
SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name: Cardiac Resynchronization Therapy Defibrillator (CRT-D)

Device Trade Names: CONTAK RENEWAL[®] 3 AVT[®] System including the CONTAK RENEWAL[®] 3 AVT[®] Models M150/M155 Cardiac Resynchronization Therapy Defibrillator, Programmer Software Application Model 2893 version 3.01, and the Model 2930 PARTNER Rhythm Assistant with Software Version 2.1

CONTAK RENEWAL[®] 3 AVT[®] HE System including the CONTAK RENEWAL[®] 3 AVT[®] HE Models M157/M159 Cardiac Resynchronization Therapy Defibrillator, Programmer Software Application Model 2893 version 3.01, and the Model 2930 PARTNER Rhythm Assistant with Software Version 2.1

Applicant's Name and Address: Guidant Corporation
Cardiac Rhythm Management
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Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P010012/S37

Date of Notice of Approval to Applicant: March 13, 2008

II. INDICATIONS FOR USE

CONTAK RENEWAL 3 AVT Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction (EF \leq 35%) and QRS duration \geq 120 ms.

CONTAK RENEWAL 3 AVT provides atrial antitachycardia pacing and atrial defibrillation treatment for patients with a history of or who are at risk of developing atrial arrhythmias.

III. CLINICAL OUTCOMES

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are approved for the following outcomes in the indicated population specified above:

- Reduction in risk of all-cause mortality or first hospitalization, where a hospitalization is defined as either:

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- Care provided at a hospital for any reason in which the duration is associated with a date change, or
 - Use of intravenous inotropes and/or vasoactive drugs for a duration > 4 hours (inpatient or outpatient).

Note: Hospitalizations associated with a device implant attempt or re-attempt are excluded.

- Reduction in risk of all-cause mortality
- Reduction of heart failure symptoms

Note: Cardiac Resynchronization Therapy in patients with a history of atrial arrhythmias has not been specifically studied in a prospective, randomized controlled clinical trial.

The CONTAK RENEWAL 3 AVT study demonstrated the device is effective in terminating atrial arrhythmias.

IV. CONTRAINDICATIONS

There are no contraindications for this device.

V. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the CONTAK RENEWAL 3 AVT Physician's Technical Manual.

VI. DEVICE DESCRIPTION

The Guidant CONTAK RENEWAL 3 AVT cardiac resynchronization therapy defibrillator (CRT-D), Models M150 and M155, and CONTAK RENEWAL 3 AVT HE CRT-D, Models M157 and M159, provide both atrial and ventricular tachyarrhythmia therapies and cardiac resynchronization therapy. Ventricular tachyarrhythmia therapy is for the treatment of ventricular tachycardia (VT) and ventricular fibrillation (VF), rhythms that are associated with sudden cardiac death (SCD). Atrial tachyarrhythmia therapy is for the treatment of supraventricular tachycardia (SVT) and atrial fibrillation (AF).

Cardiac resynchronization therapy is for the treatment of heart failure (HF) and uses biventricular electrical stimulation to synchronize ventricular contractions. The device also uses accelerometer-based adaptive-rate bradycardia therapy similar to Guidant's commercially available VENTAK® family of implantable cardioverter defibrillators (ICDs). The pulse generator has independently programmable outputs and accepts one IS-1[†] atrial lead, one LV-1 or one IS-1 coronary venous pace/sense lead, and one DF-1/IS-1 cardioversion/defibrillation lead. The pulse generator and the leads constitute the implantable portion of the CONTAK RENEWAL 3 AVT system. The device's small, physiologic shape minimizes pocket size and device migration.

[†] IS-1 refers to the international standard ISO 5841.3:2000. LV-1 refers to the Guidant LV. Proprietary connector. DF-1 refers to the international standard ISO 11318:2002.

Cardioversion/defibrillation therapies include a range of low- and high-energy shocks using either a biphasic or monophasic waveform. The CONTAK RENEWAL 3 AVT device uses the Guidant TRIAD™ electrode system for defibrillation energy delivery. By using the metallic housing of the pulse generator as an active electrode, combined with the Guidant ENDOTAK® two-electrode defibrillation lead, energy is sent via a dual-current pathway from the distal shocking electrode to the proximal electrode and to the pulse generator case. The CONTAK RENEWAL 3 AVT device also offers a wide variety of antitachycardia pacing schemes to terminate slower, more stable atrial and ventricular tachyarrhythmias. Bradycardia pacing with cardiac resynchronization therapy, including adaptive-rate features, is available to detect and treat bradyarrhythmias and to support the cardiac rhythm after defibrillation therapy.

The ZOOM® LATITUDE Programming System, which includes the Model 3120 Programmer/Recorder/Monitor (PRM), the Model 2893 CONSULT Software Application, and an accessory telemetry wand, constitutes the external portion of the CONTAK RENEWAL 3 AVT system. The external components allow interrogation and programming of the pulse generator as well as access to the device's diagnostic features. The CONTAK RENEWAL 3 AVT system can be programmed to provide a variety of therapy options. It also can provide noninvasive diagnostic testing and therapy history data.

VII. ALTERNATE PRACTICES AND PROCEDURES

Patients who have heart failure are routinely treated with medications. Cardiac resynchronization therapy (CRT) devices are also available to treat heart failure in patients already receiving optimal medications. Additional medical treatments for heart failure include, but are not limited to, exercise and nutrition programs.

VIII. MARKETING HISTORY

The CONTAK RENEWAL 3 AVT CRT-D Systems have not been marketed in the United States or any foreign country.

IX. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

OBSERVED ADVERSE EVENTS

Guidant conducted a clinical investigation to demonstrate safety and effectiveness of atrial therapies in a heart failure patient population, to confirm safety of combining ICD, CRT and atrial therapies, and to confirm delivery of CRT and ICD therapy in the presence of atrial therapies. The clinical study was a prospective, multi-center, single-arm study at 38 centers in the United States, which enrolled 170 patients. A total of 168 patients underwent a procedure to receive either the CONTAK RENEWAL 3 AVT or CONTAK RENEWAL 3 AVT HE device and an EASYTRAK/EASYTRAK 2 Lead (a left ventricular coronary venous steroid-eluting pace/sense lead) and were programmed to a biventricular pacing mode post-implant. The programmed atrial and ventricular tachyarrhythmia device therapy was left to the discretion of the investigator. Patients

underwent an evaluation of the investigational system at implant, pre-discharge, one month, three months, and quarterly thereafter.

Table 1 provides information on adverse events reported for a three-month period beginning from device implant. The adverse events are identified as *observations* and *complications*. An *observation* is defined as a clinical event that does not result in invasive intervention, injury, or death, and is not an unanticipated adverse event. A *complication* is defined as a clinical event that results in invasive intervention after implant, injury, or death. Note that the numbers of patients with observations and complications do not add up to the total number of patients experiencing an adverse event since the same patient can have both an observation and a complication.

