

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Permanent Pacemaker Electrode

Device Trade Name: Medtronic Attain Ability™ Model 4196 Lead

Applicant's Name and Address: Medtronic, Inc.
Cardiac Rhythm Disease Management
8200 Coral Sea Street
Mounds View MN 55122

Date(s) of Panel Recommendation: none

Premarket Approval Application (PMA) Number: P080006

Date of FDA Notice of Approval: April 7, 2009

Expedited: Not Applicable

II. INDICATIONS FOR USE

The Attain Ability™ Model 4196 steroid eluting, dual electrode, IS-1 transvenous lead is indicated for chronic pacing and sensing in the left ventricle via the cardiac vein, when used in conjunction with a compatible Medtronic Cardiac Resynchronization Therapy (CRT) system. Extended bipolar pacing is available using this lead in combination with a compatible CRT-D system and RV defibrillation lead or with a compatible CRT-P system and RV pacing lead.

III. CONTRAINDICATIONS

Coronary vasculature – This lead is contraindicated for patients with coronary venous vasculature that is inadequate for lead placement, as indicated by venogram.

Steroid use – Do not use in patients for whom a single dose of 232 µg of dexamethasone acetate cannot be tolerated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Medtronic Attain Ability™ Model 4196 Lead labeling.

V. DEVICE DESCRIPTION

The Medtronic Attain Ability™ Model 4196 Lead (Model 4196) is a device/drug combination product made up of two regulated components: a device (the Medtronic Attain Ability™ lead) and a drug component (dexamethasone acetate). The design characteristics of the Model 4196 lead appear in Table 1.

Table 1. Design Characteristics of Model 4196 Lead

CHARACTERISTIC		MODEL 4196
Lead Body Diameter		4 Fr (1.4 mm)
Lead Body Length		20-110 cm
Delivery System Recommended Inner Diameter		> 5.7 Fr I.D.
Fixation Method		Compound Curves
Connector		IS-1 Bipolar
Monolithic Controlled Release Devices (MCRDs) containing dexamethasone acetate at the distal (tip) and proximal (ring) electrodes		Target dose dexamethasone acetate Tip: 160 µg Ring: 72 µg
Electrodes	Material	Platinum Iridium alloy with Titanium Nitride coating
	Geometry	Tapered annular
	Surface Area	5.8 mm ²
	Molded Tip Seal	Silicone Rubber

A. Device Component Description

The Medtronic Attain Ability™ Model 4196 lead (Model 4196) is a left ventricular, 4 Fr, transvenous, steroid eluting, dual electrode, polyurethane outer insulated, single coil (co-radial) cardiac vein lead with an IS-1 connector. The Model 4196 lead has a compound curve at the distal end and can be implanted using either a guide wire or stylet. The lead is indicated for chronic pacing and sensing in the left ventricle via the cardiac vein, when used in conjunction with a compatible Medtronic Cardiac Resynchronization Therapy (CRT) system.

The Model 4196 lead was designed to provide physicians a non-invasive option to pace the left ventricle (LV) from a second location post-implant. The dual-electrode lead design features both a proximal (ring) and distal (tip) electrode. Figure 1 below provides an overall picture of the Model 4196 lead. Figure 2 below depicts the Model 4196 placed within the heart.

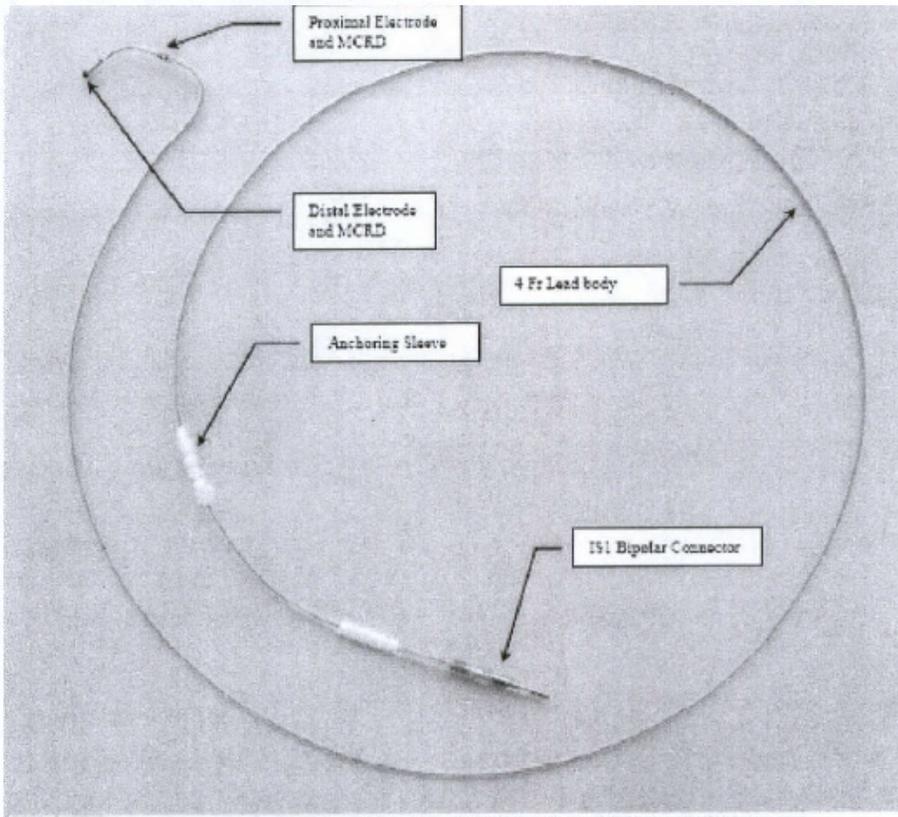


Figure 1. Medtronic Attain Ability™ Model 4196 lead

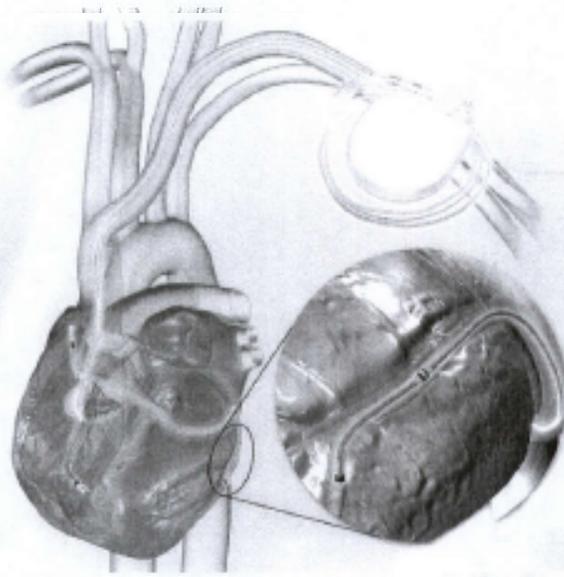


Figure 2. Model 4196 Lead in Place in the Heart

B. Drug Component Description

The active drug substance used for the Model 4196 lead is dexamethasone acetate, anhydrous, USP. The chemical name of dexamethasone acetate is 9-Fluoro-11 β ,17,21-trihydroxy-16 α -methylpregna-1,4-diene-3,20-dione 12-acetate. The chemical structure for dexamethasone acetate is shown in Figure 3.

