SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name:	Dual Chamber Implantable Cardioverter Defibrillator (ICD) with Cardiac Resynchronization Therapy
Device Trade Name:	St. Jude Medical® Epic™ HF System including the Epic™ HF Model V-338 Cardiac Resynchronization Therapy Defibrillator, the Aescula™ LV Model 1055K Lead, the QuickSite™ LV Model 1056K Lead, and the Model 3307 v4.5m Programmer Software; St. Jude Medical® Atlas® + HF System including the Atlas® + HF Model V-340 Cardiac Resynchronization Therapy Defibrillator, the Aescula™ LV Model 1055K Lead, the QuickSite™ LV Model 1056K Lead, and the Model 3307 v4.5m Programmer Software
Applicant's Name and Address:	St. Jude Medical Cardiac Rhythm Management Division 701 East Evelyn Avenue Sunnyvale, CA 94086
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P030054
Date of Notice of Approval to Applicant:	June 30, 2004

II. Indication for Use

The St. Jude Medical Epic HF and Atlas + HF Systems are intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias. The Epic HF and Atlas + HF Systems are also intended to provide a reduction of the symptoms of moderate to severe heart failure (NYHA Functional Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy (as defined in the clinical trials section), and have a left ventricular ejection fraction less than or equal to 35% and a prolonged QRS duration.

III. Contraindications

Contraindications for use of the Epic HF and Atlas + HF Systems include ventricular tachyarrhythmias resulting from transient or correctable factors such as drug toxicity, electrolyte imbalance, or acute myocardial infarction.

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

The use of QuickSite leads is contraindicated in patients who are expected to be hypersensitive to a single dose of 1.0 milligram of dexamethasone sodium phosphate.

IV. Warnings and Precautions

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

V. System Description

Epic HF/Atlas + HF Device Description

The St. Jude Medical Epic HF V-338 and Atlas + HF V-340 dual chamber implantable cardioverter defibrillator (ICD) systems are multi-programmable, implantable cardioverter defibrillators with biventricular pacing for cardiac resynchronization therapy (CRT) that monitor and regulate a patient's heart rate by providing ventricular tachyarrhythmia therapy and single- or dual-chamber bradycardia pacing with rate adaptive response (DDD(R)). The devices have five port headers (3 IS-1 Ports, 2 DF-1 Ports).

The Epic HF and Atlas + HF devices have identical circuitry, hybrids and firmware (device software), enabling them to have identical functionality in terms of biventricular pacing, sensing, and discrimination. High voltage therapy is similar, with the difference being that the Atlas + HF device has a stored energy of 42 J and maximum output of 36 J whereas the Epic HF device has a stored energy of 34 J and a maximum output of 30 J. This is the only functional difference between the Epic HF and Atlas + HF devices. The higher output in the Atlas + HF devices is achieved using a larger capacity battery and higher delivered energy high voltage capacitors, which are identical to the components used in legally marketed Atlas DR V-242 and Atlas + DR V-243.

The devices are supported on the Model 3510 programmer platform with Model 3307, version 4.5m (or higher) programmer software.

QuickSite Lead Description

The QuickSite LV Model 1056K lead is a silicone and polyurethane-insulated, steroid eluting 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 QuickSite lead is an "Over-the-Wire" design, enabling implantation using stylet placement or guidewire placement.

The QuickSite LV Model 1056K lead is a unipolar lead, having one conductor that terminates at the tip electrode.

Features of the QuickSite LV Model 1056K lead include:

- Accommodates guidewires or stylets
- Passive Fixation incorporating an s-shaped curve designed to stabilize the lead in the vein
- Steroid Elution
- Fast-Pass™ Coating to create a lubricious surface

The minimum recommended lead introducer size is 7.0 French. The lead complies with IS-1 connector standard ISO 5841-3.

Aescula Lead Description

The Aescula LV Model 1055K lead (P030035) 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 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 to create a lubricious surface

The minimum recommended lead introducer size is 7.0 French. The lead complies with IS-1 connector standard ISO 5841-3.

VI. Alternative Practices or Procedures

The present established therapies for the treatment of heart failure and sudden cardiac death and the associated signs and symptoms include pharmacological therapy, heart transplantation, other legally marketed biventricular ICDs or other surgical procedures.

VII. Marketing History

The Epic HF and Atlas + HF pulse generators and the Aescula and QuickSite leads are currently distributed commercially outside the United States. Specifically, the ICDs are market approved in the European Community, Canada and Latin America.[1]

The QuickSite lead is market approved in the European Community; Eastern Europe, Middle East, Africa (EEMEA); Latin America; and Canada.

The Aescula lead is market approved in the United States (P030035), the European Community, Canada, Australia, Eastern Europe, Middle East, Africa, and Latin America.

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

VIII. Adverse Events

As of October 31, 2003, 205 patients were enrolled at 50 clinical sites in the Resynchronization for HemodYnamic Treatment for Heart Failure Management

[1] The Epic HF and the Atlas + HF devices market released outside the United States are identical to the Epic HF V-338 and Atlas + HF V-340 devices, except they have additional features enabled by the programmer software.

(RHYTHM ICD) clinical investigation. The first Epic HF V-338 and Aescula 1055K left ventricular lead system was implanted on July 8, 2002.

The QuickSite 1056K lead was approved to be used in the RHYTHM ICD Study on March 5, 2003. As of December 3, 2003, 162 patients were enrolled at 49 clinical sites in the RHYTHM ICD/QuickSite Lead clinical investigation. The first QuickSite 1056K lead was implanted on March 26, 2003.

Potential Adverse Events

Potential adverse events (in alphabetical order) associated with the Epic HF and Atlas + HF ICDs, include, but are not limited to the following:

- Acceleration of arrhythmias (caused by device)
- Air embolism
- Allergic reaction
- Bleeding
- Cardiac tamponade
- Chronic nerve damage
- Death
- Erosion
- Exacerbation of heart failure
- Excessive fibrotic tissue growth
- Extracardiac stimulation (phrenic nerve, diaphragm, chest wall)
- Extrusion
- Fluid accumulation
- Formation of hematomas or cysts
- Inappropriate shocks
- Infection
- Keloid formation
- Lead abrasion and discontinuity
- Lead migration/ dislodgement
- Myocardial damage
- Pneumothorax
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Potential mortality due to inability to defibrillate or pace
- Thromboemboli
- Venous occlusion
- Venous or cardiac perforation.

Patients susceptible to frequent shocks despite antiarrhythmic medical management may develop psychological intolerance to an ICD system that may include the following:

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of shocking while conscious
- Fear that shocking capability may be lost
- Imagined shocking (phantom shock).

Potential adverse events (in alphabetical order) associated with the Aescula and QuickSite Lead Systems, include, but are not limited to the following:

- Allergic reaction to contrast media
- 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 dislodgement or mechanical malfunction of the pacing lead
- Myocardial irritability
- Myopotential sensing
- Pectoral/diaphragmatic/phrenic nerve stimulation
- Pericardial effusion
- Pericardial rub
- Pneumothorax/hemothorax
- Prolonged exposure to fluoroscopic radiation
- Pulmonary edema
- Renal failure from contrast media used to visualize coronary veins
- Rise in Threshold and Exit Block
- Thrombolytic or air embolism
- Valve damage

Performance of a coronary sinus venogram is unique to lead placement in the cardiac venous system, and carries risks. 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

RHYTHM ICD Study

Seventeen (17) patients enrolled in the RHYTHM ICD clinical investigation were withdrawn from the study due to death. Three (3) of the deaths occurred in patients with an unsuccessful implant, 2 deaths occurred between the implant and the Baseline visit, 8 deaths occurred between Baseline and the 6-month visit and 4 deaths occurred after the 6-month visit. Five (5) of the 17 deaths were considered to be *peri-operative mortalities* (i.e., occurred ≤ 30 days post-implant). There were no deaths classified as related to the pulse generator or lead system. Three (3) of the seventeen (17) deaths were in patients with an unsuccessful Epic HF System implantation although none of these deaths were attributed to the attempted implantations. A summary of the Events Committee death classifications is shown in Table 1 below.

TABLE 1: RHYTHM ICD DEATHS

Primary Cause	CRT OFF	CRT ON	N/A*	Total
Cardiac-Arrhythmic	0	0	0	0
Cardiac-Nonarrhythmic	1	1	4	6
Cardiac-Unknown	0	0	0	0
Non-Cardiac	2	7	1	10
Unknown	0	1	0	1
Total	**3**	**9**	**5**	**17**

**Death occurred in patients who did not have a successful Epic HF system implant (unrelated to the implant procedure) or death occurred before their Baseline visit and randomization.*

RHYTHM ICD/QuickSite Lead Study

Nine (9) patients enrolled in the RHYTHM ICD/QuickSite Lead clinical investigation were withdrawn from the study due to death. A summary of the Events Committee death classifications are shown in Table 2 below.