Table 1: Adverse Events Through Three Months

Adverse Event	Complications			Observations	
	Number Of Events (Number of Patients)	% of Patients (N Patients)	N Events/ 100 Device Months (N Events)	% of Patients (N Patients)	N Events/ 100 Device Months (N Events)
Total Adverse Events	162 (91)	23.2 (39)	9.9 (47)	40.5 (68)	24.2 (115)
Defib Lead Related Events					
Oversensing - Defibrillation lead	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
EASYTRAK 2 Lead Related Events					
Dislodgment - Elevated threshold - LV	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Dislodgment - Extracardiac stimulation - LV	3 (3)	1.8 (3)	0.6 (3)	0.0 (0)	0.0 (0)
Dislodgment - Multiple signs - LV	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Dislodgment - Unable to capture - LV	2 (2)	1.2 (2)	0.4 (2)	0.0 (0)	0.0 (0)
Extracardiac stimulation - LV	24 (19)	0.6 (1)	0.2 (1)	10.7 (18)	4.8 (23)
Unable to capture - LV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
EASYTRAK Lead Related Events					
Dislodgment - Extracardiac stimulation - LV	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Extracardiac stimulation - LV	2 (2)	0.6 (1)	0.2 (1)	0.6 (1)	0.2 (1)
PG Related Events					
Elevated DFT - Defibrillation	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Inappropriate tachy therapy - Noise	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Inappropriate tachy therapy - SVT	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Infection (> 30 days post-implant)	2 (2)	1.2 (2)	0.4 (2)	0.0 (0)	0.0 (0)
Other - PG system	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Pacemaker-mediated tachycardia (PMT)	13 (13)	0.0 (0)	0.0 (0)	7.7 (13)	2.7 (13)
Programmer / Software error code	9 (9)	0.0 (0)	0.0 (0)	5.4 (9)	1.9 (9)
Psychological effect due to device therapy	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.4 (2)

Adverse Event	Complications			Observations	
	Number Of Events (Number of Patients)	% of Patients (N Patients)	N Events/ 100 Device Months (N Events)	% of Patients (N Patients)	N Events/ 100 Device Months (N Events)
Undersensing - RA	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
RA Lead Related Events					
Elevated threshold - RA	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Oversensing - RA	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.4 (2)
Undersensing - RA	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.4 (2)
RV Lead Related Events					
Elevated threshold - RV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Extracardiac stimulation - RV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Oversensing - RV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Subtotal Device Related Events	75 (57)	8.3 (14)	2.9 (14)	28.0 (47)	12.8 (61)
Procedure Related Events					
Adverse reaction - General	7 (7)	2.4 (4)	0.8 (4)	1.8 (3)	0.6 (3)
Adverse reaction - Hypotension	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Adverse reaction - Respiratory	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Coronary venous dissection	3 (3)	0.6 (1)	0.2 (1)	1.2 (2)	0.4 (2)
Elevated DFT - Defibrillation	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Hematoma - Pocket (<=30 days post-implant)	8 (8)	0.0 (0)	0.0 (0)	4.8 (8)	1.7 (8)
Inadvertent VT/VF	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Other - PG system - Procedure	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Physical trauma	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Post-surgical infection (<= 30 days post-implant)	5 (5)	2.4 (4)	0.8 (4)	0.6 (1)	0.2 (1)
Post-surgical pocket hemorrhage	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Post-surgical wound discomfort	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.4 (2)
Subtotal Procedure Related Events	32 (24)	6.0 (10)	2.3 (11)	8.9 (15)	4.4 (21)
Cardiovascular - HF Related Events					
Dehydration - Heart failure	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)

Adverse Event	Number Of Events (Number of Patients)	Complications		Observations	
		% of Patients (N Patients)	N Events/ 100 Device Months (N Events)	% of Patients (N Patients)	N Events/ 100 Device Months (N Events)
Dyspnea - Heart failure	5 (5)	2.4 (4)	0.8 (4)	0.6 (1)	0.2 (1)
Fatigue - Heart failure	2 (2)	0.6 (1)	0.2 (1)	0.6 (1)	0.2 (1)
Heart failure symptoms	6 (6)	1.8 (3)	0.6 (3)	1.8 (3)	0.6 (3)
Heart failure symptoms - Unspecified	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Hypotension - Heart failure	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Renal insufficiency - Heart failure	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Cardiovascular - Non-HF Related Events					
Atrial fibrillation (AF)	2 (2)	0.6 (1)	0.2 (1)	0.6 (1)	0.2 (1)
Atrial flutter	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Cerebrovascular accident (CVA)	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Chest pain - Ischemic	3 (3)	0.6 (1)	0.2 (1)	1.2 (2)	0.4 (2)
Chest pain - Other	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Dizziness	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Fatigue	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Hypertension	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Hypotension	3 (3)	0.6 (1)	0.2 (1)	1.2 (2)	0.4 (2)
Mitral regurgitation	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Mitral stenosis	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Multiple symptoms	1 (1)	0.6 (1)	0.2 (1)	0.0 (0)	0.0 (0)
Nonsustained ventricular tachycardia (NSVT)	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Other SVT (AVRT, AVNRT, EAT etc.)	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Sinus tachycardia	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Syncope	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.2 (1)
Ventricular tachycardia (VT)	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.4 (2)
Subtotal Cardiovascular Related Events	40 (32)	8.3 (14)	3.8 (18)	11.9 (20)	4.6 (22)
Total Non-cardiovascular Related Events	15 (15)	2.4 (4)	0.8 (4)	6.5 (11)	2.3 (11)

A total of 11 deaths occurred in the RENEWAL 3 AVT Clinical study. These are presented in Table 2 with cause of death (as adjudicated by an independent events committee).

Table 2: Deaths in the RENEWAL 3 AVT Clinical Study

Cause of Death	Implants (N=159)	Attempts (N=9)	Total (N=168)
Cardiac: Arrhythmic	2	0	2
Cardiac: Ischemic	1	0	1
Cardiac: Pump failure	4	0	4
Noncardiac	2	0	2
Not Yet Classified*	2	0	2
Total Deaths	11	0	11

*Deaths not yet classified by the Events Committee

POTENTIAL ADVERSE EVENTS

- Acceleration of arrhythmias
- Air embolism
- Allergic reaction
- Bleeding
- Cardiac tamponade
- Chronic nerve damage
- Complications due to prolonged procedure time (e.g. hypotension, physical trauma)
- Conductor coil fracture
- Death
- Early, recurrent atrial fibrillation
- Electrolyte imbalance/dehydration
- Elevated pacing thresholds
- Erosion/extrusion
- Extracardiac stimulation (e.g., phrenic, diaphragm, chest wall)
- Fibrotic tissue formation (e.g., keloid formation)
- Fluid accumulation
- Formation of hematomas or cysts
- Heart block
- Lead displacement/dislodgment
- Lead fracture
- Lead insulation breakage or abrasion
- Lead tip deformation and/or breakage
- Local tissue reaction
- Muscle and nerve stimulation
- Myocardial infarction
- Myocardial necrosis
- Myocardial trauma (e.g., cardiac perforation, irritability, injury)
- Myopotential sensing
- Oversensing/undersensing
- Pacemaker-mediated tachycardia
- Pericardial rub, effusion
- Pneumothorax
- Pulse generator migration
- Random component failures
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Thrombosis/thromboemboli

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- Inability to defibrillate
 - Inappropriate therapy (e.g. shocks, ATP, pacing)
 - Incisional pain
 - Incomplete lead connections with pulse generator
 - Infection
 - Valve damage
 - Venous occlusion
 - Venous trauma (e.g. perforation, dissection, erosion)
 - Worsening heart failure

Patient susceptible to frequent shocks despite antiarrhythmic medical management may develop psychologic intolerance to an implantable 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

In addition to the implantation of an ICD system, potential adverse events associated with implantation of a coronary venous lead system are listed below in alphabetical order:

- Allergic reaction to contrast media
- Breakage/failure of implant tools
- Coronary venous occlusion
- Coronary venous trauma (e.g. perforation, dissection, erosion)
- Prolonged exposure to fluoroscopic radiation
- Renal failure from contrast media used to visualize coronary veins

X. SUMMARY OF PRE-CLINICAL STUDIES

Guidant conducted the following bench testing (i.e., components, assemblies, device system and software tests), biocompatibility evaluation, sterilization validation, and animal studies to support safety and effectiveness of the CONTAK RENEWAL 3 AVT System. Testing was performed using CONTAK RENEWAL 3 AVT and CONTAK RENEWAL 3 (P010012/S029, approved 8/11/2004), the device upon which CONTAK RENEWAL 3 AVT was based. These studies were performed in accordance with established national and international industry standards such as ANSI/AAMI PC69:2000; ISO 5841-3: 1992(E); ISO 11318:1993(E); prEN45502 Active Implantable Medical Devices, Part 2-1 (Requirements for active implantable medical devices intended to treat bradyarrhythmia), (draft) November 1996; and the Association for the Advancement of Medical Instrumentation (AAMI) Pacemaker Standard, August 1975; or Guidant's product specification. The test results demonstrated that the CONTAK RENEWAL 3 AVT device met the requirements set by these standards (sections that apply, as outlined in the following tables), and Guidant's specifications.

