SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name:	Implantable Pacemaker Pulse Generator and Permanent Pacemaker Electrode
Device Trade Name:	St. Jude Frontier™ Biventricular Cardiac Pacing System including the Frontier™ Model 5508 and 5508L Pulse Generators, the Aescula™ LV Model 1055K Lead and the Model 3307 v4.4.2m programmer software for use with the Model 3500/3510 Programmer
Applicant's Name and Address:	St. Jude Medical Cardiac Rhythm Management Division 15900 Valley View Court Sylmar, CA 91342
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P030035
Date of Notice of Approval to Applicant:	

II. Indication for Use

The Frontier™ Biventricular Cardiac Pacing System is indicated for maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure

III. Contraindications

Implantation of the Frontier™ Biventricular Cardiac Pacing System is contraindicated in patients who have been implanted with an implantable cardioverter-defibrillator (ICD),

The Aescula lead is contraindicated in patients who are unable to undergo an emergent thoracotomy procedure, and in patients with coronary venous vasculature that is inadequate for lead placement, as indicated by venogram.

IV. Warnings and Precautions

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

V. System Description

Frontier Device Description

The Frontier™ pulse generator is a multi-site, implantable cardiac device with biventricular sensing and stimulation capabilities, intended for use with a St. Jude Medical® left-heart pacing lead.

The Frontier device is equipped with automatic rate-adjusting algorithms, patient safety features, and diagnostic tools and tests. The Frontier device contains the Omnisense® accelerometer activity sensor to provide rate-modulated operation.

In addition, with the Frontier device, the Model 3510/3500 Programming System offers:

- On-screen Reference Manual
- Floppy disk database interface
- Continuous real-time printing of ECG, EGM, and Markers (only available on the Model 3510 Programmer).

A single setscrew for each lead secures the pin within the connector. The device header accepts unipolar or bipolar IS-1 and VS•1, or 3.2 mm leads.

The Frontier device is supported on Model 3500/3510 programmer platforms with Model 3307, v 4.4.2 m or higher programmer software.

Aescula Lead Description

The Aescula™ LV Model 1055K lead is a silicone-insulated left heart lead with a Titanium Nitride (TiN) coated platinum-iridium electrode, designed for use with implantable pulse generators for long-term cardiac pacing. The distal portion of the tip is preshaped by the silicone insulation into an "s-curve" to provide passive fixation.

The lead length is 75 centimeters, and the minimum recommended lead introducer size is 7.0 French. The lead complies with IS-1 connector standard ISO 5841-3.

The Aescula LV Model 1055K lead is a unipolar lead, having one conductor that terminates at the tip electrode.

Features of the Aescula LV Model 1055K lead include:

- Passive Fixation — incorporating an s-shaped curve designed to stabilize the lead in the vein.
- Fast-Pass® Coating — creates a lubricious surface.

VI. Alternative Practices or Procedures

The present established therapies for the treatment of patients with chronic atrial fibrillation include pharmacological therapy or standard right ventricular pacing therapy post AV nodal ablation.

VII. Marketing History

The Frontier pulse generator and the Aescula lead are currently distributed commercially outside the United States. Specifically, the Frontier pulse generator is market approved in the European Community and China. The Aescula lead is market approved in the European Community, Eastern Europe, Middle East, Africa, and Latin America.

Neither the Frontier devices nor the Aescula leads have been withdrawn from the market in any country for any reason related to safety and effectiveness.

VIII. Adverse Events

Clinical study of the Frontier™ system began on August 16, 2000. As of August 5, 2003, there were 361 attempted implants in the PAVE (Post-AV Node Ablation Evaluation) study from centers in the United States and Canada with average implant duration of 13.0 months (range: 0.1 - 35.7 months).

Potential Adverse Events

Potential adverse events associated with the use of the transvenous leads and pacing systems include:

- Body rejection phenomena
- Cardiac/coronary sinus dissection
- Cardiac/coronary sinus perforation
- Cardiac tamponade
- Coronary sinus or cardiac vein thrombosis
- Death
- Device migration and pocket erosion
- Endocarditis
- Excessive bleeding
- Hematoma/seroma
- Induced atrial or ventricular arrhythmias
- Infection
- Local tissue reaction; formation of fibrotic tissue
- Loss of pacing and/or sensing due to dislodgment or mechanical malfunction of the pacing lead
- Myocardial irritability
- Myopotential sensing
- Pectoral/diaphragmatic/phrenic nerve stimulation
- Pericardial effusion
- Pericardial rub
- Pneumothorax/hemothorax
- Pulmonary edema
- Rise in Threshold and Exit Block
- Thrombolytic or air embolism
- Valve damage

The following in addition to the above, are potential complications associated with the use of rate modulated pacing systems.

- Inappropriate, rapid pacing rates due to sensor failure or to the detection of signals other than patient activity.
- Loss of activity-response due to sensor failure.

A coronary sinus venogram is unique to lead placement in the cardiac venous system, and carries risks, such as renal failure, cardiac or coronary sinus dissection, and cardiac or coronary sinus perforation.

Potential complications reported with direct subclavian venipuncture include hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage, and rarely death.