TABLE 2: RHYTHM ICD/QUICKSITE LEAD DEATHS

Primary Cause	Total (CRT ON)
Cardiac-Arrhythmic	1
Cardiac-Nonarrhythmic	4*
Cardiac-Unknown	0
Non-Cardiac	1
Unknown	3
Total	**9**

**One patient died after undergoing unsuccessful QuickSite lead implantation. This death was unrelated to the implant procedure.*

Observed Adverse Events

RHYTHM ICD Study

The RHYTHM ICD study was a prospective, multicenter, randomized, double-blind, controlled clinical investigation designed to assess the safety and efficacy of the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Class III/IV heart failure and a prolonged QRS duration.

Adverse events were classified as complications or observations based on the following definitions:

- ***Complications*** are defined as adverse events that require invasive intervention (e.g. lead dislodgement requiring repositioning).

- ***Observations*** are defined as adverse events that can be managed without invasive intervention (e.g., oversensing or loss of pacing capture, which is then remedied by reprogramming of the pulse generator).

Table 3 lists the observations and complications reported from the RHYTHM ICD clinical trial. A total of 97 adverse events have been reported in 70 patients, of which 29 are complications and 68 are observations.

TABLE 3: RHYTHM ICD STUDY OBSERVED ADVERSE EVENTS

Event Description	# of Patients with AEs* (n = 205)	% of Patients with AEs	#AEs	AE/pt-years (n=186.07 years)
Complications (total)	**21**	**10.2%**	**29**	**0.156**
Coronary Sinus Perforation/Dissection	2	1.0%	2	0.011
Diaphragmatic/Phrenic Nerve Stimulation	3	1.5%	3	0.016
Lead Dislodgement or Migration	8	3.9%	9	0.048
Bleeding/Hematoma**	6	2.9%	6	0.032
Blood Clot/Thrombosis	1	0.5%	1	0.005
High Defibrillation/Cardioversion Requirements	2	1.0%	2	0.011
Infection	1	0.5%	1	0.005
Noise on EGM Post Shock (Non-SJM RV lead)	1	0.5%	1	0.005
Pneumothorax	2	1.0%	2	0.011
Retained Foreign Body (surgical sponge)	1	0.5%	1	0.005
Elevated Pacing Threshold – LV Lead	1	0.5%	1	0.005
Observations (total)	**57**	**27.8%**	**68**	**0.365**
Asystolic Episode during LV Lead Placement	1	0.5%	1	0.005
Bleeding/Hematoma**	10	4.9%	10	0.054
Blood Clot/Thrombosis	2	1.0%	2	0.011
Coronary Sinus Perforation/Dissection	6	2.9%	6	0.032
Diaphragmatic/Phrenic Nerve Stimulation – LV Lead	10	4.9%	10	0.054
Diaphragmatic/Phrenic Nerve Stimulation – RV Lead	2	1.0%	2	0.011
Elevated Pacing Thresholds – LV Lead	10	4.9%	10	0.054
Elevated Pacing Thresholds – RV Lead	2	1.0%	2	0.011
Heart Block at Implant	2	1.0%	2	0.011
High Defibrillation/Cardioversion Requirements	1	0.5%	1	0.005
Hypotension Requiring Ventilatory Support	1	0.5%	1	0.005
Inappropriate Therapy for SVT	10	4.9%	13	0.070
Infection	3	1.5%	3	0.016
Possible Pulmonary Embolism	1	0.5%	1	0.005
T-Wave Sensing	2	1.0%	3	0.016
Pocket Inflammation/Seroma	1	0.5%	1	0.005

**Some patients experienced more than one observation and/or complication and therefore the # of patients is less than the # of events.*

*** Fifteen (15) of the 16 patients with bleeding/hematoma related adverse events were on active anticoagulation therapy.*

An Other Reported Event is defined as any other clinical event that was reported by the investigator, which is not an Adverse Event as defined above. Table 4 contains a summary of all Other Reported Events, along with a brief description of each.

TABLE 4: RHYTHM ICD STUDY OTHER REPORTED EVENTS

Event Description	# of Patients	# of Events	Comments
Atrial arrhythmias observed	7	8	Atrial arrhythmias noted on electrograms that did not result in therapy delivery.
Bacteremia	2	2	Chronically diagnosed Gram positive bacteremia, unrelated to implant procedure, treated with antibiotics
Cardiopulmonary/ respiratory arrest	1	1	Syncopal episode leading to brief respiratory arrest probably due to vagal response while retching with spontaneous resolution following re-hydration.
Cardioversion for arrhythmias below device detection	1	1	Cardioversion for ventricular tachycardia below the programmed detection rate on a patient treated with Amiodarone.
Chest pain/tightness	3	3	ER visit for chest pain associated with pleurisy (1 pt); Chest pain associated with leaking thoracic aneurysm (1 pt); Chest pain managed medically (1 pt).
CNS related disorders	4	4	Seizure in 2 patients with history of seizure disorder and changes in mental status in 2 patients (secondary to dementia in 1 pt. and wife withheld medication for 1 pt.).
Crosstalk noted on electrogram	1	1	Resolved by reprogramming the ventricular blanking period.
Fatigue/Shortness of breath	1	1	Shortness of breath/fatigue reported on a clinic visit possibly secondary to resolving pneumonia.
Hemoptysis	1	1	Blood noted in sputum; lung biopsy performed; no further events reported.
Inflammatory response/swelling/ elevated WBCs	3	3	General clinical symptoms evaluated and treated medically; no further sequelae reported.
Elective surgery	4	4	Left hydrocelectomy; cholecystectomy; hernia repair; percutaneous transluminal coronary angioplasty.
Inappropriate mode switches	8	10	Eight events were resolved with device re-programming.
Nausea/Vomiting/ Diarrhea/Abdominal pain or bloating	6	6	GI symptoms treated medically with no further sequelae.
Nose bleed	1	1	Resulted from elevated INR while on coumadin therapy; dose adjustment and no further sequelae.
Occasional Far-R sensing noted on electrogram	2	2	Did not result in mode switching or other inappropriate device behavior; devices re-programmed.

TABLE 4: RHYTHM ICD STUDY OTHER REPORTED EVENTS (CONTINUED)

Event Description	# of Patients	# of Events	Comments
Pacing sensation	3	4	Symptoms possibly associated with pacing felt in chest. 1 pt. required re-programming.
Pain not related to procedure	2	2	Pain not associated with the device implant procedure: 1 pt was R/O ischemia and discharged and 1 pt diagnosed with gangrene of leg.
Pericardial effusion/Pericarditis	2	2	Treated medically with NSAIDs; no further sequelae.
Post-operative pain at incision site	2	3	Post surgical incisional pain treated with analgesics; no further sequelae reported.
Renal insufficiency/Elevated BUN and creatinine	1	1	Acute renal failure secondary to bilateral renal artery stenosis; treated medically with no further sequelae reported.
Respiratory related events	8	11	Reports of pneumonia, cough, bronchitis, cold, or wheezing treated medically; no further sequelae.
Shocks delivered for SVT/Afib in ventricular fibrillation zone	4	5	Therapy delivery appropriate: device performed as programmed (SVT discrimination not available to be programmed in Fib zone).
Shocks for MTD/MTF during SVT episode	2	2	Therapy delivery appropriate: device and features performed as Programmed. 1 pt. was re-programmed and 1 pt. prescribed amiodarone therapy.
Sinus bradycardia observed	4	4	2 pts. resolved by device reprogramming pacing rate; 2 pts did not require reprogramming.
Shortened AV delay caused by frequent PVC's	1	1	AV delay re-optimized by device reprogramming.
Stroke/TIA	2	2	TIA in setting of continuous AF at 3 mos. post-op in 1 pt.; Mid-cerebral artery CVA in 1 pt.
Syncope/Pre-syncope/Dizziness/ Vasovagal/ Hypotension	5	5	General clinical symptoms treated medically with IV fluids post-op (2pts.) and at rest (3pts.); no further sequelae reported.
Replacement of RA lead during initial implant procedure	1	1	Replacement of RA lead due to helix extension mechanism failure during initial implant procedure.
VF episode requiring multiple external shocks prior to Epic HF system implant	1	1	Ventricular fibrillation episode that occurred in the EP lab during initial implant procedure and reported as possibly associated with hypokalemia.
Occasional noise/EMI/ noted on electrogram	2	3	Noise observed on atrial channel of stored electrogram was not reproduced in clinic; device re-programming was not required.
TOTAL	**66***	**95**	

* *Some patients experienced more than one event, and therefore the number of patients is less than the number of events*

RHYTHM ICD/QuickSite Lead Study

The RHYTHM ICD/QuickSite Lead study was a prospective, multi-center investigation designed to evaluate the safety and effectiveness of the QuickSite left ventricular lead used with the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Class III/IV heart failure and a prolonged QRS duration.