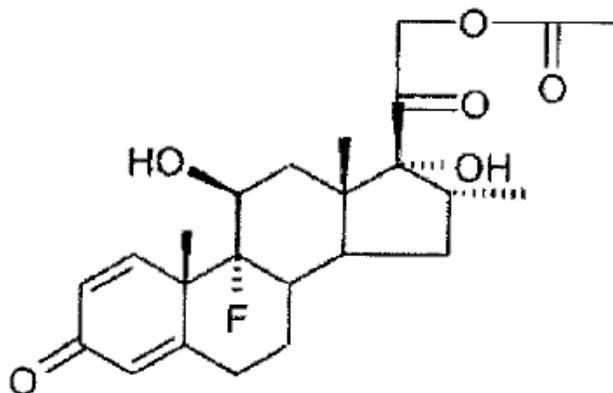


Figure 3. Chemical Structure of Dexamethasone Acetate

Dexamethasone Acetate is a non-hygroscopic, white to off-white odorless powder. The substance is an anti-inflammatory steroid that is freely soluble in acetone, alcohol, dioxane, and methanol, slightly soluble in dichloromethane and practically insoluble in water. The substance exhibits a UV maximum absorbance at 239 nm (ϵ 14900) and an optical rotation of +82° to +88° (dioxane, 25°C). The melting point is reported to be approximately 250°C with decomposition. The target dose of dexamethasone acetate on the tip MCRD is 160 μ g and the target dose of dexamethasone acetate on the ring MCRD is 72 μ g. Figure 4 illustrates the location of both MCRDs on the lead.

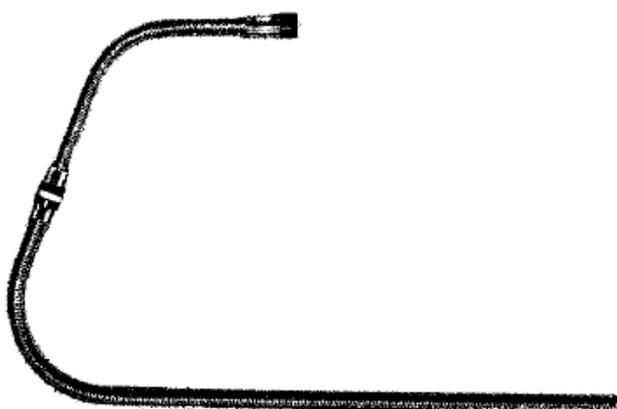


Figure 4. Illustration of Model 4196 lead showing ring and tip MCRD

C. Mechanism of Action for Dexamethasone Acetate

Steroids suppress the inflammatory response that is believed to cause threshold rises typically associated with implanted pacing electrodes. Glucocorticosteroids decrease inflammation by stabilizing leukocyte lysosomal membranes. The membrane stabilization prevents the release of destructive acid hydrolases from the leukocytes and this inhibits the accumulation of macrophages in the inflamed area. The mechanism involves the activation of glucocorticoid receptors that increase or decrease the transcription of a number of genes involved in the inflammatory process. One of the key actions is the repression of cytokine gene transcription and the other transcription factors activated in chronic inflammation. The dexamethasone is the active glucocorticoid used in this lead.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

An alternative to the Model 4196 lead for patients requiring implantation of a biventricular pacing system is the use of other commercially available left ventricular leads.

VII. MARKETING HISTORY

The Attain Ability Model 4196 Lead has not been marketed within the United States.

The Attain Ability Model 4196 Lead is currently marketed in the European Union. The lead has not been withdrawn from the market for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse events (listed in alphabetical order) related to the use of transvenous leads include, but are not limited to, the following conditions:

- Air embolism
- Avulsion or other damage to the endocardium, valve, or vein (particularly in fragile hearts)
- Cardiac dissection or perforation
- Cardiac tamponade
- Coronary sinus dissection
- Death
- Endocarditis or pericarditis
- Erosion through the skin
- Extracardiac muscle or nerve stimulation
- Fibrillation or other arrhythmias
- Heart block
- Heart wall or vein wall rupture
- Hematoma/seroma
- Infection
- Lead conductor fracture or insulation failure
- Lead dislodgement
- Myocardial irritability
- Myopotential sensing
- Pericardial effusion or rub
- Pneumothorax
- Rejection phenomena (local tissue reaction, fibrotic tissue formation)
- Threshold elevation or exit block
- Thrombosis
- Thrombotic embolism

In addition, renal failure due to contrast dye exposure is a potential risk associated with performing a venogram. For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A series of non-clinical laboratory studies was performed on the Model 4196 lead and a summary is presented in this section.

A. Biocompatibility Studies

The materials used in the Model 4196 lead that are directly exposed to body tissues or fluids are summarized in Table 2. Most of the materials are identical to materials used on previous Medtronic lead designs. Biocompatibility assessment was previously performed in accordance with ISO 10993-1, Biological Evaluation of Medical Devices: Evaluation and Testing. All materials were found to be biocompatible. Table 2 also lists which Medtronic marketed devices used these same materials. Biocompatibility testing has been performed for the new materials used in the Model 4196 lead. The testing performed was in accordance with the recommendations in International Standard ISO-10993, "Biological Evaluation of Medical Devices Part-1: Evaluation and Testing." All materials tested for use in the Model 4196 have passed biocompatibility testing.

Table 2. Biocompatibility Information

COMPONENT NAME	RAW MATERIALS	EQUIVALENT TO CURRENTLY MARKETED DEVICE	DOCUMENT CONTROL # AND (APPROVAL DATE)
Tip Seal	Silicone Rubber	4076 4193	P930039/S017 (02/09/2004) P010015/S003 (05/02/2002)
Crimp Sleeve	Titanium	4193	P010015/S003 (05/02/2002)
Electrodes	Platinum/Iridium	4076 4193	P930039/S017 (02/09/2004) P010015/S003 (05/02/2002)
Coated Electrodes	Titanium Nitride Coating	4076 3830	P930039/S017 (02/09/2004) P030036 (08/03/2005)
Electrode Ring	Silicone Adhesive	No	---
Tip to Ring Spacer	Urethane Resin	4076 4193	P930039/S017 (02/09/2004) P010015/S003 (05/02/2002)
Lead Body	Urethane Resin	4076 4193	P930039/S017 (02/09/2004) P010015/S003 (05/02/2002)
Connector Sleeve	Silicone Rubber	No	---
Strain Relief	Silicone Rubber	4076 4193	P930039/S017 (02/09/2004) P010015/S003 (05/02/2002)
Molded Silicone Rubber	Silicone Rubber	4193	P010015/S003 (05/02/2002)
Anchor Sleeve	Silicone Rubber and Pigment	4076	P930039/S017 (02/09/2004)
Lead Body	Urethane Adhesive	4076	P930039/S017 (02/09/2004)
	Silicone Adhesive	4076	P930039/S017 (02/09/2004)
		4193	P010015/S003 (05/02/2002)
	Polyurethane Adhesive	4076 4193	P930039/S017 (02/09/2004) P010015/S003 (05/02/2002)

The active pharmaceutical ingredient (API), dexamethasone acetate, is directly exposed to the physiological environment and has been used in the currently marketed, Model 4076 lead (P930039/S017, approved 02/09/2004). Biocompatibility testing per ISO 10993-1 was not performed on the dexamethasone acetate because it is an active pharmaceutical ingredient (API). The testing outlined in ISO 10993-1 is not applicable to an active pharmaceutical ingredient (API).

Each of the above-referenced materials used in the components identified are identical to the materials used in the components of the currently marketed devices as defined in Table 2 in formulation, processing, sterilization, and no other chemicals have been added with the exception of silicone adhesive used in the assembly of the electrode ring, and the silicone rubber used to manufacture the connector sleeve.

Biological testing has been performed on the new materials. In addition the materials that were used in previously approved Medtronic lead designs have been shown to be biocompatible. Medtronic has demonstrated compliance of the materials comprising the Model 4196 lead with the applicable section of ISO 10993-1 that pertain to biological effects for use in this application.

B. In-Vivo Pharmacokinetics

Pharmacokinetics – The pharmacokinetics (local drug levels and systemic levels) of dexamethasone acetate and its metabolites following placement of the Model 4196 leads were not evaluated in human clinical trials.

C. Drug Interactions

No drug interactions with dexamethasone acetate have been described. Drug interactions of dexamethasone acetate with the Model 4196 lead have not been studied.

