanism of action has been revised to reflect the *in vivo* findings.

In order to gather long-term safety and effectiveness data, the applicant has agreed to conduct post-approval studies to obtain five-year follow-up data from (a) all subjects in the clinical study who received the X STOP, and (b) a new cohort of lumbar spinal stenosis patients with moderately impaired physical function who would receive the X STOP on a post-approval basis. Both studies will utilize the same endpoints as the clinical study.

FDA worked with the applicant to review the content of the training program, and to finalize device labeling and the requirements of the post-approval studies. The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820). FDA issued an approval order on NOV 21 2005

Expedited review status of this PMA was granted on January 6, 2004, because the X STOP may offer a viable alternative to laminectomy surgery in some patients with lumbar spinal stenosis. In addition, expedited status was granted because no legally marketed device is available that does not promote fusion while treating patients with lumbar spinal stenosis.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the product 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 the Approval Order.