Adverse events were classified as complications or observations based on the following definitions:

- ***Complications*** are defined as adverse events that require invasive intervention (e.g. lead dislodgement requiring repositioning).

- ***Observations*** are defined as adverse events that can be managed without invasive intervention (e.g., oversensing or loss of pacing capture, which is then remedied by reprogramming of the pulse generator).

Table 5 lists the observations and complications reported from the RHYTHM ICD/QuickSite clinical trial. A total of 45 adverse events have been reported in 37 patients, of which 18 are complications and are 27 observations.

TABLE 5: RHYTHM ICD/QUICKSITE LEAD STUDY OBSERVED ADVERSE EVENTS

Event Description	# of Patients with AEs* (n = 162)	% of Patients with AEs	#AEs	AE/pt-years (n = 94.53 yrs)
Complications (total)	**16**	**9.9%**	**18**	**0.190**
Bleeding/Hematoma	1	0.6%	1	0.011
Diaphragmatic/Phrenic Nerve Stimulation – LV Lead	5	3.1%	6	0.063
Elevated Pacing Thresholds - LV Lead	1	0.6%	1	0.011
Infection	2	1.2%	2	0.021
Lead Dislodgement or Migration – LV Lead	1	0.6%	1	0.011
Lead Dislodgement or Migration - RA Lead	2	1.2%	2	0.021
Pericardial Effusion	1	0.6%	1	0.011
Pocket Non-Approximation	1	0.6%	1	0.011
Respiratory Arrest Requiring Ventilatory Support	1	0.6%	1	0.011
Suspected Generator Malfunction	2	1.2%	2	0.021
Observations (total)	**24**	**14.8%**	**27**	**0.286**
Bleeding/Hematoma	6	3.7%	6	0.063
Cardiac Vein Thrombus	1	0.6%	1	0.011
Diaphragmatic/Phrenic Nerve Stimulation – LV Lead	9	5.6%	9	0.095
Diaphragmatic/Phrenic Nerve Stimulation – RV Lead	1	0.6%	1	0.011
Elevated Pacing Thresholds - LV Lead	5	3.1%	5	0.053
Elevated Pacing Thresholds – RV Lead	1	0.6%	1	0.011
Inappropriate Therapy (ATP) for SVT	1	0.6%	1	0.011
Inappropriate Therapy (Shock) for SVT	1	0.6%	1	0.011
Insulation Damage to RA Lead	1	0.6%	1	0.011
Post-Operative Shoulder Pain	1	0.6%	1	0.011

**Some patients experienced more than one observation and/or complication and therefore the # of patients is less than the # of events.*

An Other Reported Event is defined as any other clinical event that was reported by the investigator, which is not an Adverse Event as defined above. Table 6 contains a summary of all Other Reported Events, along with a brief description of each.

TABLE 6: RHYTHM ICD/QUICKSITE LEAD STUDY OTHER REPORTED EVENTS

Event Description	# of Patients	# of Events	Comments
Bacteremia	1	1	Gram positive bacteremia, unrelated to implant procedure; treated with antibiotics
Chest pain/tightness	5	5	ER/hospitalizations for complaints of chest pain; all treated medically.
Inflammatory response/ swelling/elevated WBCs	3	3	General clinical symptoms evaluated and treated medically with prophylactic antibiotics; no further sequelae.
Elective surgery	1	1	Cholecystectomy.
Occasional noise noted on electrogram	1	1	Noise observed on atrial channel of stored electrogram; device re-programming was not required.
Pericarditis	2	2	Treated medically with NSAIDs; no further sequelae
Respiratory related events	4	4	COPD exacerbation in 1 patient treated medically;1 patient with upper respiratory infection treated medically; 2 patients with pneumonia treated medically.
Shocks delivered for SVT/Afib in ventricular fibrillation zone	2	2	Therapy delivery appropriate: device performed as programmed (SVT discrimination not available to be programmed in Fib zone).
Sinus bradycardia observed	1	1	Resolved by device reprogramming of pacer rate.
Dizziness/Hypotension/ Syncope	4	4	One patient developed hypotension post-op associated with rapid AF treated with IV fluids and later required diuretics for volume overload; 1 pt with orthostasis responded to decrease in diuretic dosage; 1 patient with low blood pressure treated with BV pacing; 1 patient with recurrent syncope due to hypotension was treated with IV fluids.
Shortened AV delay caused by frequent PVCs	1	1	AV delay re-optimized by device reprogramming.
Digoxin toxicity	1	1	Digoxin dose adjusted; no further sequelae
Stroke/TIA	1	1	Left upper extremity weakness later diagnosed as stroke.
Pacing sensation/palpitation	1	1	Palpitations associated with ventricular ectopy.
Inappropriate mode switches	1	1	Far-R suppression interval adjusted.
T-wave sensing not resulting in therapy	1	1	Resolved by reprogramming.
TOTAL	**30**	**30**	

IX. Summary of Pre-Clinical Studies

Epic HF and Atlas + HF Pulse Generators and Software

Verification and Validation Testing

Preclinical testing of the Epic HF and Atlas + HF Pulse Generators, presented in Table 7 below, included component, device and software testing. "Pass" as used below denotes that the device met established performance criteria and/or specifications, or was in conformance with the requirements of the standard tested to.

TABLE 7: EPIC HF AND ATLAS + HF ICD PRE-CLINICAL TESTING

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
Component Testing*			
Controller IC (integrated chip)Verification: functional, temperature characterization, visual inspection, wire bond strength, SEM(scanning electron microscope) analysis and life tests	6-105	N/A	PASS
I/O (input/output) Chip Verification: functional, visual inspection, temperature characterization, SEM analysis, wire bond strength and life tests	6-99	N/A	PASS
High Voltage PCB Assembly Verification: first article inspection, visual inspection, electrical, ionograph, thermal shock and high temperature storage tests	3-60	N/A	PASS
Isolation Transformer Module Verification: first article inspection, visual inspection, electrical, ionograph, thermal shock, mechanical shock, vibration and high temperature storage tests	60	N/A	PASS
Hybrid Verification: visual inspection, electrical, life test, temperature characterization, temperature cycling, constant acceleration, wire bond strength and die shear tests	6-28	N/A	PASS
Substrate Verification: first article, hybrid assembly and test, high voltage loop and device assembly tests	3-6	V-339**	PASS

*All components used in both the Epic HF V-338 and the Atlas + HF V-340 devices. Same components as used in the Epic DR V-233/Epic + DR V-239 and Atlas DR V-242/Atlas + DR V-243 ICDs.
**V-339 is a variant of the V-338 device.

TABLE 7: EPIC HF AND ATLAS + HF ICD PRE-CLINICAL TESTING (CONTINUED)

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
Epic HF Testing			
Battery Verification (Note: Same battery as the Photon Micro DR/VR ICDs): visual inspection, dimensional, radiographic, electrical, hermeticity, pressure, vibration, shock, temperature exposure, temperature shock, storage temperature, short circuit, forced overdischarge, abusive, end of life discharge and dimensional, accelerated pulse and varying orientation pulse tests	1-23	N/A	PASS
High Voltage Capacitor Component Verification (Note: Same capacitors as the Epic DR/VR and Epic + DR/VR ICDs): electrical, humidity, temperature cycle, storage temperature, resistance to solder heat and thickness tests	10 Pair	N/A	PASS
Connector Assembly: visual inspection, insertion and withdrawal forces, current carrying (DF-1), temperature cycling, mechanical attachment (push and torque), impedance isolation (IS-1), electrical isolation (DF-1) and dimensional examination tests	9-18	V-338	PASS
Electrical Verification: functional, detection intervals, refractory periods, PVARP, delays, escape interval, pacing pulse interval, width and amplitude, pacing output droop, burst fibber, NIPS, shock-on-T, ATP, cardioversion/defibrillation output performance (prEN45502-2-2), high voltage lead integrity check, pacing lead impedance, and signal amplitude tests	3	V-338, V-235	PASS
Mechanical Verification: functional testing, visual/x-ray inspection, physical evaluation, multiple sterilization, pressure, packaging, shipping, mechanical shock, vibration, cut open evaluation and product/package markings tests	3-6	V-338	PASS
Electromagnetic Compatibility (1975 AAMI Pacemaker standard and 2000 AAMI PC69)	3	V-338	PASS
External Defibrillation Susceptibility	3	V-338	PASS
Electrosurgical Unit Susceptibility	3	V-338	PASS
Electronic Article Surveillance (EAS) Compatibility	3	V-338	PASS

TABLE 7: EPIC HF AND ATLAS + HF ICD PRE-CLINICAL TESTING (CONTINUED)