Deaths

Fifty-one deaths occurred throughout the study. Death information was gathered and classified by an independent mortality committee of three practicing physicians according to a published classification scheme. A summary of the death classification is shown in Table 1.

Table 1- Deaths

Primary Cause	RV (N = 106)	BV (N = 146)	LV (N = 53)	Roll-in (N = 56)	Total (N = 361)
Cardiac: Arrhythmic	1	1	1	0	3
Cardiac: Other	7	3	3	2	15
Cardiac: Unknown	0	1	0	0	1
Non-Cardiac	4	2	5	4	15
Unknown	6	5	3	2	16
Total	18	12	12	8	50[1]
% Death	17.0	8.2	22.6	14.3	13.8

Observed Adverse Events

A prospective, randomized, controlled, multi-center clinical trial of patients who had received AV nodal ablation for chronic atrial fibrillation was conducted at 49 participating sites (44 in the US, 5 in Canada). The study compared the safety and effectiveness of biventricular (BV) pacing therapy, using the Frontier™ Model 5508 pulse generator and the Aescula™ 1055K Left Heart Lead (BV treatment group) to traditional right ventricular (RV) pacing therapy (RV control group) using the legally marketed pulse generators and right ventricular leads.

Of a total of 361 attempted implants, 146 patients were randomized to BV pacing, and 106 were randomized to RV pacing. In addition, 53 patients were randomized to left ventricular (LV) pacing under a previous revision of the investigational plan, and 56 were "roll-in" patients (non-randomized) who received the biventricular pacing system (Frontier pulse

1 One additional patient was consented, but died prior to any study related procedure.

generator and Aescula lead system). As per the protocol, the data from the "roll in" patients were only used in the safety endpoint analysis. All of these patients underwent a complete AV nodal ablation procedure. The study's cumulative implant duration for all enrolled patients was 4,684 months with a mean of 13.0 ± 9.6 months (range of 0.1 to 35.7 months). The cumulative duration for investigational patients (BV, LV and Roll-in groups only) was 3,129 months (260.8 years).

An adverse event is defined as an unfavorable clinical event, which impacts, or has the potential to impact, the health or safety of a clinical study participant caused by, or associated with, a study device or intervention. An adverse event is classified as a complication when it results in an injury or an invasive intervention (for example, lead repositioning after lead dislodgement) that would not have occurred in the absence of the implanted device and/or system components. An observation is defined as an adverse event that is not associated with injury to the patient or an invasive intervention, but which is associated with the system under investigation, or the programming thereof.

During the entire study period, 170 adverse events were reported including 53 complications and 117 observations. Tables 2 through 4 summarize the complications, and Tables 5 and 6 summarize the observations that occurred during the study. System-related complications and observations are based on patients with investigational systems only (BV, LV, and Roll-in groups, N = 254; RV group, N = 106). Procedure-related complications are based on patients who underwent a study-related procedure, including the AV nodal ablation procedure (BV, LV, Roll-in groups, N = 255; RV group, N = 106).

Table 2 - System-Related Complications for Investigational Group[2]

Events	BV, LV, and Roll-In (N = 254)[3]			
	# of Events	# of Patients	% of Patients	Events/Device-Months[4]
LV Lead-Related:	25	24	9.4	0.0080
Pectoral Stimulation	1	1	0.4	0.0003
Diaphragmatic Stimulation	6	6	2.4	0.009
Acute LV Lead Dislodgement	9	9	3.5	0.0029
High LV Pacing Threshold at Implant, Later System Revised	6	6	2.4	0.0019
LV Lead Loss of Capture	3	3	1.2	0.0010
RV Lead-Related:	5	4	1.6	0.0016
Acute RV Lead Dislodgement	3	2	0.8	0.0010
RV Perforation	1	1	0.4	0.0003
RV Insulation Failure	1	1	0.4	0.0003
Total System-Related	**30**	**27**	**10.6**	**0.0096**

2 Each patient may have more than one complication in more than one category.

3 System-related complications based on total number of attempted implants (N = 254).

4 Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in the BV, LV, and Roll-in groups. The cumulative duration in months in these groups was 3,129 months.

Table 3 - Procedure-Related Complications for Investigational Group [5]

Events	BV, LV, and Roll-In (N = 255)[6]			
	# of Events	# of Patients	% of Patients	Events/Device-Months[7]
Procedure-Related:	17	15	5.9	0.0054
CS Dissection at Implant	7	7	2.7	0.0022
CS Perforation at Implant	3	3	1.2	0.0010
Pneumothorax at Implant	3	3	1.2	0.0010
Arrhythmia - VT at Implant	1	1	0.4	0.0003
Pulmonary Edema Post- Ablation	1	1	0.4	0.0003
LV Lead Dislodgment During Ablation Procedure	1	1	0.4	0.0003
Cardiac Tamponade at Implant	1	1	0.4	0.0003
Total System-Related and Procedure-Related Complications	**47**	**42**	**16.5**	**0.0150**

Table 4 - Complications for Control Group

Events	RV (N = 106)			
	# of Events	# of Patients	% of Patients	Events/Device-Months[8]
Acute RV Lead Dislodgement	1	1	0.9	0.0006
RV Perforation	1	1	0.9	0.0006
RV Lead Fracture	2	2	1.9	0.0013
Infection	1	1	0.9	0.0006
Hematoma	1	1	0.9	0.0006
Total Complications	**6**	**6**	**5.7**	**0.0039**

5 Each patient may have more than one complication in more than one category.

6 Procedure-related complications based on total number of procedures (N = 255).

7 Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in the BV, LV, and Roll-in groups. The cumulative duration in months in these groups was 3,129 months.