1. DESIGN VERIFICATION TESTING (DVT)

The design verification testing supporting the RENEWAL 3 AVT pulse generator included component, electronic and mechanical tests (including packaging and shipping), electromagnetic compatibility evaluation, battery capacity test, pulse generator software design verification and programmer software application tests. The testing performed focused on evaluating the modifications that were necessary to create CONTAK RENEWAL 3 AVT relative to CONTAK RENEWAL 3 at the time that this PMA supplement was filed. The following tables provide brief descriptions of the verification tests conducted using CONTAK RENEWAL 3 AVT.

2. COMPONENT TESTING

Most of the components used in the CONTAK RENEWAL 3 AVT pulse generator are the identical components used in CONTAK RENEWAL 3 pulse generators, and were verified for pulse generator use in P010012/S008 at the time this PMA supplement was filed. The following additional components for the CONTAK RENEWAL 3 AVT were tested and passed and reviewed in this supplement.

Table 3: Component Testing

Summary of Component Testing	Sample Size	Test Results (Pass/Fail)
<p>X-ray ID in Header: Verified the correct X-ray ID tag was installed in headers. Headers were qualified by similarity to existing pulse generator headers.</p>	1	Pass
<p>Magnetic Switch: Demonstrated the supplier is capable of producing magnetic switch components that conform to specifications. Testing included the following tests:</p> <ul style="list-style-type: none"> • Visual inspection verified materials, design, construction and workmanship meet industry standards and design requirements • Dimensional inspection verified dimensions (length, width, height, tab width, inter-tab spacing) met specification • Initial Electrical test verified contact resistance, operate field strength, release field strength and alternate release field strength • Activation Cycles test verified electrical requirements are met after operation of the switch. • Production Solder and Clean test verified component meets production requirements • Thermal Shock test verified electrical requirements are met after alternating hot and cold cycles per MIL-STD-883, method 1010.8 • 85/85 Moisture Test verified electrical requirements are met after exposure to humidity chamber • Contact Sticking test verified electrical requirements are met after applying a voltage load at elevated temperature (37 C). • Destructive Physical Analysis verified design and construction of the components are consistent with supplier's specifications • Residual Magnetism test verified operate and release field strengths met requirements after holding switch under magnetic field <p>Shock and vibrations tests verified the component could withstand 4000G (shock) and 30G swept sine wave (vibration)</p>	77	Pass
<p>PEEK Tubing: Demonstrated the supplier is capable of producing PEEK tubing components that conform to specifications. Testing included the following tests:</p> <ul style="list-style-type: none"> • Visual inspection verified color of tubing and supplier certification lists correct material. • Dimensional inspection verified dimensions met specification • Pyrogenicity/Cytotoxicity tests verified absence of pyrogens and leachable toxic compounds <p>Hi-Voltage Breakdown verified tubing met minimum insulation breakdown voltage: leakage current less than 150 microamps with 1500 VAC applied</p>	69	Pass

2.1 BATTERY RESERVE CAPACITY TEST

A Battery Reserve Capacity Test was performed for the CONTAK RENEWAL 3 AVT to establish the reserve capacity between ERI (Elective Replacement Indicator) and EOL

(End Of Life) when used with the pulse generator's electronics. The test confirmed the requirement specifications were met, as described below.

Table 4: Battery Reserve Capacity Testing

Summary of Battery Capacity Testing	Sample Size	Test Results (Pass/Fail)
The Battery Reserve Capacity Test used a set of calculations, with data provided by the battery manufacturer and data measured in Guidant's laboratory, to calculate usable battery capacity. The calculated reserve capacity between ERI (Elective Replacement Indicator) and EOL (End Of Life) exceeded the amount necessary to support 10 maximum energy charges and 3 months of DDDR biventricular pacing at nominal settings.	3	Pass

2.2 ELECTROMAGNETIC COMPATIBILITY (EMC) EVALUATION

EMC testing performed previously for CONTAK RENEWAL 3 (P010012/S008) applied to CONTAK RENEWAL 3 AVT and did not require repeating.

2.3 ELECTRONIC AND MECHANICAL DESIGN VERIFICATION AND ANALYSIS TESTING

Pulse Generator Electronic and Mechanical Design Verification and Analysis Testing was performed. The RENEWAL 3 AVT was tested for functionality impacted by the new or modified features relative to CONTAK RENEWAL 3. The device met electronic and mechanical design specifications.

Table 5: Electronic and Mechanical Testing

Summary of Pulse Generator (PG) Design Testing	Sample Size	Test Results (Pass/Fail)
Electronic Design Testing		
<p>Tests were conducted in the following functional areas:</p> <ul style="list-style-type: none"> • Telemetry Distance test verified communication between PG and PARTNER™ Patient Activator within a specified distance (dependent on orientation of PG). • Atrial amplifier test sensitivity verified sensitivity after V sense and V pace is within a specified range. • Monophasic and Biphasic shock tests verified the delivered energy for each programmable (monophasic or biphasic) shock energy met a specified range, and the ratio between the peak voltage and the termination voltage met a specified range. • Watchdog Fault Detection test verified firmware notification on a watchdog time-out, generation of a fault and a non-maskable interrupt on a watchdog time-out, and verified the watchdog timeout interval met a specified range. • Magnetic switch performance in terms of switch actuation distances and voltage and appropriate switch response under electrical and mechanical influences • PEEK tubing component qualification (refer to Table 3) demonstrated PG electrical requirements were met. 	1-9	Pass
Mechanical Design Testing		
<p>Tests were conducted to verify:</p> <ul style="list-style-type: none"> • The modified X-Ray ID and pulse generator case markings are present, legible and permanent. • The new magnetic switch (in the PG) is actuated by a 90 Gauss magnet at the required distance (3 cm – 10 cm) and is deactuated when the magnet is removed. • The PG manufactured with the new magnetic switch passes the manufacturing electrical test after exposure to mechanical shock, vibration, thermal shock altitude and pressurization. 	1-6	Pass
<p>The following tests and analyses were conducted to demonstrate reliability of the PEEK tubing material as insulation for feed-through wires (high and low voltage) in pulse generator applications:</p> <ul style="list-style-type: none"> • Resistance to hydrolysis and implant environment demonstrated through the company's component testing and device testing as well as published test results referenced from the literature. • Tubing creep performance was predicted by finite element analysis and experimentally measured. The minimum tubing thickness needed to maintain required dielectric strength was met. • Resistance to stress-related cracking at room temperature (dry) and at elevated temperatures (wet) demonstrated through component testing. 	5-10	Pass

2.4 Pulse Generator Software Design Verification Test

Table 6: Pulse Generator Software Design Verification Test

Summary of Pulse Generator Software Design Verification Test:	Sample Size	Test Results (Pass/Fail)
Using an automated test system, the testing verified the proper operation and interaction of the various tasks to be executed by the software (according to the test requirements specification) and to ensure proper function, timing, and data exchange. The firmware version number is 1.1.00 with Patch A.	PG Software	Pass

2.5 PROGRAMMER SOFTWARE APPLICATION DESIGN VERIFICATION TEST

Table 7: Model 2893 Software Application DVT

Summary of Model 2893 Software Application DVT	Sample Size	Test Results (Pass/Fail)
Testing includes the functional software requirements associated with each window/feature. The software version number is Version 3.01 for use with the Model 3120 PRM.	PRM Software	Pass