D. Lead Engineering Testing

Environmental Conditioning: Model 4196 leads were subjected to four cycles of ethylene oxide (EtO) sterilization and five cycles of thermal shock (-45°C to +70°C) prior to undergoing mechanical, electrical, and steroid testing. No damage or degradation to the test leads was noted following sterilization and thermal shock. Leads were then tested according to the summary below (Table 3). Tests were also conducted on the drug component parts of the lead. The acceptance criterion for tests generating attribute data (pass/fail) is demonstration of at least 90% confidence of 90% reliability (minimum 22 specimens). The acceptance criterion for tests generating variables data is 95% confidence of 95% reliability.

Table 3. Bench Testing Summary for Attain Ability Model 4196 Lead

TEST	REQUIREMENT	RESULTS	ANALYSIS TYPE
Environmental Testing			
ETO Sterilization	No signs of damage or degradation upon visual examination (minimum magnification 3X) All samples must pass all subsequent mechanical and electrical tests	Passed	Attribute
Thermal Shock	No signs of damage or degradation upon visual examination (minimum magnification 3X) All samples must pass all subsequent mechanical and electrical tests	Passed	Attribute
Mechanical Testing			
Connector Mating Insertion/ Withdrawal	Insertion Forces ≤ 3.0 lbs Withdrawal Forces ≤ 2.5 lbs Sealing rings must not buckle or roll back during insertion	Passed	Variables
Distal Seal Leak Test	No fluid should be observed on the coil or inside the inner lumen upon visual examination when tested in water. (minimum magnification of 3X). If there is leakage at the electrode tip, repeat the test in blood on that sample(s). If the lead lumen allows full insertion and withdrawal of a guide wire following the leak test, the sample is acceptable.	Passed	Attribute
Lead Composite Pull Test	The lead must meet a minimum 1.0 lb tensile strength	Passed	Variables
Anchoring Sleeve Suture Test	≥ 0.25 lb minimum breakaway force Anchoring sleeve mobile on lead prior to suturing without sliding when the lead is held in a vertical position. There must be no damage to the coil or insulation noted upon visual examination (unaided eye)	Passed	Variables
Lead Body Flex Test (Endocardial)	B50 flex life $\geq 2.0 \times 10^5$ cycles at a bend radius of 0.236"	Passed	Attribute
Connector Flex Test	$> 82,000$ cycles at 45° bend radius without coil fracture or intermittency	Passed	Attribute
Stylet Insertion / Withdrawal	<u>Straight Stylet</u> ≤ 100 grams in connector ≤ 300 grams in lead body.	Passed	Variables

TEST	REQUIREMENT	RESULTS	ANALYSIS TYPE
Guide Wire Insertion/ Withdrawal	<u>Straight Guide Wire</u> ≤ 100 grams in connector ≤ 300 grams in distal tip.	Passed	Variables
	<u>Canted Guide Wire</u> ≤ 100 grams in connector ≤ 350 grams in distal tip.	Passed	Variables
Composite Torsional Strength	After a ten day soak in 0.9% saline solution at 37°C ± 5°C, the lead body shall be capable of withstanding 15 full rotations when held between the tip electrode and connector.	Passed	Attribute
Electrical Testing			
DC Resistance	Tip Circuit (78 cm lead) = 38Ω ± 10Ω Ring Circuit (78 cm lead) = 35Ω ± 10Ω	Passed	Variables
IS-1 Connector Leakage/Medtronic AC Impedance Test Of Unipolar Leads	Impedance > 50 kOhms	Passed	Attribute
Sterilization			
Sterilization	1 100% EtO sterilization process is used. It is considered an overkill sterilization cycle and is performed in accordance with accepted standards. Devices must have a sterility assurance of at least 10 ⁻⁶ . Sterilization validation was performed by comparison to "worst case" devices.	Passed	20 partial leads (Model 4068). Proximal and distal ends of leads were cut and capped to create a worst case condition.

Results of finished product lead analytical testing meet specifications for appearance, identification, assay, content uniformity, related substances and elution.

E. Animal Studies

The animal studies conducted for the Model 4196 lead are outlined in Table 4. Studies conducted in accordance with 21 CFR 58 (Good Laboratory Practices) are also indicated. The non-clinical laboratory testing of the Model 4196 demonstrates that the Model 4196 meets specifications.

Table 4. Summary of Animal Testing Conducted for the Model 4196 Lead

Study Number / Study Name	GLP / Non-GLP	Type/Number of Animals	Number of Leads Test/Control	Follow-up Duration / Procedure	Acceptance Criteria	Results
0052D0642 Biocompatibility	GLP	In Vitro and In Vivo (Rabbit / Rodent)	SI Polyimide coated coils	Varies depending on test	Varies depending on test	All tests were successfully completed with acceptable results.
0052D0638 Biocompatibility	GLP	In Vitro and In Vivo (Rabbit / Rodent)	Silver cored MP35N	Varies depending on test	Varies depending on test	All tests were successfully completed with acceptable results.
0120A0258 / Material Biostability Study (SI Polyimide)	GLP	Canine / 7	21 / 72	All canines terminated after implant duration of 104 weeks	The canines were sacrificed after study duration of 104 weeks and gross and histopathological assessments were made.	The gross and histopathological tissue changes observed were not excessive and were within the range expected for this procedure.
S1184 / Chronic Canine Lead Electrical Study	GLP	Canine / 6	6 / 0 (controls; reference previous LV lead animal studies; Models 2187 4193 and 4194)	Gathered electrical data at 0, 1, 2, 3, 4, 6, 8, 12 weeks post implant. Pathology performed at 12 weeks.	Acceptable electrical performance as compared to other left ventricular leads (Models 4193 and 4194 steroid eluting cardiac vein leads; Model 2187 steroid free cardiac vein lead).	The Model 4196 lead demonstrated acceptable electrical performance based on comparison to Models 2187, 4193 and 4194 leads. The gross and histological tissue changes observed were not excessive and were within the range expected for this procedure.
S1366 / Model 4196 Canine <i>In-Vivo</i> Elution Pilot Study	Non-GLP	Canine / 21	21 / 0 (explanted in groups of 3 at various time points)	Up to 1 year	Lead implanted in coronary sinus (CS) vasculature. Study is intended to determine <i>in-vivo</i> drug release profile of DXAC from the Model 4196 lead.	Study is ongoing

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness for implant and pacing and sensing in the left ventricle via the cardiac vein with the Model 4196 lead for use with a compatible Medtronic Cardiac Resynchronization Therapy (CRT) system in the US and Canada under IDE #G060193. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Subjects were enrolled (i.e. consented) starting February 5, 2007 (Canada)/March 7, 2007 (US) and continued until final implant on September 24, 2007. The database for this PMA reflected visit data collected through August 20, 2007 and included 149 subjects (US and Canada). Subjects were enrolled at 22 investigational sites (17 US and 5 Canadian).

The Model 4196 lead study was a prospective, multi-center clinical trial using objective performance criteria (OPC) to assess the safety and effectiveness of the Attain Ability™ Model 4196 left ventricular (LV) lead. Data from previous LV lead studies were used to set the Model 4196 OPC. Therefore, control subjects were not used in this study. This study was not blinded. Candidates for implant included subjects of both genders with heart failure (NYHA Class III and IV) who met all inclusion and no exclusion criteria. All subjects with a successful Model 4196 lead implant were evaluated at pre-hospital discharge, one month, three months, six months, and every six months thereafter, until study completion.