8 Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in the RV group. The cumulative duration for the RV group is 1,555 months.

Table 5 - Observations for Investigational Group[9]

Events	BV, LV, and Roll-In (N = 254)[10]			
	# of Events	# of Patients	% of Patients	Events/Device-Months[11]
Diaphragmatic Stimulation	22	19	7.5	0.0070
High LV Pacing Threshold	14	14	5.5	0.0045
Pectoral Stimulation	13	11	4.3	0.0042
Hematoma at Implant	8	8	3.1	0.0026
High LV Threshold at Implant	7	7	2.8	0.0022
Fatigue	6	6	2.4	0.0019
Infection	5	5	2.0	0.0016
LV Loss of Capture	4	4	1.6	0.0013
CS Dissection at Implant	3	3	1.2	0.0010
Telemetry Error	3	2	0.8	0.0010
Oversensing	3	3	1.2	0.0010
Thrombosis	2	2	0.8	0.0006
Hypotension	1	1	0.4	0.0003
Palpitation	1	1	0.4	0.0003
Noise on IEGM	1	1	0.4	0.0003
Arrhythmia - Torsades	1	1	0.4	0.0003
Dyspnea on Exertion	1	1	0.4	0.0003
RV Back-up Pacing Due to PVCs	1	1	0.4	0.0003
Acute LV Lead Dislodgment (minor)	1	1	0.4	0.0003
RV Loss of Capture	1	1	0.4	0.0003
LV Lead Undersensing	1	1	0.4	0.0003
Pneumothorax	1	1	0.4	0.0003
Stuck Stylet	1	1	0.4	0.0003
Syncope	1	1	0.4	0.0003
Total Events	**102**	**74**	**29.1**	**3.2600**

9 Each patient may have more than one observation in more than one category.

10 Observations based on total number of attempted implants (N = 254).

11 Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in the BV, LV, and Roll-in groups. The cumulative duration in months in these groups was 3,129 months.

Table 6 - Observations for Control Group

Events	RV (N = 106)			
	# of Events	# of Patients	% of Patients	Events/Device-Months[12]
Diaphragmatic Stimulation	1	1	0.9	0.0006
Hematoma at Implant	3	3	2.8	0.0019
Fatigue	1	1	0.9	0.0006
Hypotension	2	2	1.9	0.0013
Palpitation	2	2	1.9	0.0013
Device Site Discomfort	3	3	2.8	0.0019
Bloody Drainage from Incision Site	1	1	0.9	0.0006
High RV Pacing Thresholds	1	1	0.9	0.0006
Presyncope	1	1	0.9	0.0006
Total Observations	**15**	**15**	**14.2**	**0.0096**

IX. Summary of Pre-Clinical Studies

Frontier Pulse Generators and Programmer Software

Preclinical testing of the Frontier Pulse Generators, presented in Table 7 below, included hybrid assembly, mechanical, and electrical testing, as well as, header assembly testing.

Table 7 – Frontier Pulse Pre-Clinical Testing

	Sample Size	Model No.	Test Results (Pass**/Fail)
Hybrid Assembly: Hybrid level testing was evaluated by verifying projected longevity; pacing and sensing characterization at BOL, RRT and at EOL; and pacing rate response at RRT.	1 - 5	5508	Pass
Frontier Pulse Generator Mechanical Testing: Mechanical testing was performed to verify compliance to product specification requirements such as visual/X-ray; dimensional; marking/labeling; and document compliance.	1 - 6	5508	Pass
Frontier Pulse Generator Electrical Functional Testing: Electrical testing was performed to verify functionality of the pulse generator. Additional testing included verification of programmable parameters and crosstalk characterization.	1 - 6	5508	Pass

12 Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in the RV group. The cumulative duration for the RV group is 1,555 months.

Frontier Header Assembly: The IS-1 header connector assembly met compliance to ISO 5841-3 and included visual/dimensional requirements; insertion and extraction forces testing. Additional testing included CENELEC Leakage for lead connector impedance and lead retention using an IS-1 lead; multiple EtO sterilization; temperature cycling; torque and push test.	12 - 18	5508	Pass

* The Model 5508L Frontier device is mechanically and electrically identical to the Frontier Model 5508 except for the connector top.

** "Pass" as used here denotes that the device meets established performance criteria and/or specifications, or is in conformance with the requirements of the referenced standard.

Frontier Software Verification and Validation

Formal validation of the Frontier system was performed via User Testing to demonstrate that the clinically significant features of the Frontier system deliver the intended benefits in a "simulated as used" environment. The test activity was divided into scenarios designed to exercise the Frontier and 3500/3510 programmer system in situations representative of a clinical environment. There are no known anomalies in the software that are significant in terms of patient safety or clinical efficacy.