2.6 PARTNER (PCTA) SYSTEM DESIGN VERIFICATION

Table 8: PARTNER Design Verification Test

Summary of Model 2930 PARTNER DVT	Sample Size	Test Results (Pass/Fail)
<p>PCTA System Design verification was performed to ensure that the PARTNER™ Rhythm Assistant with the Programmer 2893 application and the RENEWAL 3 AVT device met requirements, as follows:</p> <ul style="list-style-type: none">• Pressing the Therapy or Inquire Buttons results in appropriate audible message• Telemetry transmission is attempted for specified time period /specified frequency if there is no communication with a PG after an “Inquire” or “Therapy” button press• Pressing and holding or pressing and releasing a button starts the corresponding command.• All commands from the PCTA to the PG are terminated with the “initiate daily measurement” PG command if daily measurements are delayed due to PCTA use.• An Egram recording is initiated within the PG and Shock therapy is diverted as specified in PCTA instructions for use.• A visual signal is provided when detecting atrial episodes longer than 48 hours; audible and visual signals are provided when detecting specified PG fault codes.• Successful interrogation of PG at specified distances.	1	Pass

3. SYSTEM: DESIGN VALIDATION TESTING

Design validation testing was performed to demonstrate that the CONTAK RENEWAL 3 AVT System conforms to user needs and intended use. Design validation testing included: System Features Validation, Simulated Use Testing, Arrhythmia Scenario Testing, and Animal Studies.

Table 9: System Design Validation Testing

System Design Verification and Validation Testing	Sample Size	Test Results (Pass/Fail)
System Features Tests: Tests were conducted to demonstrate functionality of features. Feature groups tested included device family, programmer support, lead support, atrial & ventricular modes/detection/ therapy, bradycardia modes/therapy, diagnostics, and faults/error handling.	1 system (pulse generator and programmer software)	Pass
Simulated Use Test: From a field user perspective, Guidant evaluated the RENEWAL 3 AVT performance and instructions for use. Clinical scenarios were simulated using the pulse generator, programmer (PRM), PRM software, and a cardiac signal simulator.	1-9	Pass
Arrhythmia Scenario Testing: A standard set of human arrhythmia test waveforms (NSR, AF/SVT combined with various ventricular rhythms, and VF/VT) were injected into a pulse generator. The devices sensed all monomorphic R-waves one-to-one, appropriately detected monomorphic and polymorphic rhythms above the specified rate threshold (VT and VT/VF), detected and classified AF vs SVT, and detected all NSRs.	3	Pass
Animal Study: The study verified that the components of the CRT-D System were compatible and performed safely in an acute <i>in-vivo</i> canine model. Details provided in Section 7.	3 animals	Pass

4. SAFETY AND RISK ANALYSIS

The safety and risk analysis of the RENEWAL 3 AVT system was conducted to identify potential hazards and their causes, and to take appropriate actions to minimize patient and user risk. Analysis included a Hazard Analysis, Failure Modes and Effects Criticality Analysis (FMECA), and Reliability Prediction Analysis (per the “Parts Stress Analysis Prediction” procedure in MIL-HDBK-217F). The safety and risk analysis demonstrated that the residual safety risk associated with the system is acceptable for normal product use. The potential hazards that could result from using the CONTAK RENEWAL 3 AVT system have been identified and documented, the relevance of mitigations for each hazard have been peer reviewed and approved, the results of the hazard analysis have been peer reviewed and approved, and the remaining risks are acceptable when weighed against the intended benefits to the patient.

5. BIOCOMPATIBILITY EVALUATION

The biocompatibility of the tissue contacting materials used in the CONTAK RENEWAL 3 AVT has been established in previous PMA applications (P890061, P910077, P960040,

and P010012). These materials include: polyurethane, titanium, and silicone rubber that are all currently used in Guidant's commercially available implantable cardioverter defibrillator (ICD) devices. There were no new tissue-contacting materials or processes used that would introduce new issues of biocompatibility.

6. STERILIZATION VALIDATION

Sterilization assessment was performed and validated that the CONTAK RENEWAL 3 AVT could be effectively sterilized with the 100% ethylene oxide (EtO) sterilization process. This process is identical to the process used for Guidant's commercially available ICD pulse generators.

7. ANIMAL STUDIES

Guidant conducted an animal study with the CONTAK RENEWAL 3 AVT System in an acute *in vivo* canine model to evaluate the safety and performance of the RENEWAL 3 AVT device. The animal study also addressed the compatibility of the system components. The animal study was performed in accordance with Good Laboratory Practices (GLP) regulations (21 CFR § 58). The study verified that the components were compatible, and the system performed safely as a cardiac rhythm management system. For each animal, the testing was conducted within one day to demonstrate the following system performance:

- Implanted PG was successfully interrogated using the telemetry wand and programmer
- PG status indicators were updated following capacitor reform and battery test
- Lead signals met minimum implant acceptance values for sensing, impedance, and pacing threshold
- System provided good quality surface ECG and Egrams
- QuickCheck was used to obtain thresholds, impedances and P- and R-wave amplitudes
- Bradycardia pacing when LRL > intrinsic rate; no pacing when LRL < intrinsic rate; rate-adaptive pacing up to (but not above) MSR
- EEHF was used to determine programmable settings
- Shock lead integrity test was used to verify electrical integrity
- VF and AF induction methods were used to deliver programmed induction stimuli, sense tachyarrhythmias, and deliver appropriate therapy in the atrium and in the ventricle
- Commanded ATP Delivery, Commanded Atrial ATP, STAT SHOCK, STAT SHOCK Divert, and STAT PACE, and save-to-disk features were demonstrated
- PG demonstrated appropriate DOO pacing during electrocautery and appropriate pacing/sensing after electrocautery was demonstrated
- PCTA features (indicators, therapy delivery and therapy divert) were demonstrated
- System was able to withstand a transthoracic shock

Animal testing was also performed in an *in vivo* rabbit model to demonstrate the biostability of polyetheretherketone (PEEK), in the form of molded test samples, in a long-term implant application. Samples were implanted subcutaneously. Explants taken at 12, 26, and 52 weeks post-implant were tested and results compared to pre-implant

properties to assess potential degradation of PEEK. Results showed no onset of degradation of PEEK when implanted *in vivo* for 52 weeks (12 months). The following tests were conducted: Scanning Electron Microscopy (SEM), tensile strength, Differential Scanning Calorimetry (DSC), Gel Permeation Chromatography (GPC) and Fourier Transform Infrared Spectroscopy (FTIR).

XI. SUMMARY OF CLINICAL STUDIES

1. PRIOR CLINICAL STUDY POPULATIONS

Guidant CRT-Ds, when compared to optimal pharmacological therapy (OPT) alone, have been demonstrated with reasonable assurance, to be safe and effective in significantly reducing: the risk of a composite of all-cause mortality or first hospitalization by 20%, the risk of all-cause mortality by 36%, and heart failure symptoms in patients who have moderate to severe heart failure (NYHA III/IV) including left ventricular dysfunction (EF \leq 35%) and QRS duration \geq 120 ms and remain symptomatic despite stable, optimal heart failure drug therapy, based on the Guidant sponsored COMPANION clinical study – reviewed in P010012/S026, approved 9/14/2004. (Guidant devices were the only devices studied in the COMPANION clinical trial.)

Guidant CRT-Ds have been demonstrated to be safe and effective in ICD-indicated patients who have moderate to severe heart failure (NYHA Class III/IV) including left ventricular dysfunction (EF \leq 35%) and QRS duration \geq 120 ms and remain symptomatic despite stable, optimal heart failure drug therapy, based on the Guidant sponsored CONTAK CD clinical study – reviewed in P010012, approved 5/2/2002. (Guidant devices were the only devices studied in the CONTAK CD clinical trial. The trial demonstrated these devices to be safe and effective in the CONTAK CD population.)