Sample Size Justification

The safety endpoint criteria drove the sample size for the study, consistent with other left heart leads. To evaluate the primary safety objective, a minimum sample size of 63 subjects followed to one month was needed for evaluation of the endpoint. Additionally, the effectiveness endpoints were powered to determine the follow-up performance of the tip and ring electrodes. The attrition rate was calculated step-wise from the number of patients consented to those that will contribute to the endpoints. For example, based on their venous anatomy, not all patients were attempted with or received a Model 4196 LV lead. Additional US enrollments were requested to allow for physician experience with the lead for a total US sample size of 150. In addition, the sponsor also reported on 50 subjects enrolled in Canada.

Monitoring of investigative sites was performed by trained Medtronic Monitors and includes the following activities: verification of inclusion/exclusion criteria, verification of data to available source documents, confirmation of protocol required testing, verification of investigational device disposition logs, review of informed consent documents, review of compliance to, or documented deviations from, the Clinical Investigational Plan and the review of all required study correspondence and regulatory documents.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the study was limited to patients who met the following inclusion criteria:

- Subject had demonstrated prolonged QRS defined as an intrinsic QRS \geq 120 ms (test documented within 6 months of Baseline)
- Subject had a Left Ventricular Ejection Fraction (LVEF) \leq 35% (test documented within 12 months of Baseline)
- Subject was diagnosed with NYHA Class III or IV despite optimal medical therapy which is defined as:
 - ACE inhibitor or Angiotensin Receptor Blocker (ARB), if tolerated, for at least one month prior to implant

- Beta-blockers for at least three months preceding implant, if tolerated, and stable for one month. Stable is defined as no upward titration of beta-blockers.

OR

- Subject had an urgent medical need for an implantable cardioverter defibrillator (ICD) that precludes waiting the one or three months for medication requirement for ACE inhibitor, ARB or beta blocker.
- Subject was indicated for ICD implantation for the treatment of life threatening ventricular arrhythmias¹
- Subject signed and dated the study-specific informed consent form
- Subject was 18 years of age or older
- Subject was expected to remain available for follow-up visits
- Subject was willing and able to comply with the protocol

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Subject had a previous complete atrial based biventricular CRT system
- Subject had a previous LV lead implanted or previous implant attempt within 30 days of implant or ongoing adverse events from previous unsuccessful attempt
- Subject had unstable angina pectoris or who have had an acute MI within the past month
- Subject had a coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA) within the past three months
- Subject had chronic (permanent) atrial arrhythmias
- Subject had contraindications for standard transvenous cardiac pacing (e.g. mechanical right heart valves)
- Subject had a heart transplant (subjects waiting for heart transplant are allowed in the study)
- Subject was contraindicated for < 1mg dexamethasone acetate
- Subject was enrolled in any concurrent drug and/or device study that may confound the results of this study
- Subject had a terminal illness and was not expected to survive more than three months
- Subject was a woman who was pregnant, or had child-bearing potential and was not on a reliable form of birth control (pregnancy test required within seven days prior to implant for females with child bearing potential)
- Subject was unable to tolerate an urgent thoracotomy

2. Follow-up Schedule

All subjects with a Model 4196 lead implanted were scheduled to return for follow-up examinations at pre-hospital discharge, one month, three months, six months, and every six months thereafter, until study completion. Subjects who had at least one Model 4196 lead attempt, but who did not ultimately receive a Model 4196 lead implant were

¹ In accordance with Class I or II ICD indications as specified in the current ACC/AHA/HRS practice guidelines at the time of implant.

followed at pre-hospital discharge and one month, unless there were ongoing relevant implant related adverse events, in which case they were followed until those events resolved before being exited from the study.

Preoperatively, the following baseline information was obtained:

- Demographic data
- Inclusion / Exclusion criteria verified, including:
 - Informed consent form completed
 - NYHA classification
 - QRS duration
 - LVEF
 - Pregnancy test date (if applicable)
 - ICD Indication
- Cardiovascular medical history
- Cardiovascular medication list
- Adverse events (if applicable)
- Subject study deviations (if applicable)

At the time of implant, the following information was obtained:

- Surgical data (date and time of implant)
- Cannulation data (tools used and length of procedure)
- Venous imaging data (tools used)
- LV lead implant data (per attempt: lead model, times, location, outcome)
- System configuration data (model, manufacturer)
- Final electrical data (pace/sense parameters, extrastimulation check, programmed LV polarity)
- Total fluoroscopy time
- Total surgical time
- Stylet usage data
- Guide wire data (manufacturer, model, diameter, insertion force)
- Lead handling assessment
- Final device interrogation
- Adverse events (if applicable)
- Subject study deviations (if applicable)

Postoperatively, the objective parameters measured during the study included the information listed in Table 5. Adverse events and complications were recorded at all visits.

The key time points are shown below in the tables summarizing safety and effectiveness.

Table 5. Summary of Post-Implant Collected Data

	PRE-HOSPITAL DISCHARGE	ONE MONTH	THREE MONTH	SIX MONTH +	INTERIM
Date of Follow-Up	X	X	X	X	X
Initial Device Interrogation	X	X	X	X	(X)
Cardiovascular Medications	X	X	X		(X)
Pacing/Sensing Evaluation, LV programmed polarity	X	X	X	X	(X)
NYHA Classification		X	X	X	
Final Device Interrogation	X	X	X	X	(X)
Adverse Events	(X)	(X)	(X)	(X)	(X)
Deviations	(X)	(X)	(X)	(X)	(X)

X = Required

(X) = If Applicable

3. Clinical Endpoints

With regards to safety, the Model 4196 lead was considered safe if the complication free rate from Model 4196 lead related complications at the end of the one month follow-up window was greater than 80%.

Primary Safety Objective

The Model 4196 lead was considered safe if the complication free rate from Model 4196 lead related complications at the end of the one month follow-up window was greater than 80%.

$H_0: p(\text{Model 4196 one month complication free rate}) \leq 80\%$

$H_A: p(\text{Model 4196 one month complication free rate}) > 80\%$

The Model 4196 lead was considered safe if the one sided 95% lower confidence bound was greater than 80%.

With regards to effectiveness, the Model 4196 lead was considered effective if the mean left ventricular voltage threshold (at 0.5 ms) at the one month visit using the tip electrode was less than 3.0 volts and if the mean left ventricular voltage threshold (at 0.5 ms) at the three month visit using the ring electrode was less than 4.0 volts.

Primary Effectiveness Objectives

The distal tip electrode of the Model 4196 lead was considered effective if the mean left ventricular voltage threshold (at 0.5 ms) at the one month visit using the tip electrode was less than 3.0 volts.

$H_0: \mu$ (Model 4196 one month voltage threshold) ≥ 3.0 V
 $H_A: \mu$ (Model 4196 one month voltage threshold) < 3.0 V

The Model 4196 lead was considered effective if the one-sided p-value of the above hypothesis test was less than or equal to 0.05.

The proximal ring electrode of Model 4196 lead was considered effective if the mean left ventricular voltage threshold (at 0.5 ms) at the three month visit using the ring electrode was less than 4.0 volts.

$H_0: \mu$ (Model 4196 ring electrode three month voltage threshold) ≥ 4.0 V
 $H_A: \mu$ (Model 4196 ring electrode three month voltage threshold) < 4.0 V

The Model 4196 lead ring electrode was considered effective if the one sided p-value of the above hypothesis test was less than or equal to 0.025.

Secondary Objectives

The secondary objectives were descriptive in nature and were intended to provide additional information about the Model 4196 lead. There were no established performance requirements related to the secondary objectives.

- To characterize the LV voltage thresholds, LV sensing, and LV pacing impedance of the Model 4196 lead tip electrode at implant and follow-up.
- To characterize the LV voltage thresholds, LV sensing (implant only), and LV pacing impedance of the Model 4196 lead ring electrode at implant and follow-up.
- To evaluate the implant success rates of the Model 4196 lead and the Attain™ family of leads.
- To evaluate the following implant related times: total implant, fluoroscopy, coronary sinus cannulation, and placement of the Model 4196 lead.
- To evaluate the Model 4196 lead handling characteristics such as pushability, steerability, and stability.
- To characterize all adverse events, excluding unavoidable adverse events.