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
Atlas + HF Testing			
Battery Verification (Note: Same battery as the Atlas + DR/VR ICDs): visual inspection, dimensional, radiographic, electrical, hermeticity, pressure, vibration, shock, temperature exposure, temperature shock, storage temperature, short circuit, forced overdischarge, abusive, end of life discharge and dimensional, accelerated pulse and varying orientation pulse tests	1-23	N/A	PASS
High Voltage Capacitor Component Verification (Note: Same capacitors as the Atlas + DR/VR ICDs): electrical, shelf life, maximum exposure temperature, maximum operating temperature, storage temperature, temperature cycling, vibration, solvent resistance and vacuum/temperature exposure tests	10 pair	N/A	PASS
Connector Assembly: visual inspection, insertion and withdrawal forces, current carrying (DF-1), temperature cycling, mechanical attachment (push and torque), impedance isolation (IS-1), electrical isolation (DF-1) and dimensional examination tests	9-18	V-340	PASS
Electrical Verification: functional, cardioversion/ defibrillation output (prEN45502-2-2) and high voltage lead integrity check tests	1	V-341***	PASS
Mechanical Verification: functional testing, visual/x-ray inspection, physical evaluation, multiple sterilization, pressure, packaging, shipping, temperature cycle, mechanical shock, vibration, cut open evaluation and product markings tests	3	V-340	PASS
Electromagnetic Compatibility (1975 AAMI Pacemaker standard and 2000 AAMI PC69)	3	V-340	PASS
External Defibrillation Susceptibility	3	V-340	PASS
Electrosurgical Unit Susceptibility	3	V-340	PASS
Electronic Article Surveillance (EAS) Compatibility	3	V-341	PASS

*** V-341 is a variant of the V-340 device.

TABLE 7: EPIC HF AND ATLAS + HF ICD PRE-CLINICAL TESTING (CONTINUED)

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
Software Testing			
Device software (firmware) per Verification Test Plan	Firmware	N/A	PASS
Programmer Software per Verification Test Plan	Program-mer Software	3307	PASS
Programmer Software User Testing per User Test Plan	Program-mer Software	3307	PASS
System Validation Testing			
Epic HF System Validation Testing	6	V-338	PASS
Atlas + HF System Validation Testing	1	V-340	PASS
Epic HF Acute GLP Animal Study (Canine)	3	V-338	PASS

Biocompatibility

All materials used for the Epic HF and Atlas + HF pulse generators are currently used in legally marketed St. Jude Medical pulse generators and have been previously tested and approved for their biocompatibility. All materials used in these devices have previously been assessed for biocompatibility (per ISO 10993) with respect to biological response and lack of harmful effects to patients.

Sterilization, Packaging and Shelf Life

The sterilization of the Epic HF and Atlas + HF devices is identical to the sterilization process of the legally marketed Epic DR/VR and Atlas + DR/VR ICDs. 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 Epic HF and Atlas + HF devices is also identical to the packaging of the legally marketed Epic DR/VR and Atlas + DR/VR ICDs, with the exception of the inner seal tray, which has been modified in size.

Based on battery longevity testing, the shelf life for the Epic HF and Atlas + HF ICDs was established and approved at 12 months. This is identical to that of the Epic DR/VR and Atlas + DR/VR ICDs.

Aescula and QuickSite Left Ventricular Leads

The testing that was completed for the Aescula and QuickSite LV leads is summarized below in Table 8. Testing included mechanical, electrical and in vivo characterization in canines. All tests were completed successfully and the leads met all required specifications for human clinical use in accordance with established National and International industry standards, or St. Jude Medical specifications. "Pass" as used below denotes that the lead met established performance criteria and/or specifications, or was in conformance with the requirements of the standard to which it was tested.

TABLE 8: SUMMARY OF PRECLINICAL LABORATORY TESTING – LV LEADS

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
Aescula Testing			
Aescula Lead Verification 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

TABLE 8: SUMMARY OF PRECLINICAL LABORATORY TESTING – LV LEADS (CONTINUED)

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
Aescula Testing (continued)			
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 to determine distal end reliability subjected to 400 million flex cycles.	10	1055K	PASS
Animal Study (Canine) conducted to assess performance of the lead in a canine model.	6	1055K	PASS
QuickSite Testing			
QuickSite Lead Verification 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; connector set-screw deformation. Additional testing verifying compliance to prEN45502-2-1 included connector flex; lead body flex; lead sensing impedance; temperature cycling; lead durability; insulation integrity and lead composite pull test.	12-24	1056K	PASS
QuickSite Lead Biocompatibility/Sterilization Tests: particulate release, sterilization efficiency, biocompatibility, bioburden, and EtO residuals	5-30	1056K	PASS

TABLE 8: SUMMARY OF PRECLINICAL LABORATORY TESTING – LV LEADS (CONTINUED)

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
QuickSite Testing (continued)			
Multiple sterilization tests to determine effects of multiple sterilization exposures.	24	1056K	PASS
UPS ship test to ensure conditions of general shipping and handling were met.	12	1056K	PASS
Polarization test to measure polarization of fully assembled leads.	24	1056K	PASS
Temperature Storage test to determine the effects of long-term storage at high and low temperatures on lead integrity.	36	1056K	PASS
Temperature Shock test to determine the effects of rapid temperature changes on lead integrity.	36	1056K	PASS
Suture Sleeve test to ensure that the suture sleeve will slide properly along the lead.	24	1056K	PASS
Guidewire Insertion test to assess ease of guidewire insertion into the lead.	24	1056K	PASS
Stylet Insertion test to assess ease of stylet insertion into the lead.	24	1056K	PASS
Flushing Tool Performance test to assess installation and performance of flushing tool.	24	1056K	PASS
S Shape Retention test to ensure proper lead body shape is retained after multiple stylet insertions.	24	1056K	PASS
Lead Dimensional test to verify lead passage through a 6 French introducer.	24	1056K	PASS
Steroid Ring Swelling Evaluation to verify that after steroid ring expansion a guidewire can still pass through the tip.	10	1056K	PASS
Steroid Extraction Verification to verify total amount of steroid does not exceed 1 mg.	3-7	1056K	PASS

TABLE 8: SUMMARY OF PRECLINICAL LABORATORY TESTING – LV LEADS (CONTINUED)

Test Performed	Sample Size	Model No.	Test Results (Pass/Fail)
QuickSite Testing (continued)			
Distal Tip Fatigue Testing to determine distal end reliability subjected to 400 million flex cycles.	24	1056K	PASS
Animal Study (Canine) conducted to assess performance of the lead in a canine model.	9	1056K	PASS

Biocompatibility

The Aescula and QuickSite lead blood/tissue contact materials have a long history of successful use in long-term implants and are identical to those used in other SJM products. All materials used in these leads have been assessed for biocompatibility (per ISO 10993) with respect to biological response and lack of harmful effects to patients. For more information, you may reference the SSED for the Aescula lead, approved under P030035 on May 13, 2004.

Sterilization, Packaging and Shelf Life

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

Packaging of the Aescula and QuickSite leads is identical to that of other St. Jude Medical leads, including the Passive Plus DX family of leads. UPS shipping testing was performed (See Table 8) to ensure that the product and product packaging can withstand the conditions of general shipping and handling.

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

X. Summary of Clinical Investigations

The St. Jude Medical, Inc. Resynchronization for HemodYnamic Treatment for Heart Failure Management (RHYTHM) ICD and RHYTHM ICD/QuickSite Lead clinical studies were conducted under an IDE (investigational device exemption).

RHYTHM ICD Clinical Investigation

The RHYTHM ICD study was a prospective, multicenter, randomized, double-blind, controlled clinical investigation designed to assess the safety and efficacy of the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Classification of III or IV and a prolonged QRS duration. The products being evaluated were the Epic HF V-338 ICD and the Aescula and QuickSite LV leads. The objective of this clinical study was to verify the safety and efficacy of the Epic HF ICD (Model V-338) system in an ICD indicated patient population with advanced heart failure (NYHA Classification III or IV) and prolonged QRS duration.

Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

1. Approved indication for implantation of an ICD for treatment of a life-threatening ventricular tachyarrhythmia(s).
2. Symptomatic, advanced heart failure (ischemic or non-ischemic) not due to reversible causes, diagnosed for at least 6-months.
3. New York Heart Association (NYHA) Classification of III or IV, despite receiving a minimum of 90 days of appropriate pharmacological therapy.
4. Receive optimal pharmacological therapy for CHF (including angiotensin converting enzyme inhibitor and beta blocker, as tolerated) which has been stable during the 30 days prior to enrollment.
5. Left ventricular ejection fraction (LVEF) $\leq$ 35%.
6. Ventricular conduction delay manifested as a QRS duration $\geq$150 msec.
7. Ability to complete cardiopulmonary exercise stress testing and 6-Minute hall walk test, with the only limiting factor(s) being fatigue and/or shortness of breath.
8. Ability to independently comprehend and complete a quality of life questionnaire (Minnesota Living with Heart Failure).
9. Ability to provide informed consent for study participation and be willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

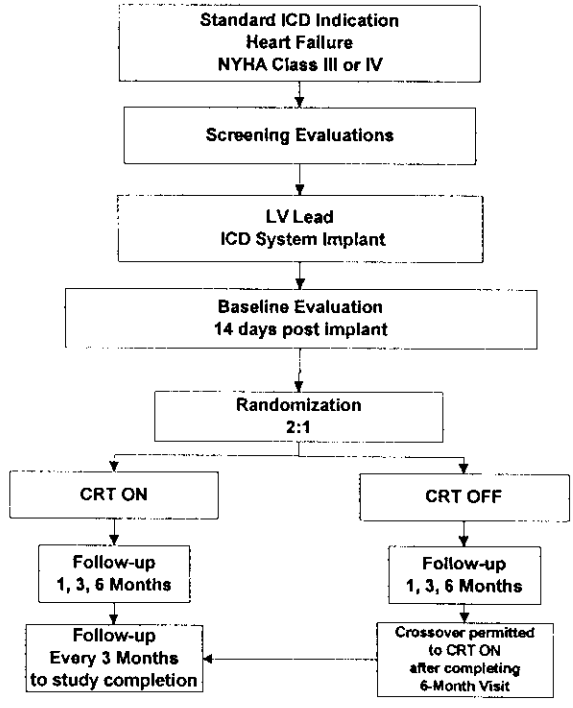
Exclusion Criteria

1. Standard bradycardic indication for pacing.
2. History of chronic atrial fibrillation (continuous AF lasting > 1 month) within 1 year prior to enrollment or have undergone cardioversion for AF in the past month.
3. Ability to walk > 450 meters during the 6-Minute walk test.
4. NYHA Classification of I or II.
5. Contraindication for an emergency thoracotomy.
6. Classification of Status 1 for cardiac transplantation or consideration for transplantation over the next 6-months.
7. Recent myocardial infarction, unstable angina or cardiac revascularization (PTCA or CABG) within 1 month of enrollment.

8. Recent CVA or TIA - within 3 months of enrollment.
9. Severe musculoskeletal disorder(s).
10. Pregnant or planning for pregnancy in next 6-months.
11. Participating in, or has participated in any clinical investigation within the last 30 days. (Note: the only exception being that of a registry trial)
12. Life expectancy of less than 6 months.
13. Less than 18 years of age.

Figure 1 outlines the study design for the trial. As of March 17, 2004, the total time of follow-up from the time of successful implant was 2205 patient months. The average time of follow-up was 12.1 ± 3.4 (range 0.3 to 20.3) patient months.

FIGURE 1: RHYTHM ICD STUDY OVERVIEW



Patient Population

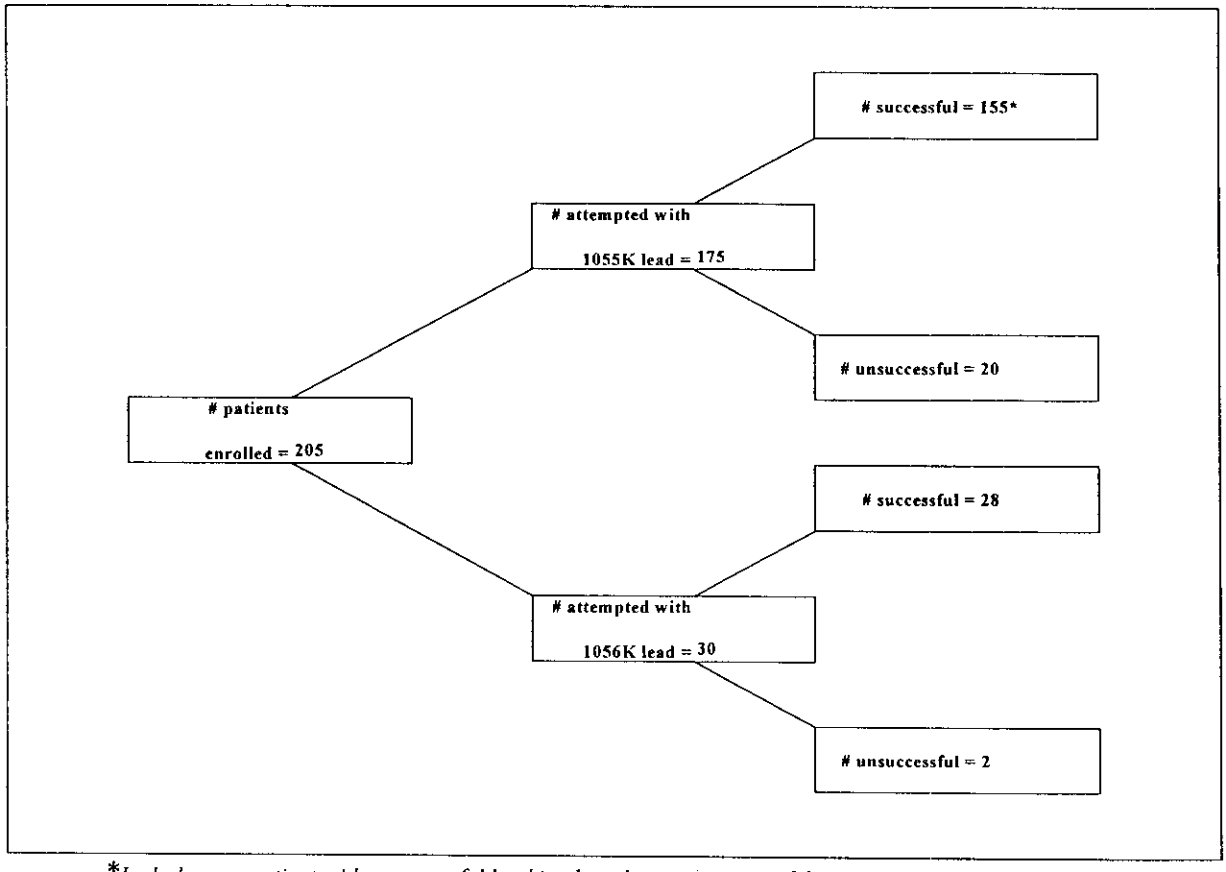
Of the 205 patients enrolled in the RHYTHM ICD study, one hundred and eighty-three (183) lead implant attempts were successful (180 successful on the first attempt and 3 successful on the second attempt). One additional patient had a successful left ventricular lead implant, but had high defibrillation thresholds (DFTs). This patient was withdrawn from the study and received a heart transplant, leaving a total of 182 successful system implants. Table 9 has a breakdown of the reasons for the 23 unsuccessful implants.

TABLE 9: UNSUCCESSFULL IMPLANTS (N=23)

Reason	Number of Patients
LV Lead Related:	
Unable to Cannulate the CS	7
Unable to Obtain Distal Placement	6
Unable to Obtain Stable Lead Position	3
High Pacing Thresholds	3
CS Dissection	3
Other:	
High Defibrillation Threshold (DFT)	1
TOTAL	**23**

Figure 2 displays the leads used and the number of successful system implants for each category of leads.

FIGURE 2: NUMBER OF PATIENTS ATTEMPTED AND IMPLANTED WITH MODEL 1055K AND 1056K LEADS



**Includes one patient with a successful lead implant, but an unsuccessful system implant due to high DFTs.*

Patients who were successfully implanted with the Epic HF ICD system had a Baseline visit approximately two weeks after implant, during which the following tests/assessments were performed: Electrical measurements on RA, RV and LV leads, cardiopulmonary exercise (CPET) test, echocardiogram, NYHA class assessment, 6

minute walk test, and Minnesota Living with Heart Failure questionnaire. Of the 182 patients with successful implants, two patients expired and one patient withdrew from the study before the Baseline visit and therefore, 179 patients had a Baseline visit. One additional patient who had a Baseline follow-up visit refused randomization and all the Baseline evaluations except device interrogation and electrical measurements, but remained in the study. Therefore, a total of 178 patients completed the requirements of the Baseline visit.

Table 10 summarizes all the reported data on the 178 patients available for analysis at the Baseline visit, as well as broken down by randomization group.