Guidant ICDs have been demonstrated to be safe and effective in patient populations including, but not limited to, those with:

- Prior myocardial infarction and an ejection fraction (EF) $<$ 30%, based on the Guidant sponsored MADIT II clinical study. (Guidant devices were the only devices studied in the MADIT II clinical trial – reviewed in P960040/S026 and P910077/S037, approved 7/18/2002. The trial demonstrated these devices to be safe and effective in the MADIT II population.)
- Prior myocardial infarction, left ventricular ejection fraction of $<$ 35%, and a documented episode of nonsustained ventricular tachycardia (VT), with an inducible ventricular tachyarrhythmia, based on the Guidant sponsored MADIT clinical study. (Guidant devices were the only devices studied in the MADIT clinical trial. The trial demonstrated these devices to be safe and effective in the MADIT population.)

2. CLINICAL STUDY SUMMARIES FOR CONTAK RENEWAL 3 AVT

CONTAK RENEWAL 3 AVT Study

The CONTAK RENEWAL 3 AVT trial, a prospective clinical study, was conducted using the CONTAK RENEWAL 3 AVT CRT-D Systems in patients with a history of atrial tachyarrhythmias (AT) and with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction ($EF \leq 35\%$), and QRS duration ≥ 120 ms. This study was designed to demonstrate safety and effectiveness of atrial therapies in a heart failure patient population, to confirm the safety of combining ICD, CRT and atrial therapies, and to confirm the delivery of CRT and ICD therapy in the presence of atrial therapies.

COMPANION Study Retrospective Sub-analysis

The COMPANION study supports safety and effectiveness of Guidant CRT-D devices, like RENEWAL 3 AVT, in patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction ($EF \leq 35\%$), and QRS duration ≥ 120 ms.

Guidant performed a retrospective sub-analysis of patients within the COMPANION study to compare patients with previously reported paroxysmal or persistent atrial arrhythmias (atrial flutter, SVT or AF) prior to enrollment to those patients without a prior history. Physician notation of the arrhythmia on the enrollment/screening case report form was used as the basis for documentation. Patients with chronic AF (does not terminate spontaneously and cannot be terminated with medical intervention) at the time of enrollment were excluded from the COMPANION study and thus are not a part of this analysis. Patients who did not have previously reported atrial arrhythmias (AA) at enrollment, but who developed an AA during the trial were included in the non-AA subgroup. The following outcomes were compared between these two patient subgroups: complication rate, 6 Minute Walk, Peak VO_2 , New York Heart Association classification, and Quality of Life. This retrospective sub-analysis was performed in order to explore whether or not CRT provides observed effectiveness in patients with a history of atrial arrhythmias with no added risk attributable to CRT therapy and AF interaction.

Summary

In summary, two clinical data sets – the CONTAK RENEWAL 3 AVT IDE study in combination with the COMPANION Study retrospective sub-analysis – provide the clinical data that was evaluated to support safety and effectiveness of the CONTAK RENEWAL 3 AVT CRT-D device in a patient population with heart failure and a history of atrial arrhythmias. A description of the results, analyses, and conclusions for these study components are provided in greater detail below.

3. CONTAK RENEWAL 3 AVT IDE STUDY

A. STUDY DESIGN

This clinical investigation was a 170 patient prospective, multi-center, single-arm study at 38 centers in the United States. One hundred sixty eight (168) patients underwent a procedure to receive the CONTAK RENEWAL 3 AVT or CONTAK RENEWAL 3 AVT HE device and the EASYTRAK/EASYTRAK 2 pace/sense lead. Patients underwent an evaluation of the investigational system at implant, pre-discharge, one month, three months, and quarterly thereafter. Patients were programmed to a biventricular pacing mode during the three-month study period post-implant. The programmed atrial and ventricular tachyarrhythmia device therapy was left to the discretion of the investigator.

Evaluation of the EASYTRAK 2 lead, consisting of measurement of left ventricular pacing thresholds, left ventricular lead impedances, and left ventricular R-wave amplitudes, was performed at each scheduled visit.

1. Inclusion Criteria

Patients enrolled in the study were required to meet the following inclusion criteria:

- Meet all device indications and contraindications (LVEF and QRS must be documented within 90 days prior to enrollment. NYHA must be documented at time of enrollment.)
- Willing and capable of providing informed consent, undergoing a device implant, participating in all testing associated with this clinical investigation at an approved clinical investigational center and at the intervals defined by this protocol
- Prescribed to stable optimal pharmacologic therapy for heart failure as defined below:
 - Beta Blockers: All patients must be prescribed to beta blockers for 90 days prior to enrollment, and on a stable dose (e.g., no greater than a 50% increase or decrease in dosage) for the 30 days prior to enrollment unless the patient is not indicated, is contraindicated, is intolerant, or has developed a recent ICD indication that necessitates ICD therapy concurrent with the optimization of beta blocker therapy. The choice of selective or non-selective beta-blocker use is left to the investigator's discretion.
 - Angiotensin Converting Enzyme (ACE) Inhibitors: All patients must be prescribed to stable ACE inhibitor therapy for 30 days or angiotensin receptor blocker (ARB) unless the patient is not indicated, contraindicated, is intolerant, or has developed a recent ICD indication that necessitates ICD therapy concurrent with the optimization of ACE inhibitor therapy.
- Creatinine < 2.5 mg/dL obtained no more than two weeks prior to enrollment
- Age 18 or above, or of legal age to give informed consent specific to state and national law
- Geographically stable residents who are available for follow-up

-
- Able to provide documented** evidence of one or more episodes of AF/AT within 12 months of implantation

** Source documentation includes but is not limited to one or more of the following: 12-lead ECG, telemetered rhythm strips, Holter and event monitor recordings, physician reports, and/or medical records/progress notes.

Note: Guidant recommends anticoagulation therapy per physician discretion.

2. Exclusion Criteria

Patients were excluded from the investigation if they met any of the following criteria:

- Have a preexisting non-Guidant left ventricular lead
- Have a preexisting unipolar pacemaker that will not be explanted/abandoned
- Documented life expectancy of less than six months or expected to undergo heart transplant within the next six months
- Have an atrial tachyarrhythmia that is permanent (i.e., does not terminate spontaneously and cannot be terminated with medical intervention) within 180 days prior to enrollment
- Have a known hypersensitivity to a 0.7 mg dose of dexamethasone acetate
- Have surgically uncorrected primary valvular heart disease
- Currently requiring hemo-dialysis
- Have had a myocardial infarct, unstable angina, percutaneous coronary intervention, or coronary artery bypass graft during the preceding 30 days prior to enrollment
- Have hypertrophic obstructive cardiomyopathy or infiltrative cardiomyopathy (e.g., amyloidosis, sarcoidosis)
- Have a mechanical tricuspid heart valve
- Enrolled in any concurrent study, without Guidant written approval, that may confound the results of this study
- A Cerebral Vascular Event/Transient Ischemic Attack within 12 months of implantation
- During the four weeks prior to implantation, a patient experiences an episode of AF \geq 48 hours in duration and was not anticoagulated at an adequate therapeutic level for the 4 weeks prior to enrollment with an INR = 2.0-3.0 at enrollment

Note: If above criteria is not met or adequate documentation on anticoagulation does not exist, then the patient may be included if a routine transesophageal echocardiogram (TEE) is negative for intracavitary "smoke" or thrombus at the time of implant.

- Women who are pregnant or plan to become pregnant

Note: Women of childbearing potential must have a negative pregnancy test within 7 days of enrollment.