With regard to success/failure criteria of the overall trial, success was defined as meeting the primary safety endpoint and both the effectiveness endpoints.

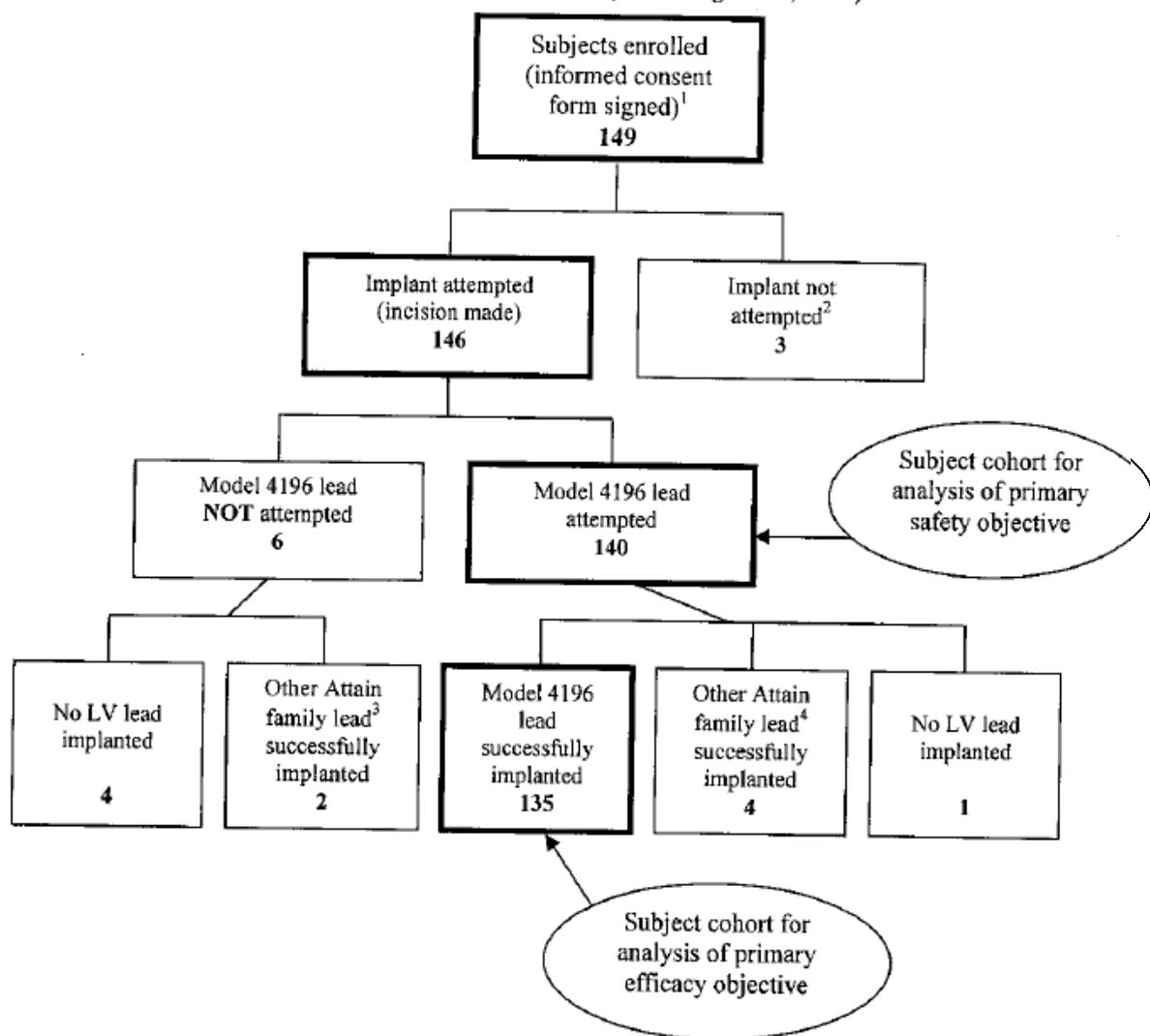
B. Accountability of PMA Cohort

At the time of the PMA database lock on August 20, 2007, of 149 subjects enrolled in PMA study, 94% subjects were available for safety analysis and 90.6% were available for effectiveness analysis.

Data was collected for a total of 149 US subjects enrolled with 146 subjects having implant attempts (incision made). A total of 140 subjects underwent an implant attempt of the Model 4196 lead. A summary of the enrollment status is presented in Figure 5. After providing consent and a successful baseline evaluation, eligible subjects underwent a cardiac

resynchronization therapy (CRT) system implant attempt. The protocol advised physician that a market-released right atrial lead and a market-released Medtronic right ventricular lead may be implanted. For the purposes of the study, the implanted system had to include a Medtronic market released CRT device which can be programmed to utilize both electrodes, i.e. Concerto™ Model C154DWK or Concerto-AT™ Model C174AWK. The Model 4196 lead could also be attempted but was not required. If the Model 4196 lead was not attempted at the time of implant or was unable to be implanted, any market released left ventricular (LV) lead labeled for biventricular pacing systems could have been used. The physicians were trained to make their LV lead selections based on experience, handling preference and subject anatomy.

Figure 5. Enrollment Status (As of August 20, 2007)



¹ Adverse events are reported for all subjects enrolled through the time of exit.
² Two subjects did not meet inclusion/exclusion criteria after signing the informed consent. One subject was exited prior to implant because the physician opted for a different treatment for patient.
³ The “Other Attain Family Leads” implanted in the subjects not attempted with the Model 4196 were both Model 4194 leads.
⁴ The “Other Attain Family Leads” implanted in the subjects attempted with the Model 4196 were two Model 4194 leads, one Model 4193 lead, and one Model 4195 lead (in Canada).

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a left ventricular lead study performed in the US and are summarized in Table 6 below.

Subjects ranged in age from 33 to 86.7 years, with a mean age of 68.7 years. One hundred ten (110) of the subjects (75.3%) were male and 36 of the subjects (24.7%) were female and the population was predominantly Caucasian (88.4%). The majority of subjects were NYHA Class III (144, 98.6%), and the remaining patients were NYHA Class IV (2, 1.4%). The subject cohort had a mean intrinsic QRS width of 151.8ms (SD = 24.5) and a mean LV ejection fraction of 23.9% (SD = 6.9).

Table 6. Subject Demographics

CATEGORY	SUBJECTS WITH IMPLANT ATTEMPT (N = 146) ¹
Gender, N (%)	
Male	110 (75.3%)
Female	36 (24.7%)
Age (years)	
Mean	68.7
Standard deviation	11.7
Range	33.0-86.7
NYHA functional classification, N (%)	
Class III	144 (98.6%)
Class IV	2 (1.4%)
Primary Inclusion Criteria Values	
LV Ejection Fraction (mean %)	23.9
Intrinsic QRS Width (mean ms)	151.8
Pre-existing IPG/ICD Status	
None	99 (67.8%)
ICD	33 (22.6%)
IPG	14 (9.6%)

¹Subjects who underwent an implant attempt (incision made) were included in the study population analysis.

Only CRT-D system implants were allowed by the protocol. Table 7 summarizes the ICD indications (from ACC/AHA/HRS practice guidelines at the time of implant) collected at baseline for each subject.