TABLE 10: SUMMARY OF BASELINE VARIABLES AND COMPARISONS BETWEEN CRT OFF AND CRT ON GROUPS

Demographic variable	Overall group (N = 178)*	CRT OFF (N = 59)	CRT ON (N = 119)	p-value (CRT ON vs. CRT OFF)
NYHA Class, n (%):				0.61
I	3 (1.7%)	2 (3.4%)	1 (0.8%)	
II	10 (5.6%)	4 (6.8%)	6 (5.0%)	
III	154 (86.5%)	50 (84.7%)	104 (87.4%)	
IV	11 (6.2%)	3 (5.1%)	8 (6.7%)	
LV Ejection Fraction (%) - ECHO:				
Mean ± SD	24.8 ± 7.7	23.3 ± 6.4	25.6 ± 8.3	0.07
Range	(9, 48)	(11, 43)	(9, 48)	
QRS Duration (ms):				
Mean ± SD	168 ± 15	167 ± 15	169 ± 16	0.40
Range	(120, 210)	(130, 200)	(120, 210)	
LVEDD (mm):				
Mean ± SD	66.2 ± 8.8	66.0 ± 9.4	66.2 ± 8.5	0.88
Range	(47.7, 85.9)	(50.1, 84.2)	(47.7, 85.9)	
LVESD (mm):				
Mean ± SD	57.0 ± 9.87	56.9 ± 10.5	57.1 ± 9.4	0.93
Range	(37.1, 78.2)	(37.9, 78.2)	(37.1, 76.2)	
Quality of Life Score:				
Mean ± SD	48 ± 24	46 ± 24	48 ± 24	0.53
Range	(0, 103)	(4, 100)	(0, 103)	
Six-Minute Walk (meters):				
Mean ± SD	280 ± 99	291 ± 89	275 ± 103	0.30
Range	(31, 561)	(31, 480)	(37, 561)	

** Of the 182 patients that had successful system implants, two patients expired and one patient withdrew from the study before their Baseline visit; one additional patient refused randomization and all Baseline evaluations, except device interrogation and electrical measurements, and therefore, is not included.*

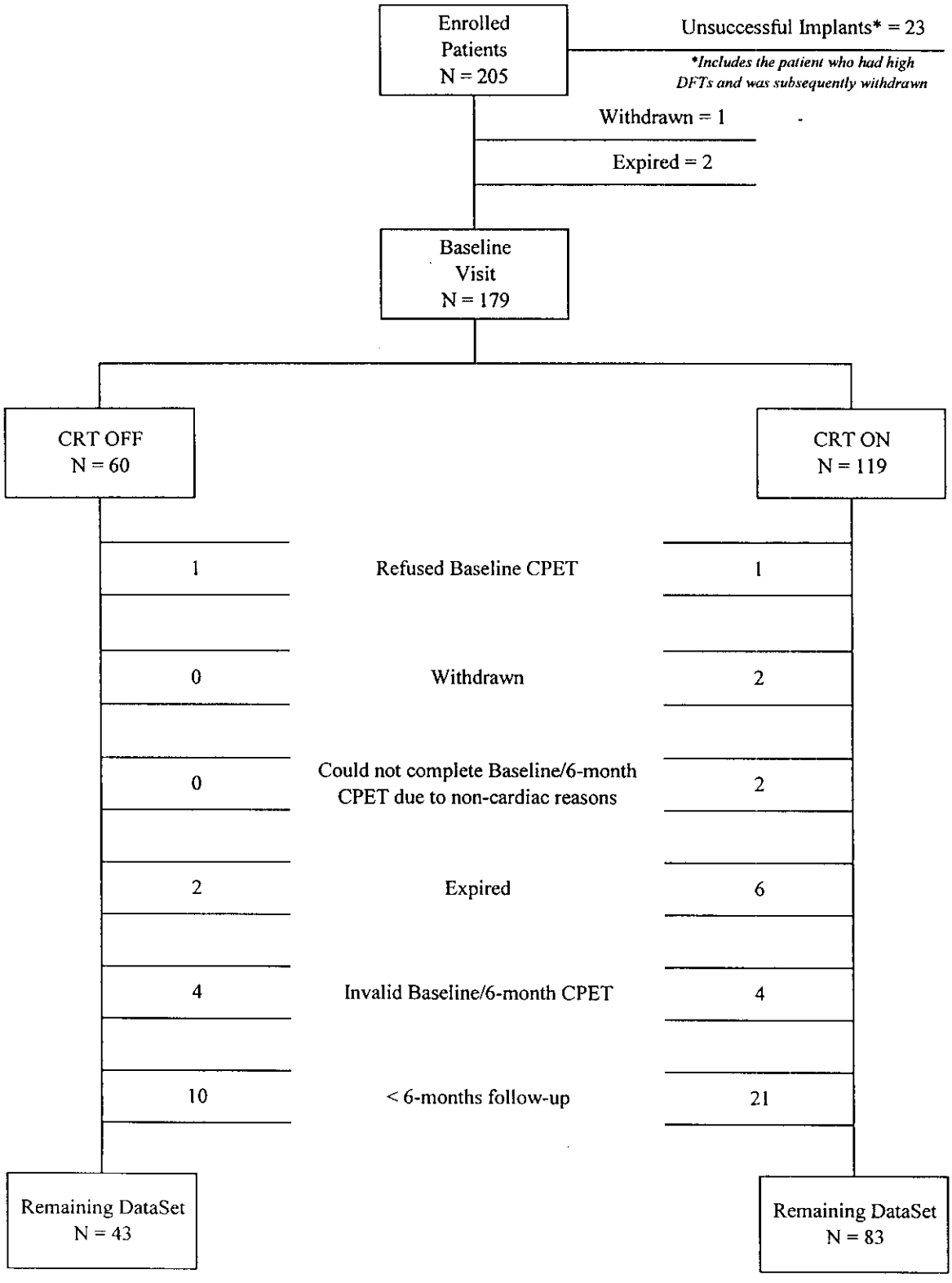
TABLE 10: SUMMARY OF BASELINE VARIABLES AND COMPARISONS BETWEEN CRT OFF AND CRT ON GROUPS (CONTINUED)

Demographic variable	Overall group (N = 178)*	CRT OFF (N = 59)	CRT ON (N = 119)	p-value (CRT ON vs. CRT OFF)
Cardiopulmonary Exercise Test:				
Peak VO_2 (ml/kg/min):				
Mean ± SD	11.3 ± 3.3	12.3 ± 3.5	10.8 ± 3.0	0.006
Range	(4.3, 26.9)	(6.0, 23.1)	(4.3, 26.9)	
Exercise Time (minutes):				
Mean ± SD	8.3 ± 3.3	8.9 ± 3.6	8.0 ± 3.2	0.08
Range	(0.7, 19.8)	(2.3, 19.8)	(0.7, 16.5)	
Baseline Medications, n (%):				
ACE Inhibitors/Substitutes	129 (72.5%)	44 (74.6%)	85 (71.4%)	0.79
Beta Blockers	147 (82.6%)	52 (88.1%)	95 (79.8%)	0.24
Angiotensin Receptor Blockers	34 (19.1%)	10 (16.9%)	24 (20.2%)	0.76
Diuretics	157 (88.2%)	54 (91.5%)	103 (86.6%)	0.47
Positive Inotropics/Glycoside	112 (62.9%)	39 (66.1%)	73 (61.3%)	0.65
Nitrates	62 (34.8%)	23 (39.0%)	39 (32.8%)	0.51
Anti-Coagulants and Anti-Platelets	150 (84.3%)	48 (81.4%)	102 (85.7%)	0.59
Calcium Channel Blockers	20 (11.2%)	9 (15.3%)	11 (9.2%)	0.35
Anti-Arrhythmics	42 (23.6%)	13 (22.0%)	29 (24.4%)	0.87

** Of the 182 patients that had successful system implants, two patients expired and one patient withdrew from the study before their Baseline visit; one additional patient refused randomization and all Baseline evaluations, except device interrogation and electrical measurements, and therefore, is not included.*

Figure 3 outlines the patient population for the effectiveness analysis.

FIGURE 3: ANALYZABLE PATIENT GROUP FOR PRIMARY RESYNCHRONIZATION EFFECTIVENESS ANALYSIS



Primary Objectives and Results

1. *LV Lead-Related Complications (at 6 Months)*

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula lead-related complications through six months will not be less than 75%.

Results: One hundred and fifty-five (155) patients who had a successful 1055K LV lead implant were analyzed for this endpoint. A total of 11 patients experienced 13 1055K LV lead related complications. The survival from 1055K lead related complications at 6-months was calculated as 92.8% with a 95% lower confidence bound of 89.4%. Objective met.

2. *Epic HF System-Related Complications (at 6 Months)*

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Epic HF system-related complications through six months will not be less than 70%.

Results: One hundred and eighty-two (182) patients who had a successful Epic HF system implant with either the Aescula or QuickSite LV lead were analyzed for this endpoint. A total of 13 patients experienced 16 Epic HF system-related complications. The survival from system-related complications at 6-months was calculated as 93.4% with a 95% lower confidence bound of 90.6%. Objective met.

3. *Defibrillation System Effectiveness: VF Detection/Redetection Times*

Objective: The upper bound of the one-sided 95% confidence interval of the median VF detection time will be less than 3.4 seconds. The upper bound of the one-sided 95% confidence interval of the median VF redetection time will be less than 1.9 seconds.

Results: Detection and redetection times for induced VF episodes (including Ventricular Fibrillation, Polymorphic Tachycardia, and Ventricular Flutter) during biventricular pacing were included in the analysis. Detection and redetection times were calculated for each episode from the stored electrograms or rhythm strip from an external recorder. A total of 440 episodes in 172 patients were analyzed for detection times, and 90 episodes in 55 patients were analyzed for redetection times. The 95% upper confidence bound for the mean detection time was 3.11 seconds and that for the redetection time was 1.61 seconds. Objective met.