3. Follow-Up Schedule

Enrollment: Initial assessment of patient eligibility; patient history

Implant: Implant of investigation device and acute device testing

Routine Follow-up: Routine evaluation of device function and patient condition at pre-discharge, one-month, three-month

Quarterly Visits: After the 3-month follow-up patients were seen for routine evaluation of device function and patient condition

4. Endpoints

The RENEWAL 3 AVT clinical study consisted of:

4.1 Primary Endpoints

- Safety Endpoint: System Complication-Free Rate

Objective: To show that the RENEWAL 3 AVT system functions safely

- Effectiveness Endpoint: Atrial Fibrillation Shock Conversion Rate

Objective: To demonstrate the effective termination of induced episodes of atrial fibrillation by cardioversion

- Effectiveness Endpoint: Appropriate Detection and Classification of Atrial Arrhythmias

Objective: To correctly detect and classify atrial arrhythmias (AF and/or SVT) from all other rhythms

4.2 Secondary Endpoints

- Safety Endpoint: Ventricular Fibrillation (VF) Detection Time

Objective: To confirm normal ICD sensing and detection in the presence of atrial therapies

- Safety Endpoint: Percent Biventricular (BiV) Pacing

Objective: To confirm CRT pacing is delivered in the presence of atrial therapies

- Safety Endpoint: Rate of Inappropriate Response to BiV Trigger Feature

Objective: To confirm BiV Trigger does not induce ventricular arrhythmias

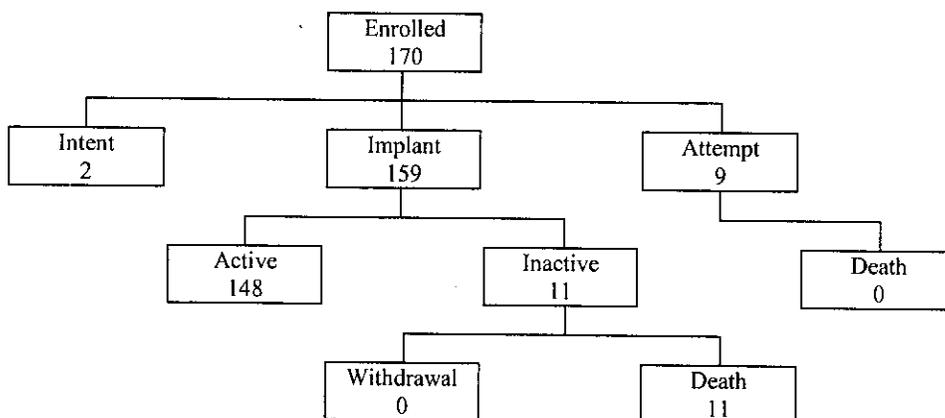
- Safety Endpoint: EASYTRAK 2 Lead Complication-Free Rate

Objective: To show that the EASYTRAK 2 lead functions safely

Note that during the course of the RENEWAL 3 AVT trial, the EASYTRAK 2 Coronary Venous pace/sense lead was established as safe and effective in a separate clinical study and was approved for commercial distribution (P010012/S024, 8/6/04). Refer to the commercially available EASYTRAK 2 Coronary Venous pace/sense lead labeling for clinical safety and performance characteristics.

B. STUDY RESULTS

1. Patient Accountability



2. Patient Characteristics

Table 10: Characteristics of Patient Population

Characteristic	Measurement	Result
Age at Implant (years)	N	168
	Mean ± SD	70.7 ± 10.3
	Range	40.8 - 87.6
Gender [N (%)]	Male	142 (85)
	Female	26 (15)

Characteristic	Measurement	Result
NYHA Class [N (%)]	III	147 (88)
	IV	21 (12)
LVEF (%)	N	168
	Mean ± SD	22.6 ± 6.4
	Range	10.0 - 35.0
QRS Duration (ms)	N	167
	Mean ± SD	150 ± 25
	Range	120 - 237
Concomitant Medications* [N (%)]	ACE Inhibitor or ARB	129 (77)
	Aldosterone Antagonist	59 (35)
	Anticoagulant	150 (90)
	Beta Blocker	111 (66)
	Loop Diuretic	149 (89)
Etiology [N (%)]	Ischemic	131 (78)
	Nonischemic	37 (22)
Conduction Disorder [N (%)]	Left Bundle Branch Block	107 (64)
	Nonspecific Intraventricular Delay	34 (20)
	Right Bundle Branch Block	27 (16)
Primary Tachy Arrhythmia [N (%)]	Monomorphic VT (MVT)	44 (26)
	Nonsustained VT with inducible MVT	24 (14)
	Ventricular Fibrillation (VF)	18 (11)
	Inducible VT	9 (5)
	Non-sustained VT	7 (4)
	Ventricular Tachycardia (VT)	3 (2)
	Polymorphic VT (PVT)	2 (1)
	Other	2 (1)
	None‡	59 (35)
Primary Atrial Arrhythmia [N (%)]	Atrial Fibrillation (AF)	120 (71)
	Atrial Flutter	21 (13)
	Paroxysmal Atrial Fibrillation	10 (6)
	Paroxysmal Atrial Tachycardia (PAT)	10 (6)
	PSVT	5 (3)
	Other	2 (1)

* Patients may appear more than once.

‡ Patients without a primary tachyarrhythmia had the following indications: MADIT II and/or HF

3. Primary Endpoints

3.1 Primary Safety Endpoint 1: System-Related Complication-Free Rate

The safety of the investigational system was assessed by the system related complication-free rate observed in the period between implant and the three-month follow-up visit in all patients attempted or implanted with a RENEWAL 3 AVT system.

The system related complication free rate at three months was 85.1% with a lower 95% confidence bound of 79.8%. These data met the primary safety endpoint – system related complication-free rate of greater than 70% – and demonstrate device safety of the RENEWAL 3 AVT system.

Table 11: System Related Complications

Complication	Number of Events	Number of Patients	Complication Free Rate	Lower One-Sided 95% Confidence Bound
LV Lead	10	10	94.0	90.1
EASYTRAK 2 Lead	8	8	95.2	91.6
EASYTRAK Lead	2	2	98.8	96.3
PG	4	4	97.6	94.6
Procedure	12	11	93.5	89.4
Total	26	25	85.1	79.8

An additional analysis using the Kaplan-Meier method was performed with results demonstrating a 3-month event free rate of 85.7% with a lower confidence bound of 81.1%. This bound is similar to that resulting from the straight rate and is still above the acceptance criterion.

Figure 1 demonstrates the time to first system related complication using a Kaplan-Meier analysis and details are provided in Table 12.

Figure 1: Time to System Related Complications

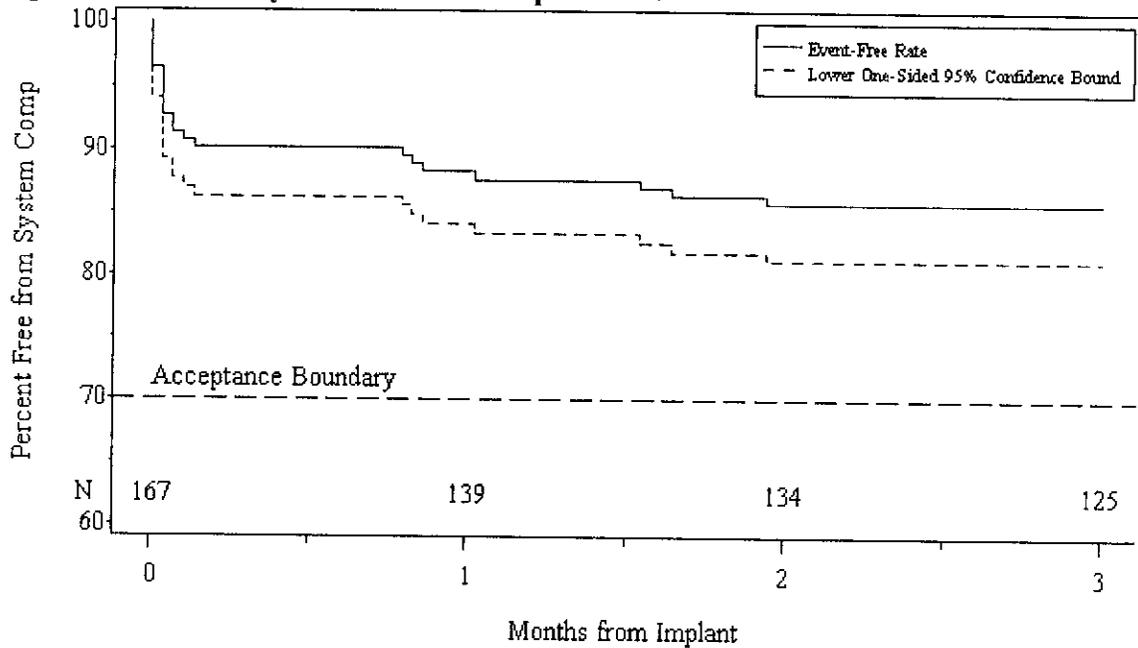


Table 12: Details for Time to System Related Complications

Statistic	Start of Interval (Months from Implant)			
	0	1	2	3
Number at Risk at Start of Interval	167	139	134	125
Number of Events in Interval	19	4	0	0
Cumulative Number of Events	19	23	23	23
Number Censored in Interval	9	1	9	125
Cumulative Number Censored	9	10	19	144
% Freedom from Event	100.0	88.2	85.7	85.7
Lower One-Sided 95% Confidence Limit	100.0	84.0	81.1	81.1