Programmer Software Verification

The programmer software verification underwent extensive testing for Model 3307, v 4.4.2 m, which supports the Frontier pulse generator on Model 3500/3510 programmer platforms. The results of the programmer verification testing demonstrate that the requirements have been met. There are no known anomalies in the software that are significant in terms of patient safety or clinical efficacy.

Biocompatibility

The blood and tissue contacting materials (Hysol epoxy, titanium, ETR silicone) are the same as in the commercially available Affinity family of pulse generators, except for polysulfone (included in the QuickLock connector only). The polysulfone has gone through extensive biocompatibility testing, which has been reviewed and accepted by FDA.

All materials listed above have been assessed for biocompatibility with respect to biological response and lack of harmful effects to patients. All materials were tested to and comply with ISO 10993.

Electromagnetic Compatibility

The Frontier device has an identical filtered feedthrough as in the commercially available Affinity device. EMI testing was conducted on the Affinity device in accordance with the preliminary version of ANSI/AAMI PC69 and the released AMSI/AAMI PC69:2000. Therefore, no additional testing was conducted on the Frontier device for EMI susceptibility.

Sterilization, Packaging and Shelf Life

The sterilization of the Frontier pulse generator is identical to the sterilization process of the commercially available Affinity DR Model 5330. Routine validation is performed in accordance with the Association for the Advancement of Medical Instrumentation. Medical Device – Validation and routine control of ethylene oxide sterilization (ANSI/AAMI/ISO 11135:1994).

The packaging process of the Frontier pulse generator is also identical to the packaging of the commercially available Affinity DR Model 5330 device, with the exception of the inner seal tray, which has been reduced in size by approximately one-half.

Based on the above the shelf-life of the Frontier is identical to that of the Affinity DR Model 5330 and set at 18 months.

Aescula Lead

Preclinical testing of the Aescula lead, presented in Table 8 below, included mechanical, electrical and in vivo characterization in canines.

Table 8 – Aescula Lead Pre-Clinical Testing

	Sample Size	Model No.	Test Results (Pass*/Fail)
Aescula Lead Qualification Testing: Lead testing verifying conformance to IS-1 standard per ISO 5841-3 requirements included visual inspection; IS-1 connector dimensional; DC resistance; connector insertion/withdrawal; set screw deformation and marking. Additional testing verifying compliance to prEN45502-2-1 included connector flex; conductor flex; temperature cycling; lead durability; insulation integrity and lead pull test.	6 - 12	1055K	Pass
Multiple sterilization tests to determine effects of multiple sterilization exposures.	12	1055K	Pass
UPS ship test to ensure conditions of general shipping and handling were met.	12	1055K	Pass
Polarization test to measure polarization of fully assembled leads.	12	1055K	Pass
Temperature Storage test to determine the effects of long-term storage at high and low temperatures on lead integrity.	12	1055K	Pass
Temperature Shock test to determine the effects of rapid temperature changes on lead integrity.	12	1055K	Pass
Suture Sleeve test to ensure that the suture sleeve will slide properly along the lead.	12	1055K	Pass
Stylet Insertion test to assess ease of stylet insertion into the lead.	12	1055K	Pass
Air Leak test to determine bond integrity under pressurized conditions.	12	1055K	Pass
Shape Retention test to ensure proper lead body shape is retained after multiple stylet insertions.	12	1055K	Pass
Joint Bond strength test to determine the integrity of the lead bonds.	12	1055K	Pass

Lead Introducer test to verify lead passage through a 6 French introducer.	12	1055K	Pass
Distal Tip Fatigue Testing is to determine distal end reliability subjected to 400 million flex cycles.	10	1055K	Pass

* "Pass" as used here denotes that the device meets established performance criteria and/or specifications, or is in conformance with the requirements of the referenced standard.

Biocompatibility

The following materials used in the Model 1055K lead come in contact with the patients' blood and/or tissue while the lead is implanted:

- Silicone Rubber
- Photo Active Polyvinyl Pyrolidone Coating ("Fast Pass")
- Titanium Nitride
- Platinum/Iridium

All materials listed above have been assessed for biocompatibility with respect to biological response and lack of harmful effects to patients. All materials were tested to and comply with ISO 10993.

Sterilization, Packaging and Shelf Life

The 100% EtO sterilization process and packaging process of the Aescula lead are identical to the process used for the legally marketed Passive Plus DX lead (P960030, approved January 29, 1998).

Packaging of the Model 1055K lead is identical to that of other St. Jude Medical leads, including the Passive Plus DX family of leads. The Model 1055K lead is packaged in double aseptic package composed of Polyethylene Terephthalate Glycol copolyester (PETG) with a Tyvek lid. The lidding stock is coated with a water soluble adhesive and is bonded to the tray using heat and pressure.

Based on the above the shelf-life of the Aescula lead is identical to that of the Passive Plus DX family of leads and set at 3 years.

Aescula Lead Chronic Animal Study

The Aescula lead has been tested in a canine model to confirm that the lead effectively captures the left ventricle via the coronary sinus. This animal study provided information on pacing thresholds, signal amplitudes, lead impedance and stability data. The study demonstrated acceptable performance of the Aescula lead in this animal study.