4. *Cardiac Resynchronization Therapy Efficacy* (Peak VO_2)

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: In the intention-to-treat analysis, patients who crossed over from the CRT OFF group to the CRT ON group during the study were analyzed according to the original treatment group they belonged to. Table 11 contains a summary of the improvement in peak VO_2 values in the two treatment groups for this analysis. The average improvement in the CRT ON group over the CRT OFF group was approximately 1.9 ml/kg/min. The p-value for this analysis was 0.001. Objective met.

TABLE 11: IMPROVEMENT IN PEAK VO_2 VALUES (ML/KG/MIN) INTENTION-TO-TREAT ANALYSIS (N = 126)

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	12.8 ± 3.7	11.2 ± 3.0
6-months	11.4 ± 5.6	11.7 ± 3.2
Change	-1.41 ± 4.6	0.52 ± 2.5

In the per-protocol analysis, patients who crossed over from the CRT OFF group to the CRT ON group during the study were analyzed according to the new treatment group they belonged to. Of the 126 patients who were part of the peak VO_2 endpoint analysis, two patients crossed over from the CRT OFF group to the CRT ON group due to symptoms attributed to worsening heart failure before their 6-month follow up visit. Table 12 displays a summary of the improvement in the two groups for this analysis. The CRT ON group showed an average improvement of approximately 2.0 ml/kg/min over the CRT OFF group. The p-value for this analysis was 0.001. Objective met.

TABLE 12: IMPROVEMENT IN PEAK VO_2 VALUES (ML/KG/MIN) PER-PROTOCOL ANALYSIS (N = 126)

	CRT OFF	CRT ON
N	41	85
Mean ± SD	-1.47 ± 4.7	0.52 ± 2.5

Secondary Objectives and Results

1. *Improvement in NYHA Class at 6-months Over Baseline*

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: Table 13 shows the average change in NYHA Class from Baseline to 6-months for each group.

TABLE 13: BASELINE AND 6-MONTH NYHA CLASS (N = 126)

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	2.86 ± 0.52	3.01 ± 0.33
6-months	2.58 ± 0.73	2.53 ± 0.69
Change	-0.28 ± 0.63	-0.48 ± 0.65

The two-sample t-test for the NYHA hypothesis resulted in a p-value of 0.048; therefore, the CRT ON group shows a statistically significant improvement in NYHA Class over the CRT OFF group. Objective met.

2. *Improvement in Quality of Life at 6-months over baseline*

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: Patient quality of life (QOL) was assessed with the Minnesota Living with Heart Failure questionnaire. A lower score indicates an improvement in quality of life. Table 14 contains a summary of the improvement in Quality of Life in the two groups from baseline to 6 months.

TABLE 14: IMPROVEMENT IN QUALITY OF LIFE SCORE (N = 126)

	CRT OFF Mean ± SD (N = 43)	**CRT ON Mean ± SD (N = 83)**
Baseline	42.0 ± 23	48.3 ± 24
6-months	45.4 ± 31	40.4 ± 22
Change	3.4 ± 31	-7.8 ± 22

The average improvement in the CRT ON group over the CRT OFF group was approximately 11 points. The p-value for this analysis was 0.009. Objective met.

3. *Improvement in Six-Minute Hall Walk at 6-months Over Baseline*

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: Table 15 contains a summary of the improvement in 6-minute walk distance between baseline and 6 months.

TABLE 15: IMPROVEMENT IN 6-MINUTE WALK DISTANCE (METERS) (N = 126)

	CRT OFF Mean ± SD (N = 43)	**CRT ON Mean ± SD (N = 83)**
Baseline	298 ± 94	284 ± 105
6-months	283 ± 150	297 ± 122
Change	-15 ± 142	13 ± 74

The average improvement in the CRT ON group over the CRT OFF group was approximately 28 meters. The p-value for this analysis was 0.07.

4. *Aescula Left Ventricular Lead Performance*

Objective: The lower bound of the one-sided 95% confidence interval of the percent successful implant will not be less than 80%.

Results: Of the175 patients who were attempted with the Aescula 1055K lead, 155 patients, or 88.6% had a successful implant. The 95% lower confidence bound on the percent successful implant was 83.8%. Objective met.

5. Aescula LV Lead Pacing Capture Threshold at 6-Months

Objective: The upper bound of the one-sided 95% confidence interval of the LV lead pacing capture threshold is less than 3 V.

Results: The 95% upper confidence limit for the mean LV lead capture threshold at 6 months was 2.37 V. The average pacing capture threshold was 2.2 ± 1.5 V. Objective met.

Additional Data

1. Biventricular Pacing at 6-months

The average percentage of biventricular pacing at the 6-month visit in the 83 patients who were in the CRT ON group among the 126 patients in the primary resynchronization cohort was 95% ± 6%, with a range of 70% to 100%.

2. Echocardiographic Data

Echocardiographic analysis was performed at the baseline and 6-month follow-up visits. The following parameters were evaluated from the echocardiographic analysis: LVEDD, LVESD, LVEF, MR, E/A Wave Point Ratio, and Sphericity Index. Cardiac dyssynchrony (including Pre-Ejection Delay Time and Intraventricular Mechanical Delay) was also evaluated at baseline and 6-Months. Table 12 displays summaries of the improvement in these parameters between baseline and 6-months.

TABLE 16: IMPROVEMENT IN ECHOCARDIOGRAPHY PARAMETERS

Parameter	CRT OFF (N = 40) Mean ± SD	CRT ON (N = 82) Mean ± SD
LVEDD (mm)	-2.4 ± 6.5	-4.3 ± 5.4
LVESD (mm)	-3.0 ± 6.4	-4.6 ± 7.0
LVEDV (ml)	-37 ± 53	-43 ± 69
LVESV (ml)	-36 ± 47	-43 ± 58
LVEF (%)	2.9 ± 6.2	4.3 ± 9.9
MR (grade)	0.10 ± 0.50	-0.06 ± 0.74
E/A Wave Point Ratio	-0.02 ± 1.2	-0.08 ± 0.8
Sphericity Index	0.02 ± 0.1	-0.02 ± 0.1
Pre-Ejection time (ms)	7.3 ± 33	-1.5 ± 52
IVMD (ms)	-6.4 ± 48	-14.5 ± 52
Tei Index	-0.05 ± 0.5	-0.4 ± 0.8
Contraction Interval (ms)	-55 ± 103	-94 ± 124

3. Patient Discontinuation/Withdrawals

A total of 41 patients participating in the RHYTHM ICD study were withdrawn from the study. Twenty (20) patients (including the 19 patients with unsuccessful LV lead implants and the one patient with an unsuccessful system implant due to high defibrillation thresholds) were withdrawn approximately one month after unsuccessful system implants in accordance with the protocol. Seventeen (17) patients died and were also withdrawn from the study. Three of the 17 deaths occurred in patients who had previously unsuccessful implants. In addition to these 20 unsuccessful implants and 17 deaths, 4 additional patients were withdrawn from the study. Table 17 summarizes the reason for these 4 patient withdrawals.

TABLE 17: PATIENT DISCONTINUATIONS/WITHDRAWALS
(Excludes Withdrawals for Deaths and After Unsuccessful Implants)

Reason for Withdrawal	CRT Group	Days after Implant
System Explant	N/A*	1
Heart Transplant	ON	75
Patient Request	ON	28
Patient's Family Request	ON	293

** Patient was withdrawn before the Baseline visit and randomization*

RHYTHM ICD/QuickSite Lead Clinical Investigation

The RHYTHM ICD/QuickSite Lead study was a prospective, multi-center investigation designed to evaluate the safety and effectiveness of the QuickSite left ventricular lead system in an ICD indicated patient population with advanced heart failure (NYHA Classification III or IV) and prolonged QRS duration. The objective of this clinical study was to verify the safety and efficacy of the QuickSite Model 1056K left ventricular pacing lead in an ICD indicated patient population with advanced heart failure (NYHA Classification III or IV) and prolonged QRS duration.

Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

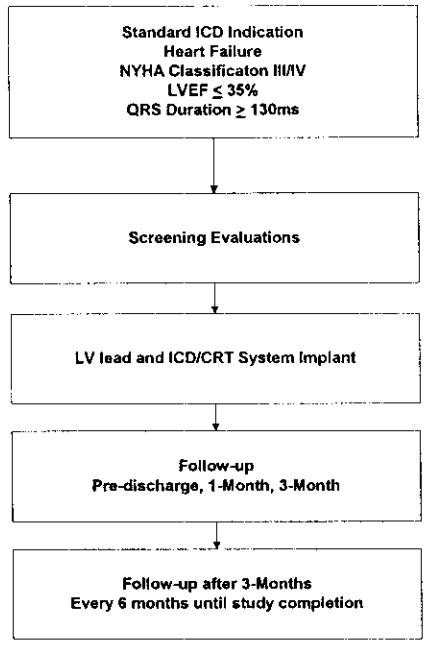
1. Approved indication for implantation of an ICD for treatment of a life-threatening ventricular tachyarrhythmia(s).
2. Symptomatic heart failure with a New York Heart Association (NYHA) Classification of III or IV, despite optimal pharmacological therapy.
3. Left ventricular ejection fraction (LVEF) ≤ 35%.
4. Ventricular conduction delay manifested as a QRS duration ≥130 msec.
5. Ability to provide informed consent for study participation and be willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Exclusion Criteria

1. NYHA Classification of I or II.
2. Contraindication for an emergency thoracotomy.
3. Hypersensitivity to single 1.0mg dose of dexamethasone sodium phosphate.
4. Classification of Status 1 for cardiac transplantation or consideration for transplantation over the next 3-months.
5. Recent myocardial infarction, unstable angina or cardiac revascularization (PTCA, Stent or CABG) within 30 days of enrollment.
6. Currently participating in a clinical investigation that includes an active treatment arm.
7. Pregnant or a planning for pregnancy in the next 6-months.
8. Life expectancy of less than 6-months.
9. Less than 18 years of age.

Figure 4 outlines the study design for the trial. As of December 3, 2003, 162 patients were enrolled at 49 clinical sites in the RHYTHM ICD/QuickSite Lead clinical investigation. The first QuickSite 1056K lead was implanted on March 26, 2003.

FIGURE 4: RHYTHM ICD/QUICKSITE LEAD STUDY OVERVIEW



Patient Population

Of the 162 patients enrolled in the RHYTHM ICD/QuickSite Lead study, one hundred and fifty-three (153) lead implant attempts were successful. Table 18 has a breakdown of the reasons for the 9 unsuccessful implants.

TABLE 18: UNSUCCESSFULL IMPLANTS (N=9)

Reason	Number of Patients
LV Lead Related:	
Unable to Cannulate the CS	4
Unable to Obtain Distal Placement	3
Unable to Obtain Stable Lead Position	2
TOTAL	**9**

Table 19 contains a summary of the pre-implant assessment information on all patients included in the RHYTHM ICD/QuickSite Lead Study patient cohort (162 patients).

TABLE 19: PRE-IMPLANT ASSESSMENT INFORMATION

Demographic Variable	Overall Group (N = 162)
Age (years):	
Mean ± SD	68.8 ± 9.9
Range	(39, 86)
Gender, n (%):	
Male	132 (81.5%)
Female	30 (18.5%)
NYHA Class, n (%):	
III	149 (92%)
IV	13 (8%)
LV Ejection Fraction (%):	
Mean ± SD	22.5 ± 6.7
Range	(10, 35)
QRS Duration (ms):	
Mean ± SD	166 ± 21
Range	(130, 240)
Cardiomyopathy Classification:	
Ischemic, n (%)*:	**126 (77.8%)**
Myocardial Infarction	119 (94.4%)
CABG	86 (68.3%)
PTCA	57 (45.2%)
Unstable Angina	42 (33.3%)
Non-Ischemic, n (%):	**36 (22.2%)**
Idiopathic	19 (52.8%)
Hypertensive	6 (16.7%)
Familial/Congenital	2 (5.6%)
Alcoholic	4 (11.1%)
Valvular	2 (5.6%)
Other	3 (8.3%)
Other Medical History, n (%)*:	
Hypertension	99 (61.1%)
Diabetes	59 (36.4%)
OPD	36 (22.2%)
Other	115 (71.0%)
None	13 (8.0%)
Intrinsic Ventricular Conduction, n(%):	112 (69.1%)
LBBB	27 (16.7%)
RBBB	23 (14.2%)
IVCD	

TABLE 19: PRE-IMPLANT ASSESSMENT INFORMATION (CONTINUED)

Demographic Variable	Overall Group (N = 162)
Intrinsic Ventricular Conduction, n(%):	
LBBB	112 (69.1%)
RBBB	27 (16.7%)
IVCD	23 (14.2%)
Primary Indication for ICD, n (%):	
VT	25 (15.4%)
VF	7 (4.3%)
VT and VF	11 (6.8%)
Primary Prevention	64 (39.5%)
Upgrade	44 (27.2%)
Syncope	5 (3.1%)
Did not have Class I/II indic	6 (3.7%)
Pre-Implant Medications, n (%):	
ACE Inhibitors/substitutes	112 (69.1%)
Beta Blockers	131 (80.9%)
Angiotensin Receptor Blockers	31 (19.1%)
Diuretics	150 (92.6%)
Positive Inotropics/Glycoside	95 (58.6%)
Nitrates	54 (33.3%)
Anti-Coags and Anti-Platelets	145 (89.5%)
Calcium Channel Blockers	8 (4.9%)
Anti-Arrhythmics	45 (27.8%)

** Individual patients may be included in more than one subcategory*

Primary Objectives and Results

1. *LV Lead-Related Complications (at 3 Months)*

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from QuickSite™ lead-related complications through six months will not be less than 80%.

Results: One hundred and fifty-three (153) patients who had a successful QuickSite 1056K LV lead implant were analyzed for this endpoint. A total of 6 patients experienced 8 LV lead related complications. The survival from QuickSite 1056K LV lead related complications at 3-months was calculated as 96.1% with a 95% lower confidence bound of 93.5%. Objective met.

2. *QuickSite LV Lead Implant Success*

Objective: The lower bound of the one-sided 95% confidence interval of the percent successful implant will not be less than 80%.

Results: Of the 162 patients who were attempted with the QuickSite 1056K lead, 153 patients, or 94.4% had a successful LV lead implant. The 95% lower confidence bound on the percent successful implant is 90.5%. Objective met.

3. QuickSite LV Lead Pacing Capture Threshold at 3-Months

Objective: The upper bound of the one-sided 95% confidence interval of the LV lead pacing capture threshold is less than 3 V.

Results: The 95% upper confidence limit for the mean LV lead capture threshold at 6 months was 1.81 V. The average pacing capture threshold was 1.6 ± 1.4 V. Objective met.

Additional Data

1. LV Lead Handling Characteristics

The handling of the LV lead was rated by the implanting physicians on how easily the lead was able to be navigated in the coronary venous system. Table 20 provides the lead handling data.

TABLE 20: LV LEAD HANDLING CHARACTERISTICS SUCCESSFUL IMPLANTS (N=153)

Handling Characteristic	Number of Patients	% of Patients
Easy	98	64.1%
Acceptable	39	25.5%
Poor	12	7.8%
Not Rated	4	2.6%
TOTAL	**153**	**100%**

2. Implantation Procedure Times

Table 21 summarizes the total fluoroscopic exposure times, time to CS cannulation and total procedure times.

TABLE 21: IMPLANTATION PROCEDURE TIMES SUCCESSFUL IMPLANTS (N = 153)

	Mean ± SD Range (minutes)
Fluoroscopic Exposure Time	32 ± 24 (5, 128)
Time to CS Cannulation	46 ± 40 (2, 211)
LV Lead Placement Time	87 ± 55 (16, 330)
Total Procedure Time	137 ± 69 (34, 490)

The average fluoroscopic time for the unsuccessful LV lead implants was 78 ± 41 (range 20 to 158) minutes.

XI. Conclusions Drawn the Study

Safety of the Epic HF ICD system including either the Aescula or the QuickSite LV leads was characterized by examining survival from LV lead and ICD system related complications. Survival from all complications at 6-months, including procedural complications and patients with unsuccessful implants, was determined to be acceptable in this study. The RHYTHM ICD study showed that the ICD portion of the Epic HF device was not adversely affected by the addition of biventricular pacing as shown by acceptable ICD detection and redetection times and appropriate termination of spontaneous arrhythmic episodes.

In terms of effectiveness, the Epic HF ICD cardiac resynchronization system demonstrated a statistically significant overall improvement between Baseline and 6-months in cardiopulmonary exercise testing (mean peak VO_2) compared to the CRT OFF group. Additionally, the Epic HF system demonstrated a six month improvement in the quality of life and a reduction in the NYHA functional class which were two of the secondary endpoints of the study.

The Atlas + HF V-340 device is functionally identical to the Epic HF V-338 device, except it can deliver up to 36 J of output instead of 30 J. The intended use remains the same. Therefore, no additional clinical investigation was required to support the safety and effectiveness of the Atlas + HF V-340 ICDs.

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 P030054 on June 30, 2004. Conditions of approval included a postapproval study to characterize the incidence of all-cause and cause-specific mortality associated with the Epic HF and Atlas + HF CRT-D systems. In addition, this study will provide a 3-year evaluation of the chronic electrical and clinical performance of the QuickSite LV Model 1056K Lead.

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.