3.2 Primary Effectiveness Endpoint 1: AF Shock Conversion Rate

AF Shock Conversion Rate was calculated from induced and spontaneous episodes classified as AF that received verifiable shock therapy and compared to conversion rates for conventional pharmacological options and other commercially available devices.

A total of 152 AF episodes had verifiable conversion data of which 138 were successfully converted, for an AF Shock Conversion Rate of 90.8%. The RENEWAL 3 AVT AF Shock Conversion Rate met the pre-specified and agreed upon performance criteria of greater than 60% ($p < 0.001$). An additional generalized estimating equations (GEE) analysis to account for the correlation due to multiple episodes per patient produced an adjusted rate of 91.3% with a 95% confidence interval of (85.2, 95.0). Table 13 contains

details of AF Shock Conversion Rate, First Shock Conversion Rate and Clinical Conversion Rate (defined as sinus rhythm two minutes post shock, induced episodes only) for all AF episodes. Separate device conversion efficacies are also shown for induced and spontaneous AF episodes.

Table 13: Atrial Fibrillation Shock Conversion

	AF Episodes (N)	Successful Conversions (N)	Conversion Rate
AF Shock Conversion Rate - All AF Episodes	152	138	91%
AF Shock Conversion Rate - Induced	140	127	91%
AF Shock Conversion Rate - Spontaneous	12	11	92%
First Shock Conversion Rate	152	118	78%
Clinical Conversion Rate - Induced	140	121	86%

3.2 Primary *Effectiveness Endpoint 2: Appropriate Detection and Classification of Atrial Arrhythmias*

Appropriate Detection and Classification of Atrial Arrhythmias is measured by sensitivity, defined as the number of atrial arrhythmias identified by the device divided by the total number of documented atrial arrhythmias. Any sustained atrial episode not detected, or incorrectly classified by the device, was counted against this endpoint.

A total of 184 episodes of the 188 induced atrial episodes in 133 patients were appropriately detected and classified resulting in a sensitivity of 97.9%. Three patients had 4 episodes that were not detected as AF/AT due to P-wave undersensing related to the patient's underlying medical condition. The sensitivity of RENEWAL 3 AVT met the pre-specified and agreed upon criteria of greater than 83% ($p < 0.001$). An additional GEE analysis to account for the correlation due to multiple episodes per patient produced an adjusted sensitivity of 97.8% with a 95% confidence interval of (93.5, 99.2). The RENEWAL 3 AVT device is effective at discriminating atrial arrhythmias from all other rhythms. The Appropriate Detection and Classification endpoint was met.

4. Secondary Endpoints

4.1 *Secondary Safety Endpoint: VF Detection Time*

VF detection time was evaluated with the typical CRT/ICD features and the addition of the RENEWAL 3 AVT atrial features (Atrial Shocks, Atrial ATP, ARC, APP, Post A Therapy APP, and ProACT) enabled. Ventricular Fibrillation Detection Time was defined as the interval starting from 250 ms after the last induction artifact (the time of the post induction ventricular refractory period) and ending at the "V-Episode Declared" marker on real-time electrograms. A mean VF detection time was calculated for each patient.

A total of 150 patients had successful VF inductions at implant. The atrial features (Atrial Shocks, Atrial ATP, ARC, APP, Post Atrial APP, and ProACT) were required to

be programmed ON. Average VF detection time with all features ON was 2.5 ± 0.6 seconds. The RENEWAL 3 AVT VF detection time met the pre-specified and agreed upon performance criteria of less than 4.1 seconds based on the CONTAK CD study. The results for VF detection time are shown in Table 14.

Table 14: VF Detection Time

Number of Patients	Mean	SD	p-value*
150	2.5	0.6	<0.001

*p-value determined using a one sample t-test

4.2 Secondary Safety Endpoint: Percent Biventricular Pacing

The safety of CRT therapy provided by the investigational system was assessed by the percent of time a patient is appropriately paced, as recorded by the device counter, at the three-month visit. The appropriateness of CRT delivery was defined by whether the device delivered CRT in accordance with the physician's programming. The objective of this endpoint was to demonstrate that patients receive continuous appropriate pacing from the device during activities of daily living. For each patient, the value for percent of time LV paced as recorded by the device counter was collected at the 3-month follow-up.

As shown in Table 15, the mean percentage of appropriately paced beats during activities of daily living was 95.8 ± 7.1 with a median of 98.0, which meets the pre-specified and agreed upon performance criteria of 85%. These data demonstrate device safety of the RENEWAL 3 AVT in providing continuous appropriate CRT during activities of daily living.

Table 15: Percent BiV Pacing

Number of Patients	Mean +/- SD	Range	Median	p-value*
132	95.8 ± 7.1	33 - 100	98	<0.001

*p-value calculated from a signed-rank test.

4.3 Secondary Safety Endpoint: Rate of Inappropriate Response to BiV Trigger Feature

Biventricular (BiV) Trigger was designed to promote synchronized right and left ventricular contractions by pacing the right and left ventricle immediately after a sensed right ventricular event. The BiV Trigger feature was evaluated in all patients by the investigator at each follow-up visit by reviewing the VT/VF episodes to determine whether any events were associated with a BiV trigger pace. A VT/VF episode was considered associated with BiV Trigger if the first beat of the event onset was immediately preceded by a BiV Trigger pace marker.

The acceptance criterion for this secondary endpoint was defined as a response rate of zero (0). The failure criterion for this endpoint is defined as one or more incidences of inappropriate response.

There were no VT/VF episodes caused by BiV Trigger in the 432 VT/VF episodes from 71 patients reviewed by the investigators. The BiV Trigger feature is safe and is not proarrhythmic.

5. Ancillary Data Analysis

5.1 Concomitant Arrhythmia Testing

To determine the ability of the RENEWAL 3 AVT device to discriminate between atrial and ventricular arrhythmias, patients were also induced into AF plus VT/VF. There were 114 successful inductions of AF plus VF/VT at implant. All ventricular episodes were appropriately declared by the device.

The addition of atrial features and therapies (Atrial Shocks, Atrial ATP, ARC, APP, Post A Therapy APP, and ProAct) had no effect on the ability of the RENEWAL 3 AVT device to successfully detect ventricular fibrillation demonstrating that the RENEWAL 3 AVT device is safe and effective in the detection of ventricular fibrillation.

5.2 Spontaneous Ventricular Episodes

A total of 1049 spontaneous ventricular episodes were recorded during the clinical investigation in 49 patients. Seventy-five (75) episodes received therapy (ATP and/or shocks). The remainder of spontaneous ventricular episodes were non-sustained. The breakdown of classification of episodes receiving therapy can be found in Table 16.