Table 7. ICD Indications

DESCRIPTION	N	Percent %
Cardiac arrest due to VF or VT not due to a transient or reversible cause	3	2.1%
Spontaneous sustained VT in association with structural heart disease	8	5.5%
Syncope of undetermined origin with clinical relevant, hemodynamically significant sustained VT or VF induced at EP study when drug therapy is ineffective, not tolerated, or not preferred	3	2.1%
Nonsustained VT in patients with coronary artery disease, prior MI, LV dysfunction, and inducible VF or sustained VT at EP study that is not suppressible by a Class I antiarrhythmic drug	2	1.4%
Spontaneous sustained VT in patients who do not have structural heart disease that is not amendable to other treatments	1	0.7%
Subject with LVEF of less than or equal to 30% at least one month post MI and three months post coronary artery revascularization surgery	15	10.3%
Familial or inherited conditions with a high risk for life-threatening ventricular arrhythmias such as long-QT syndrome or hypertrophic cardiomyopathy	1	0.7%
Nonsustained VT with coronary artery disease, prior MI, LV dysfunction and inducible VT or VF induced at EP study	2	1.4%
Syncope in subject with advanced structural heart disease in which thorough invasive and noninvasive investigation has failed to define a cause	1	0.7%
EF < 35%, NYHA Class II or III, regardless of etiology	110	75.3%

D. Safety and Effectiveness Results

1. **Safety Results**

The analysis of safety was based on the cohort of 140 patients who underwent a Model 4196 lead attempt. The key safety outcomes for this study are presented below in Tables 8 to 11. Adverse effects are reported in these tables.

Adverse effects that occurred in the PMA clinical study:

The dataset includes adverse events for all subjects between the first enrollment, February 5, 2007, and the visit data cut-off date of August 20, 2007. During this period of time a total of 146 subjects underwent an LV lead implant attempt. Of these, 140 subjects had a Model 4196 lead implant attempt, and 135 subjects were successfully implanted with a Model 4196 lead. As of August 20, 2007, evaluation of the Model 4196 lead included 216.9 device months of experience. Subject follow-ups ranged from 0 to 6.2 months and averaged 1.5 ± 1.3 months (median = 1.2 months). Note at the time of this analysis the clinical study was still ongoing. The last subject was implanted in the Model 4196 clinical study on Sept 24, 2007, and this additional implant and follow-up experience was summarized at a later date in a progress report².

² Attain Ability Model 4196 Left Ventricular Lead FDA Annual Progress Report, Version 1, 27 Feb 2008

A total of 132 adverse events were reported in the subject cohort and are presented in Table 8. Thirty eight (28.8%) of the events were classified as complications and 94 (71.2%) were classified as observations.

For the purpose of the Model 4196 lead study, an adverse event was defined as any undesirable clinical occurrence in a subject, whether or not related to the investigational device. The center categorized adverse events by event code, and then further classified by relatedness. Medtronic reviewed each event and the treatment associated with the event to determine if the event was a complication or an observation. All adverse events were adjudicated by the Adverse Events Advisory Committee (AEAC) based on the event code, relatedness, and complication/observation. The definition for each follows:

Complication: An adverse event that results in invasive intervention, or the termination of significant device function regardless of other treatments. Intravenous (IV) and intramuscular (IM) therapies are considered invasive treatment.

Observation: An adverse event that is not a complication.

Relatedness: All adverse events were classified by their relatedness to the components, the CRT system, implant tools, therapy, or procedure.

Table 8 provides a summary of all adverse events by relatedness including incidence rates by complication or observation. Incidence rate per subject month were calculated by dividing the number of events by the total time (month) when subjects were exposed to the risk for having event. The subject cohort for left ventricular lead related events were subjects who underwent an model 4196 implant attempt; the subject cohort for right ventricular lead related events, cardiac resynchronization device related events, cardiac resynchronization system related events, implant tool related events and implant procedure related events were subjects who underwent an implant attempt; the subject cohort for not cardiac resynchronization system related events were all subjects enrolled in this study.

Table 8. Summary of All Adverse Events

RELATEDNESS	COMPLICATIONS		OBSERVATION	
	Number of Events	Incidence Rate (events per subject month)	Number of Events	Incidence Rate (events per subject month)
Model 4196 LV Lead	6	0.0277	10	0.0461
Right Ventricular Lead	2	0.0090	2	0.0090
Cardiac Resynchronization Device	0	0.0000	3	0.136
Cardiac Resynchronization System	0	0.0000	2	0.0090
Implant Tool	1	0.0045	5	0.0226
Implant Procedure	2	0.0090	8	0.0362
Not Related to Cardiac Resynchronization System	27	0.1182	64	0.2802

RELATEDNESS	COMPLICATIONS		OBSERVATION	
	Number of Events	Incidence Rate (events per subject month)	Number of Events	Incidence Rate (events per subject month)
Total	38	0.1664	94	0.4116

Of the 146 subjects who underwent an implant attempt, 140 subjects underwent a Model 4196 lead attempt and are included in the safety endpoint. Among the 105 subjects who completed a one month follow-up or a later follow-up, 101 subjects did not experience any Model 4196 lead related complications. One additional subject did not complete their one month follow-up; however, a Model 4196 related complication was observed prior to their one month visit window cut-off date. Since documentation of the complication was complete and valid, this complication was considered confirmed and reportable, hence included in the primary endpoint analysis (i.e. the patient was included in the denominator of the analysis and the complication was counted against the numerator). Table 9 presents the results of the safety endpoint analysis - rate of freedom from Model 4196 lead related complications at one month. At one month, five subjects had experienced a total of six Model 4196 lead related complications.

Table 9. Freedom from Model 4196 Lead Related Complications at One Month

Number of Subjects ¹	Number of subjects with events (cumulative)	Observed Complication-Free Rate	95% Lower Confidence Bound (1-sided)	Predetermined Acceptance Criteria	OBJECTIVE MET
106	5	95.3%	90.3%	80%	Yes

¹Includes all subjects who completed a one month follow-up or a later follow-up, or experienced a Model 4196 lead related complication within the one month follow-up window.

Table 10 summarizes the Model 4196 lead related complications at one month and their treatments.

Table 10. Treatment of Model 4196 Lead Related Complications through One Month

EVENT (6 events in 5 subjects)	TREATMENT	N
Lead Dislodgement	Lead Repositioned	3
	Lead Replaced ¹	2
	LV Lead Programmed Off ²	1

¹One subject had the Model 4196 lead replaced with a Model 4194 lead and a second subject had it replaced with a Model 4193 lead.

²One subject was awaiting LV lead repositioning at the time of the visit cut-off date.

In the Model 4196 clinical study there were 10 adverse events (in 9 subjects) reported for extracardiac stimulation caused by LV pacing (see Table 11 below). There were no subjects that required surgical intervention in order to eliminate the extracardiac stimulation while maintaining biventricular pacing, so all ten of the events were classified as observations. Three of the events were treated by utilizing an alternate electrode configuration and seven of the events were treated by changing the pacing output.

Table 11. Events Related to LV Pacing and Programming Treatment (N=140)

ADVERSE EVENT	NUMBER OF EVENTS (SUBJECTS)	PERCENT OF SUBJECTS WITH EVENT (%)	TREATMENT (NUMBER OF EVENTS)
Chest wall stimulation	1 (1)	0.7	Changed pacing output (1)
Possible chest wall stimulation	1 (1)	0.7	Changed pacing output (1)
Muscle stimulation-diaphragm	8 (7)	5.0	Utilized an alternate configuration (3) Changed pacing output (5)

In addition to the 10 events described above related to LV pacing, there were 6 adverse events (in 5 subjects) reported for LV lead dislodgement. For each of these subjects there was visual evidence, e.g. Chest X-ray or fluoroscopy, which confirmed a lead dislodgment that necessitated additional treatment beyond reprogramming. Therefore, the six LV lead dislodgments were all classified as complications because they resulted in invasive intervention or termination of significant device function (see Table 10 above).

2. Effectiveness Results

The analysis of effectiveness was based on the 135 evaluable at the 1 and 3 month time point. Key effectiveness outcomes are presented in Table 12-15 and Figure 6.