Conclusions Drawn from the Pre-Clinical Studies

The results of a comprehensive program of hardware qualification and software verification and validation tests performed on the Frontier system provide a reasonable level of assurance that this device will be safe and effective when utilized in accordance with the intended use stated in the product labeling.

X. Summary of Clinical Investigation

A prospective, randomized, controlled, multi-center clinical trial conducted at 49 participating sites (44 in the US, 5 in Canada) compared the safety and effectiveness results for patients receiving the Frontier™ Model 5508 pulse generator and the Aescula™ 1055K Left Heart Lead to those receiving legally marketed right ventricular pulse generators and standard leads following an AV nodal ablation for chronic atrial fibrillation (AF). Chronic AF is defined as persisting without interruption for at least one month.

The purpose of this investigation was to study the benefit of biventricular pacing over traditional RV pacing for those patients electing to undergo AV nodal ablation for treatment of chronic atrial fibrillation. The primary effectiveness objective of the study was to compare exercise performance data, as measured by the 6-minute walk test, for patients with biventricular (BV) pacing versus RV pacing at baseline and 6-months follow-up. Electrical and safety performance data of the Aescula lead as well as the safety performance of the entire implanted pacing system were evaluated as primary safety endpoints. Functional capacity as measured by peak VO_2 and Quality of Life were evaluated as secondary effectiveness endpoints.

Patients who satisfied the inclusion and exclusion criteria underwent a pre-implant baseline evaluation to determine study eligibility. Patient inclusion criteria included:

1. Patients who will undergo complete AV nodal ablation for chronic atrial fibrillation resulting in complete AV Block (chronic atrial fibrillation is defined as persisting without interruption for at least 1 month).
2. Patients who are on a stable medical therapy regimen. Stable medical therapy is defined as either ON or OFF drug therapy for 5 drug half-lives at the time of enrollment. If the eligible candidate is being treated with Amiodarone therapy, the dosage at the time of enrollment must be stable for at least 30 days prior to implant.
3. Patients who are able and have completed the 6-minute walk test as outlined in this protocol with the only limiting factor(s) being fatigue and/or shortness of breath.
4. Patients who will provide informed consent for study participation and, are willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

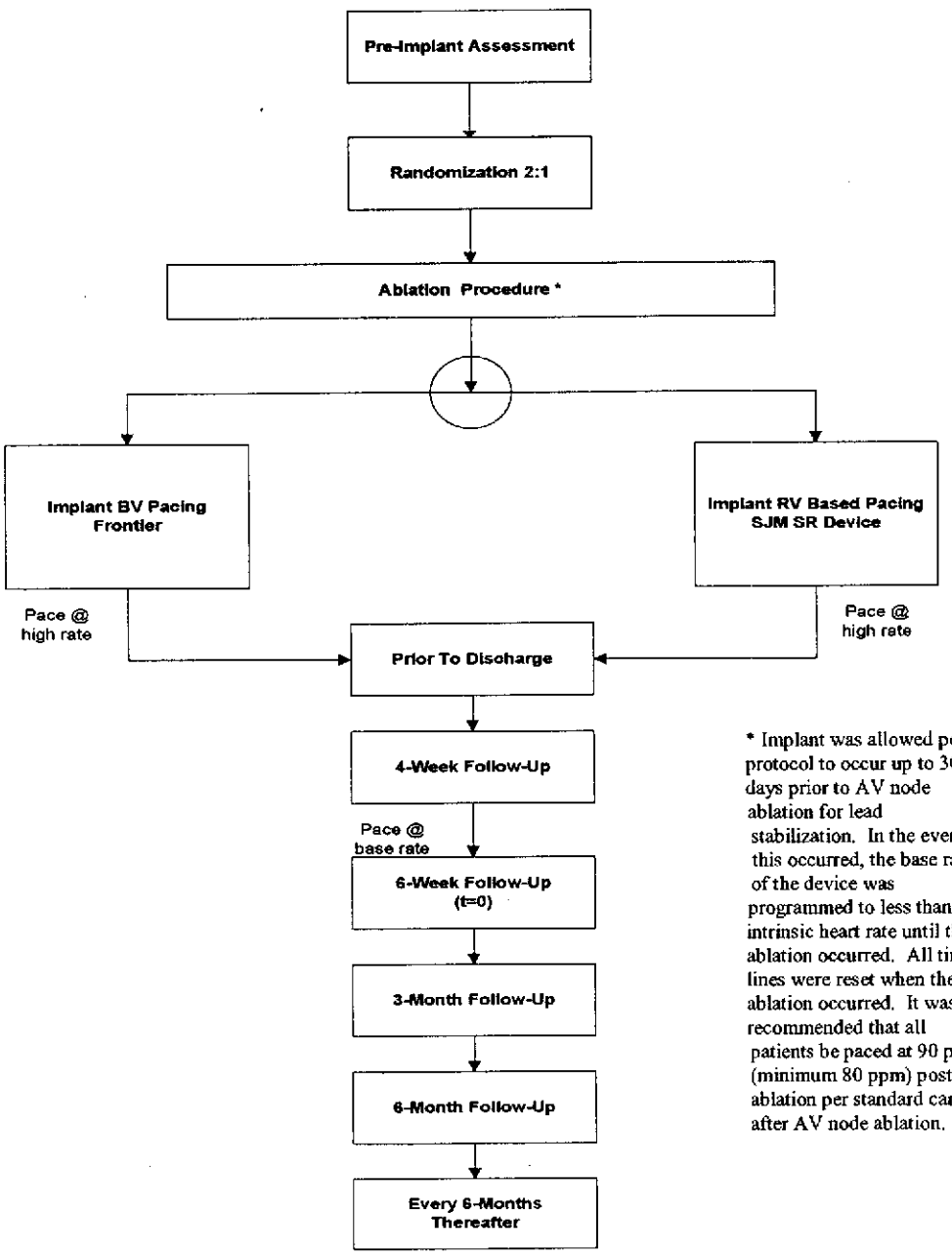
Patient exclusion criteria were:

1. Patients who are classified as NYHA class IV.
2. Patients who can walk >450 meters while using the 6-minute walk test.
3. Patients who have an implanted ICD or, are being considered for implantation of an ICD.
4. Patients who are contraindicated for an emergency thoracotomy.
5. Patients who are being considered for cardiac surgery within the next 6 months.
6. Patients with prosthetic valve replacements.
7. Patients with severe musculoskeletal disorder(s).
8. Patients under the age of 18 years.
9. Current or planned pregnancy in the next 6 months.
10. Current participation or participation in the past 30 days in any clinical investigation.
11. Patients with life expectancy less than 6 months.

12. Patients who cannot independently comprehend and complete the Quality of Life (QoL) questionnaire.
13. Patients allergic to dexamethasone sodium phosphate (DSP).

Figure 1 outlines the study design for the trial. Patient cross-over was not allowed in the study and every effort was made to maintain randomized configuration throughout the trial period. The study's cumulative implant duration was 5,742 months with a mean of 15.9 ± 10.8 months (range of 0.13 to 40.0 months).

FIGURE 1: STUDY OVERVIEW

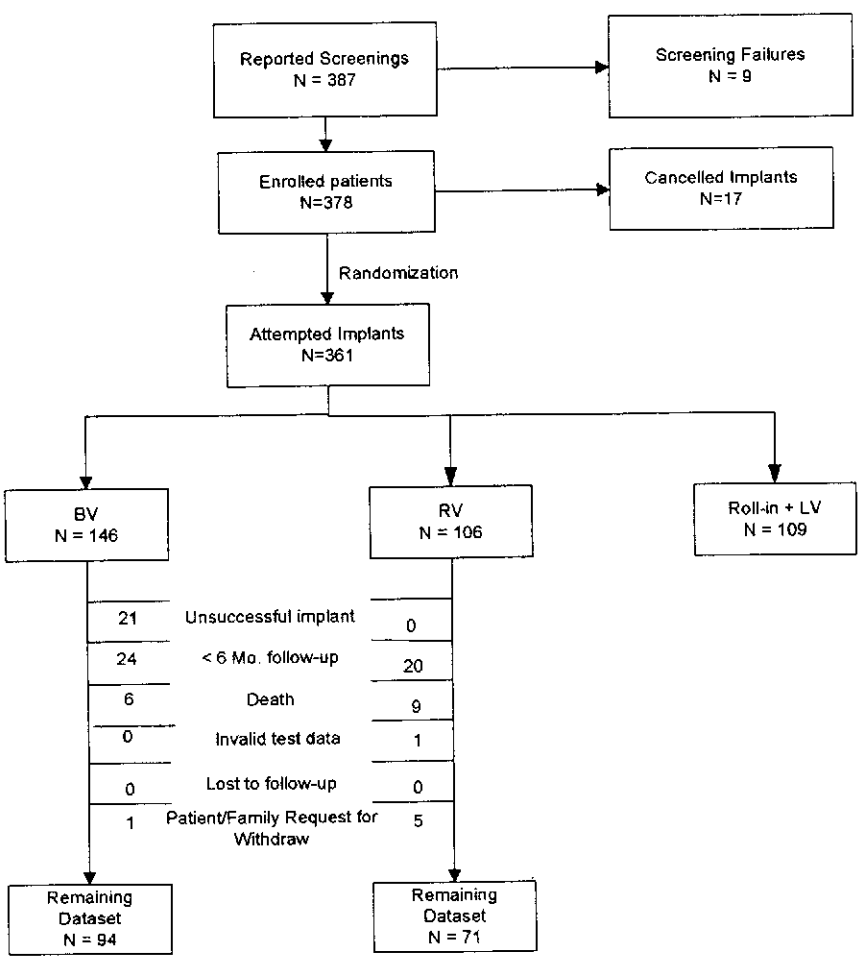


* Implant was allowed per protocol to occur up to 30 days prior to AV node ablation for lead stabilization. In the event this occurred, the base rate of the device was programmed to less than the intrinsic heart rate until the ablation occurred. All time lines were reset when the ablation occurred. It was recommended that all patients be paced at 90 ppm (minimum 80 ppm) post ablation per standard care after AV node ablation.