Table 12. Summary of Primary Effectiveness Objectives Results

PRIMARY OBJECTIVE	RESULTS	OBJECTIVES MET
<u>Effectiveness:</u> The distal tip electrode of the Model 4196 lead will be considered effective if the mean LV voltage threshold (at 0.5 ms) at the one month visit using the tip electrode is less than 3.0 volts	Observed mean Model 4196 LV tip electrode voltage threshold at one month = 1.1 V One-sided 95% confidence interval upper bound = 1.2 V	Yes
<u>Effectiveness:</u> The proximal ring electrode of the Model 4196 lead will be considered effective if the mean LV voltage threshold (at 0.5 ms) at the three month visit using the ring electrode is less than 4.0 volts	Observed mean Model 4196 LV ring electrode voltage threshold at three months = 1.8 V One-sided 97.5% confidence interval upper bound = 2.3 V	Yes

As demonstrated in the table above, sufficient statistical evidence exists to reject the null hypothesis for both the tip and ring electrodes.

3. Secondary Results

Table 13 presents a summary of the secondary objectives results. The secondary objectives summarize the Attain family and Model 4196 lead implant success, lead placement and procedure time, lead handling, additional electrical performance, and all adverse events (see Table 8) reported in the study.

The results of the secondary objectives confirmed that the Model 4196 lead can be successfully and safely implanted, and that electrical performance values were stable over time and were within expected values based on Medtronic market-approved LV leads.

Table 13. Summary of Secondary Objectives Results

SECONDARY OBJECTIVE	RESULTS
Evaluate the Attain leads implant success	All transvenous LV leads success = 96.6% (141/146) All transvenous LV leads success after cannulation = 98.6% (141/143) Attain family success = 96.6% (141/146) Model 4196 lead success = 96.4% (135/140)
Evaluate total implant, fluoroscopy, cannulation and Model 4196 lead placement time (Mean ± standard deviation)	Cannulation time = 11.5 min ± 4.0 Fluoroscopy time = 25.6 min ± 18.3 Model 4196 lead placement time = 12.2 min ± 10.0 Total implant time = 119.2 min ± 104.0
Evaluate lead handling	Ability to Push (Good or Fair) = 98.5% (135/137) Ability to Navigate (Good or Fair) = 99.3% (138/139) Stability at final location (Good or Fair) = 94.2% (131/139) Stability while slitting (Good or Fair) = 97.8% (136/139) Acceptability = 98.6% (137/139)
Characterize the electrical performance of the Model 4196 LV lead tip electrode (Mean ± standard deviation) <ul style="list-style-type: none"> • LV R-wave amplitude • LV lead impedance • LV Voltage thresholds measured at 0.5 ms 	Model 4196 Lead Electrical Performance at Implant <ul style="list-style-type: none"> • R-Wave Amplitude = 17.1 mV ± 7.1 (N = 129) • Impedance = 674.1 Ohms ± 217.2 (N = 135) • Voltage Threshold = 1.0 V ± 0.9 (N = 135) Model 4196 Lead Electrical Performance at Discharge <ul style="list-style-type: none"> • R-Wave Amplitude = 16.7 mV ± 5.7 (N = 127) • Impedance = 494.4 Ohms ± 168.4 (N = 130) • Voltage Threshold = 1.2 V ± 1.2 (N = 125) Model 4196 Lead Electrical Performance at One month <ul style="list-style-type: none"> • R-Wave Amplitude = 17.6 mV ± 6.3 (N = 97) • Impedance = 496.4 Ohms ± 128.5 (N = 98) • Voltage Threshold = 1.1 V ± 0.8 (N = 99) Model 4196 Lead Electrical Performance at Three months <ul style="list-style-type: none"> • R-Wave Amplitude = 17.8 mV ± 6.2 (N = 48) • Impedance = 519.4 Ohms ± 170.5 (N = 50) • Voltage Threshold = 1.0 V ± 0.7 (N = 50)
Characterize the electrical performance of the Model 4196 LV lead ring electrode (Mean ± standard deviation) <ul style="list-style-type: none"> • LV R-wave amplitude (implant only) • LV lead impedance • LV Voltage thresholds measured at 0.5 ms 	Model 4196 Lead Electrical Performance at Implant <ul style="list-style-type: none"> • R-Wave Amplitude = 15.3 mV ± 6.9 (N = 129) • Impedance = 588.3 Ohms ± 246.3 (N = 135) • Voltage Threshold = 1.8 V ± 1.9 (N = 126) Model 4196 Lead Electrical Performance at Discharge <ul style="list-style-type: none"> • Impedance = 399.0 Ohms ± 94.2 (N = 128) • Voltage Threshold = 2.2 V ± 2.1 (N = 112) Model 4196 Lead Electrical Performance at One month <ul style="list-style-type: none"> • Impedance = 509.1 Ohms ± 309.9 (N = 98) • Voltage Threshold = 2.0 V ± 2.0 (N = 88) Model 4196 Lead Electrical Performance at Three months <ul style="list-style-type: none"> • Impedance = 515.4 Ohms ± 315.7 (N = 50) • Voltage Threshold = 1.8 V ± 2.0 (N = 42)

With the dual electrode design, the Model 4196 lead provides the physician a second option to pace the LV. Table 14 below summarizes the pacing configuration selected at implant and the start of each follow-up visit. Table 15 and Figure 6 summarize the voltage thresholds for the permanent programmed pacing configuration.

Table 14. LV Permanently Programmed Configuration

VISIT	N	LV TIP TO RV COIL	LV RING TO RV COIL	OTHER
Implant	135	103 (76.3%)	30 (22.2%)	2 (1.5%) ¹
Pre-hospital discharge	133	101 (75.9%)	29 (21.8%)	3 (2.3%) ²
One month	101	73 (72.3%)	26 (25.7%)	2 (2.0%) ³
Three month	50	35 (70.0%)	15 (30.0%)	0 (0.0%)
Six month	1	1 (100%)	0 (0.0%)	0 (0.0%)

¹ Two subjects were programmed to the bipolar (LV tip/LV ring) configuration.

² Two subjects were programmed to the bipolar (LV tip/LV ring) configuration. A subject had the LV lead programmed off following the implant, but prior to the pre-hospital discharge visit.

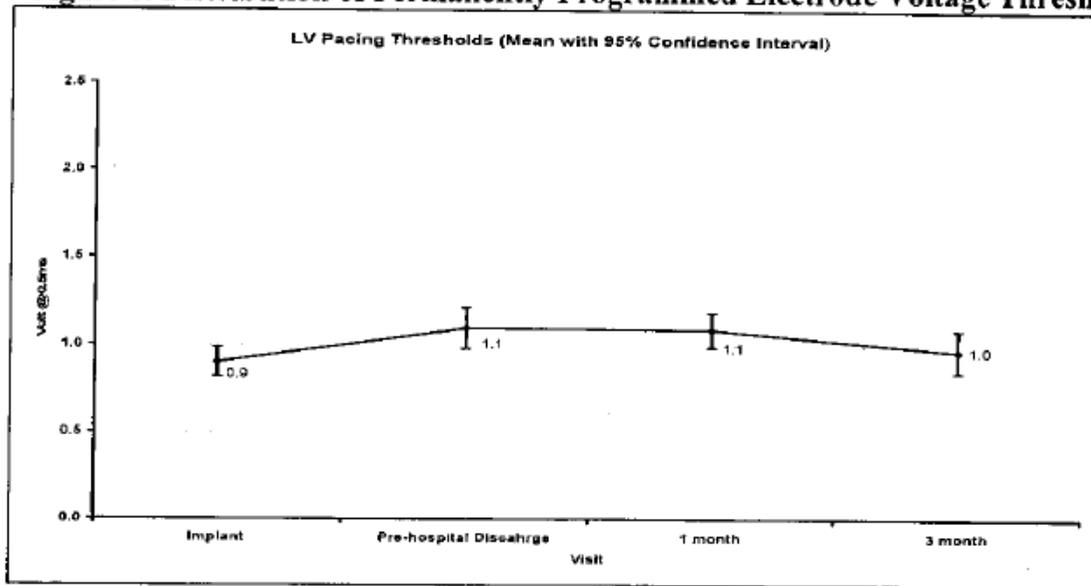
³ One subject was programmed to the bipolar (LV tip/LV ring) configuration. A subject had the LV lead programmed off due to dislodgement.