Patient Population

The overall study population included 361 patients. One hundred and forty-six (146) patients were randomized to BV and 106 were randomized to RV. In addition, 53 were randomized to LV pacing under the original revision of the investigational plan (although, this arm was subsequently dropped as St. Jude elected not to pursue this therapeutic option). Fifty-six (56) patients were "roll-in" patients (non-randomized, 2 per center) and received the bi-ventricular pacing system (Frontier pulse generator and Aescula lead system). As per the protocol, effectiveness analyses were based on patients randomized to the RV and BV groups only. Safety analyses include all patients with the Frontier pulse generator and the Aescula left heart lead, including LV and Roll-in patients. All patients had a permanent pacemaker implant indication following an elective AV nodal ablation for chronic atrial fibrillation. The mean age was 69.23 ± 9.98 years and there were 34.3% female and 65.7% male. Fifteen percent (15%) of the patients had no heart failure or had heart failure and were NYHA Class I, 48% were NYHA Class II, and 37% were NYHA Class III prior to implant. Figure 2 outlines the patient population for the effectiveness analysis.

FIGURE 2: PATIENT POPULATION FOR EFFECTIVENESS ANALYSIS



Primary Objectives and Results

1. **FREEDOM FROM SYSTEM-RELATED COMPLICATIONS THROUGH SIX MONTHS**
   Objective: The lower bound of the one-sided 95% confidence interval of the freedom from system-related complications for the BV group will not be less than 70%. A system-related complication was defined as a complication that is caused by a failed pacing system. A pacing system refers to all implanted components, including the pulse generator, leads, and the interaction of these components.

   Results: There were 29 system-related complications in 26 patients within six months follow-up. The freedom from system-related complications is 87.8% with a lower bound of 84.0%. Objective met.

2. **FREEDOM FROM PULSE GENERATOR-RELATED COMPLICATIONS THROUGH SIX MONTHS**
   Objective: The lower bound of the one-sided 95% confidence interval of the freedom from pulse generator-related complications for the BV group through six months will not be less than 90%.

   Results: There were no pulse generator-related complications through six months. The survival rate is 100% with a lower bound of 98.6%. Objective met.

3. **FREEDOM FROM AESCULA™ LEAD-RELATED COMPLICATIONS THROUGH SIX MONTHS**
   Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula™ lead-related complication for the BV group through six months will not be less than 75%.
   Results: There were 25 Aescula lead-related complications in 24 patients through six months follow-up. The freedom from Aescula lead-related complications is 88.2% with a lower bound of 84.4%. Objective met.

4. **RATE OF SUCCESSFUL IMPLANTATION OF THE AESCULA™ LEAD**
   Objective: The lower bound of the one-sided 95% confidence interval of the successful implantation rate of the Aescula lead for the BV group will not be less than 80%. The success rate was defined as the proportion of patients who received the complete pacing system.

   Results: One hundred and forty-six patients randomized to BV underwent attempted implants. One hundred and twenty-five were successfully implanted. The rate of successful implant of the Aescula lead for BV group is 86% with a lower bound of 81%. Objective met.

5. AESCULA™ LEAD PACING THRESHOLD AT SIX MONTHS

Objective: The upper bound of the one-sided 95% confidence interval of mean capture threshold will not be greater than 3.0 V for the BV group at six months.

Results: The pacing threshold at six months for the BV group is 2.27 V ± 1.66 V with an upper bound of 2.53 V. Objective met.

6. EXERCISE CAPACITY AS MEASURED BY DISTANCED WALKED IN SIX-MINUTE WALK TEST

Objective: To determine if the treatment group (BV) shows a statistically significant improvement over the control group (RV) at the six months follow-up time.

Results: The treatment group (BV) showed statistically significant improvement over the control group (RV) in distance walked from pre-implant to six months ($p = 0.03$). The BV group also had a greater percentage of patients showing improvements than the RV group ($p = 0.035$). Figure 3 illustrates the improvement in the six-minute walk between BV and RV groups. Table 9 outlines the improvement distribution in the six-minute walk between BV and RV groups.

Figure 3- Improvements in Six-minute Walk Distance in BV and RV Groups ($p = 0.03$)