Table 15. Permanently Programmed Electrode Voltage Threshold at 0.5ms

VISIT	UTC	N	MEAN (VOLTS)	MEDIAN	STD. DEV.	RANGE
Implant	0	135	0.9	0.6	0.8	0.3 - 4.5
Pre-hospital discharge	1 ¹	125	1.1	0.5	1.0	0.5 - 6.0
One month	1 ¹	99	1.1	1.0	0.8	0.5 - 5.0
Three month	0	50	1.0	0.5	0.7	0.5 - 3.0
Six month	0	1	1.0	1.0	-	1.0 - 1.0

¹ Two subjects are listed as UTC at the permanently programmed configuration and LV lead dislodgements were confirmed.

Figure 6. Distribution of Permanently Programmed Electrode Voltage Thresholds



4. Subject Exits and Deaths

Of the 149 subjects enrolled, 17 subjects exited the study. Three subjects exited prior to any implant attempt, six exited because they did not have a Model 4196 lead attempted, and three exited because they did not have a successful Model 4196 lead implant. Two subjects had a Model 4196 lead explanted and were subsequently exited from the study. One subject requested to withdraw from the study and two subjects exited due to death. One of the deaths was classified as non-cardiac-related, and the other death as having an unknown cause. Neither of the patient deaths were thought to be LV lead-related.

5. Subgroup Analyses – Gender Bias

A subgroup analysis by gender determined that there is no significant difference in the primary safety and the ring electrode efficacy endpoint between men and women. The female cohort reported a statistically significantly higher tip threshold as compared to the men (p-value = 0.041); however the mean threshold for both groups is well below the pre-specified objective performance criteria (3.0V @ 0.5msec). The poolability analysis results support that the Model 4196 Lead is safe and effective for both genders.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Of the 146 subjects that were consented and underwent baseline screening and an implant attempt, 144 (98.6%) met all inclusion criteria/exclusion criteria. A total of 50 deviations were reported in 36 subjects. All protocol deviations are summarized in Table 16 below. Protocol deviations were reviewed and deemed not to affect the overall results.

Table 16. Protocol Deviation Summary

DEVIATION DESCRIPTIONS	n	Percent %
Informed consent	2	4.0%
Subject did not meet inclusion/exclusion criteria	2	4.0%
Visit compliance	8	16.0%
Protocol required data collection/testing	30	60.0%
Protocol required implanted system – outside inclusion/exclusion criteria	1	2.0%
Regulatory compliance	3	6.0%
Source documents	4	8.0%

XII. PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION

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 Systems 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. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

Investigators at 22 centers (17 in the US and 5 in Canada) enrolled 149 subjects as of August 20, 2007. Implant attempts occurred in 146 subjects, with 140 undergoing a Model 4196 lead attempt. Of the subjects who had a Model 4196 lead attempt, 135 (96.4%) had a successful Model 4196 lead implant. Safety was demonstrated by the complication free rate of 95.3% from Model 4196 lead related complications at one month.

The results of the secondary objectives confirm that the Model 4196 lead can be successfully and safely implanted and that the general electrical performance (e.g. sensing, impedance, etc.) is stable over time and within expected values and when compared to market released LV leads.

The adverse effects of the device are based on data collected in a clinical study conducted to support PMA approval as described above.

B. Effectiveness Conclusions

Effectiveness of the tip electrode was demonstrated by the mean Model 4196 lead voltage pacing threshold of 1.1 V (at 0.5 ms) at one month. Effectiveness of the ring electrode was demonstrated by the mean Model 4196 lead voltage pacing threshold of 1.8 V (at 0.5 ms) at three months.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

Medtronic conducted a hazard analysis on the Model 4196 lead and then conducted non-clinical laboratory tests and a clinical study to evaluate the lead. All test results were found to be acceptable.

The Model 4196 Lead met both the safety and effectiveness performance criteria and has been determined to be safe and effective for human use. The clinical study of the Model 4196 Lead has shown that the lead has statistically and clinically acceptable pacing thresholds and sensing performance. The clinical study also demonstrated that the Model 4196 has acceptable handling performance during implant.

The safety and biocompatibility of the Model 4196 lead was evaluated in a series of non-clinical tests and animal studies. The animal studies were conducted in accordance with 21 CFR 58 (Good Laboratory Practices) with the exception of the S1366/Model 4196 Canine In-Vivo Elution Pilot Study, which was found to be acceptable. The results of the animal studies support the safety and biocompatibility of the Model 4196 lead.

XIV. CDRH DECISION

CDRH issued an approval order on April 7, 2009.

The safety and effectiveness of the Medtronic Attain Ability Model 4196 lead was demonstrated in the results of bench testing, animal studies, and a clinical trial. The Model 4196 lead passed all preclinical tests and had acceptable handling, acceptable pacing and sensing electrical performance, acceptable adverse events rates, and met the predefined safety and effectiveness objective performance criteria. CDRH believes that the sponsor has adequately addressed all of FDA's questions related to the safety and effectiveness of the lead.

The final conditions of approval cited in the approval order are described below.

1. Medtronic commits to provide a report with the complete elution profile data for the tip and ring at 50 rpm and 100 rpm from all the lots that are manufactured during the first post-approval year. Based on the elution data provided in this report, a decision on the rotation speed and/or the acceptance criteria for the tip and ring will be made by the Agency. If a change is to be made (to the method and/or the acceptance criteria), Medtronic will submit a supplement for the change.
2. Medtronic will conduct a post-approval study to characterize chronic performance of the Medtronic Attain Ability™ Model 4196 Lead as presented in your protocol submitted January 26, 2009 and February 10, 2009 which incorporates the following:

- a. A prospective study design to characterize chronic lead performance following device implant, and will contain a retrospective arm to include subjects from the IDE cohort;
- b. A post-approval study duration of at least 5 years;
- c. A sample size that results in a 2-sided 95% upper confidence bound of no more than 1.0% for individual adverse event rates, assuming an expected rate of 0.4%, using the exact binomial method;
- d. A total enrollment which accounts for estimated attrition, and an enrollment plan which attempts to fully enroll the study within 21 months of market release, based on current sales estimates. Medtronic will reassess the actual enrollment rate and actual sales of the Model 4196 lead compared to projections. If actual data differs significantly from the initial projections, Medtronic agrees to re-evaluate the enrollment strategies being implemented;
- e. A primary safety endpoint is the complication-free rate greater than 92.5% at 5 years. The complication-free rate will be estimated based on clinical adverse events included in the primary safety objective (excluding events collected and reported as secondary objectives);
- f. A rigorous process to monitor the status of all study subjects, to actively follow-up missed visits, and to document the reason for all subject dropouts;
- g. Inclusion of a trend analysis process in the protocol to provide a robust early warning mechanism to identify, characterize, and report adverse events, failure modes, and failure rates;
- h. Post-approval study status reporting at least every 6 months and a mechanism for providing non-scheduled trend analysis reports for new information;
- i. Inclusion of a full list of complications, failure modes, and definition of terms within the study protocol; and
- j. Collection of secondary data including implant data, demographic information, lead-related adverse events, electrical performance, returned product analyses, and other parameters of interest. Additionally, data on unanticipated adverse events that are determined to be possibly related or related to the lead will be collected and reported in the 6-month PAS progress reports.

The applicant's manufacturing facilities were inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.