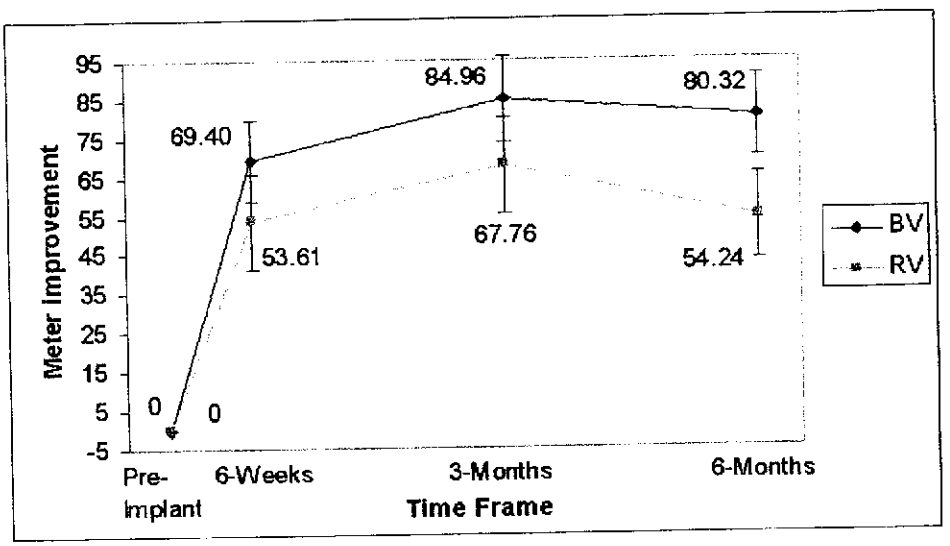


Table 9 - Distribution of Improvement in BV and RV Group in Six-Minute Walk ($p = 0.035$)

	RV (N = 66)	BV (N = 84)
Improved (> 5 m)	46 (69.70%)	69 (82.14%)
No Change (-5 to 5 m)	4 (6.06%)	4 (4.76%)
Worsened (< -5 m)	16 (24.24%)	11 (13.10%)

Secondary Objectives and Results

1. QUALITY OF LIFE AS MEASURED BY SF-36 SCORE

Objective: To determine if the BV group shows improvement over the RV group at the six-month follow-up in the health-related quality of life as measured by the SF-36 score.

Results: Using the SF-36 Quality-of-Life questionnaire, a standardized measurement of quality of life, the study found that for the six-week to six-month visit time period, the improvement in SF-36 scales was not different between groups.

2. FUNCTIONAL CAPACITY AS MEASURED BY PEAK VO_2

Objective: To determine if the BV group shows improvement in functional capacity, as measured by peak VO_2, from the six-week follow-up to the six-month follow-up.

Results: The BV group showed an improvement of 0.86 ml/kg/min in peak VO_2 from six weeks to six months measured during CPX testing ($p = 0.03$). The BV group also had a greater percentage of patients showing improvement in peak VO_2 ($p = 0.02$). Figure 4 illustrates the improvement in peak VO_2 in BV and RV groups. Table 10 outlines the distribution of improvement in peak VO_2 between BV and RV groups.

Figure 4 - Improvements in Peak VO_2 in BV and RV Groups ($p = 0.03$ within BV Group)

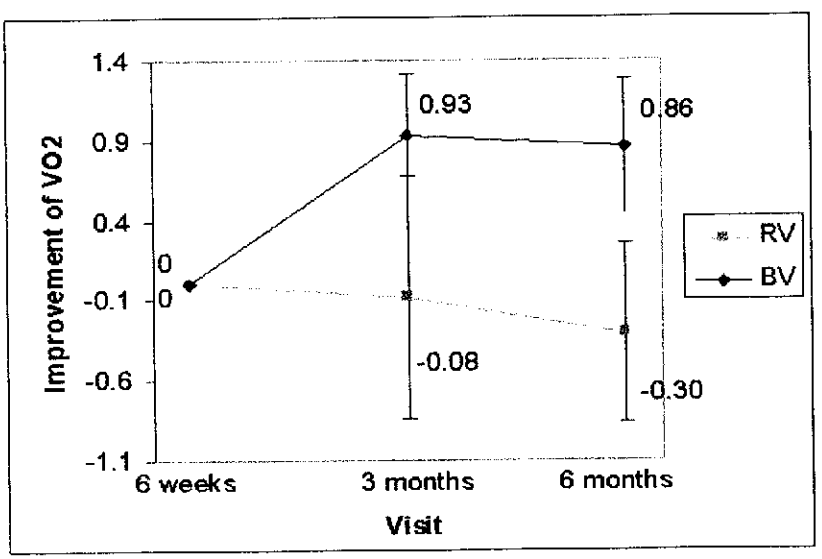


Table 10 - Distribution of Improvements in VO2 in BV and RV groups

Change in Peak VO_2(ml/kg/min)	RV (N = 10)	BV (N = 35)
Improved (> 0.5)	4 (40%)	21 (60.0%)
No Change (-0.5 to 0.5)	0 (0%)	4 (11.4%)
Worsened (<-0.5)	6 (60%)	10 (28.6%)
p-Value Within Group	0.38	0.02

XI. Conclusions Drawn from the Clinical Study

The results of the PAVE Study provide reasonable assurance of safety and effectiveness of the St. Jude Frontier™ Biventricular Cardiac Pacing System including the Frontier™ Model 5508 and 5508L Pulse Generators, the Aescula™ LV Model 1055K Lead and the Model 3307 v4.4.2m programmer software for use with the Model 3500/3510 Programmer when used as indicated in accordance with the directions for use.

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

XIII. CDRH Decision

FDA issued an approval order for P030035 on May 13, 2004. Conditions of approval included a 3-year evaluation of chronic lead performance, including electrical performance and adverse clinical events.

The sponsor's manufacturing facilities were inspected and determined to be in compliance with the Quality System Regulation (21 CFR Part 820).

XIV. Approval Specifications

Directions for Use:	See labeling
Hazards to Health from Use of the Device:	See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.
Post-approval Requirements, Restrictions:	See approval order.