Table 16: Spontaneous Ventricular Episodes Receiving Therapy

Ventricular Episode Classification	N	%
VF Episodes	4	5.3
VT Episodes	68	90.7
Other	3	4.0
Total	75	100.0

Of the 4 spontaneous VF episodes, all received shock therapy and were successfully converted with the device, giving a VF shock conversion rate of 100%. VF and VT shock conversion efficacies are shown in Table 17.

Table 17: Spontaneous Episode Shock Conversion Efficacy

Ventricular Episode Classification	Number of Episodes Receiving Shock Therapy	Number of Successful Conversions	Conversion Rate
VF Episodes	4	4	100%
VT Episodes	24	24	100%

5.3 Atrial ATP Conversions of SVT

Successful conversion of an SVT (non-AF) episode is defined by conversion to one of the following: sinus rhythm, sinus tachycardia, or atrial pacing within one-minute post therapy delivery.^{1,2}

Forty-one (41) patients experienced 1104 episodes of SVT (8 induced, 1096 spontaneous). Conversion efficacy at one minute was 65.7% (725/1104). The GEE adjusted rate at one minute was 56.8%.

SVT was terminated with ATP 65.7% of the time.

5.4 Expert Ease for Heart Failure +

Expert Ease for Heart Failure + (EEHF+) is designed to provide suggested settings for programming the device for CRT in a manual and automatic mode. EEHF+ evaluates right and left ventricular response to both atrial sensed and atrial paced events to determine suggested settings for the AV Delay, Sensed AV Offset, and Ventricular Pacing Chamber.

This data shows that out of 112 eligible EEHF+ uses, the EEHF+ recommended AV delay was programmed in the RENEWAL 3 AVT device by the physician 88 times (79%). There were no adverse events related to the use of EEHF+.

C. CONTAK RENEWAL 3 AVT STUDY CONCLUSIONS

1. Safety

The adverse event rate was well within acceptable limits. The lower one-sided confidence bound was 79.8%, which met the primary safety endpoint of greater than 70%. The safety performance of the CONTAK RENEWAL 3 AVT System compares favorably with the safety performance observed with other commercially available CRT-D devices.

2. Effectiveness

The atrial shock therapy conversion rate for CONTAK RENEWAL 3 AVT was compared to the conversion rate associated with conventional pharmacological options and other commercially available devices in converting AF using shock and met the pre-specified performance criteria of greater than 60%. AF can be safely and effectively terminated with atrial shocks in patients with heart failure. Additionally, the RENEWAL 3 AVT device is effective at discriminating atrial arrhythmias from all other rhythms.

4. COMPANION RETROSPECTIVE SUB-ANALYSIS

Guidant conducted a retrospective analysis of the COMPANION trial to explore the safety and effectiveness of CRT therapy in heart failure patients with a history of paroxysmal or persistent atrial arrhythmias (HF-AA patients). The COMPANION CRT-

D and CRT-P randomized groups have been combined into a “CRT” group, except in the mortality analysis. This CRT group and the OPT group were then sub-divided into atrial arrhythmia (AA) and no-AA groups. As a result of this stratification, the following four sub-groups were utilized in the analysis:

- CRT-AA: HF-AA patients who received OPT and CRT during the therapy period
- CRT-no AA: HF patients without AA who received OPT and CRT
- OPT-AA: HF-AA patients who received OPT only
- OPT-no AA: HF patients without AA who received OPT only

A. ANALYSES PERFORMED

1. Effectiveness Analysis

The COMPANION trial collected data for multiple effectiveness variables as part of the secondary endpoints and this retrospective sub-analysis utilizes this data to demonstrate the effectiveness of the therapy.

Peak VO₂ – A Peak VO₂ improvement of 1.0 mL/kg/min is clinically meaningful.^{3,4,5}

Six Minute Walk – A 25 meter improvement is clinically meaningful.^{6,7,8}

Quality of Life Questionnaire (QOL)⁹ - A 5-point reduction is clinically meaningful.

NYHA Class – A one class reduction (e.g., IV to III) is clinically meaningful.

All effectiveness analyses include data for patients who had a baseline value and at least one additional 3 and/or 6 month measurement.

2. Safety Analysis

The measurement of system safety for this retrospective sub-analysis involved analyzing complications.

3. Mortality Analysis

In addition to the analysis of effectiveness variables for HF, a mortality analysis was performed. CRT-D and CRT-P were analyzed separately for mortality. Guidant included the CRT-D portion of this analysis because the RENEWAL 3 AVT device has defibrillator function, which may have an important mortality effect above and beyond CRT-P.

B. RESULTS OF ANALYSES

1. Patient Baseline Characteristics

In total, the COMPANION trial included data from 1,520 patients (1,212 CRT, 308 OPT). Using the criterion for atrial arrhythmia history, 22.1% of the CRT (268/1212) and 23.4% of the OPT (72/308) patients were included in the AA sub-groups. This was

consistent with literature that reported roughly 15%-30% of NYHA Class III/IV patients have atrial arrhythmias.^{10,11,12}

Tables 18 and 19 provide the baseline characteristics for each of the four groups.

Table 18: Baseline Characteristics of the CRT group

Baseline Characteristic		CRT-AA (N=268)	CRT-no AA (N=944)	Total (N=1212)
Age (years)	Mean +/- SD	68.2 +/- 10.1	64.7 +/- 11.7	65.5 +/- 11.5
Gender [N (%)]	Female	56 (20.9)	340 (36.0)	396 (32.7)
	Male	212 (79.1)	604 (64.0)	816 (67.3)
NYHA Class [N (%)]	III	229 (85.4)	820 (86.9)	1049 (86.5)
	IV	39 (14.6)	124 (13.1)	163 (13.5)
Ischemic [N (%)]	Ischemic	172 (64.2)	484 (51.3)	656 (54.1)
	Non-Ischemic	96 (35.8)	460 (48.7)	556 (45.9)
Medications	ACE Inhibitor or Angiotensin II [N (%)]	168 (62.7)	675 (71.5)	843 (69.6)
	Beta Blocker [N (%)]	146 (54.5)	677 (71.7)	823 (67.9)
	Digoxin [N (%)]	194 (72.4)	699 (74.0)	893 (73.7)
	Amiodarone, Sotalol and/or Dofetilide [N (%)]	103 (38.4)	54 (5.7)	157 (13.0)
	History of Valve Disease [N (%)]	24 (9.0)	52 (5.5)	76 (6.3)
	History of Diabetes [N (%)]	102 (38.1)	382 (40.5)	484 (39.9)
	History of Renal Disease [N (%)]	78 (29.1)	191 (20.2)	269 (22.1)
	History of Pulmonary Hypertension [N (%)]	44 (16.4)	140 (14.8)	184 (15.2)
	History of Carotid Artery Disease [N (%)]	34 (12.7)	99 (10.5)	133 (11.0)
LVEF (%)	Mean +/- SD	21.9 +/- 6.9	22.4 +/- 6.8	22.3 +/- 6.8
PR Interval	Mean +/- SD	216 +/- 43	201 +/- 36	204 +/- 37.9
QRS Width	Mean +/- SD	161 +/- 28	159 +/- 23	159 +/- 24.5
Body Mass Index	Mean +/- SD	28 +/- 6	28 +/- 6	28 +/- 6.1

Table 19: Baseline Characteristics of the OPT group

Baseline Characteristic		OPT-AA (N=72)	OPT-no AA (N=236)	Total (N=308)
Age (years)	Mean +/- SD	71.1 +/- 8.2	65.4 +/- 11.0	66.7 +/- 10.7
Gender [N (%)]	Female	19 (26.4)	78 (33.1)	97 (31.5)
	Male	53 (73.6)	158 (66.9)	211 (68.5)
NYHA Class [N (%)]	III	56 (77.8)	197 (83.5)	253 (82.1)
	IV	16 (22.2)	39 (16.5)	55 (17.9)
Ischemic Heart Disease [N (%)]	Ischemic	45 (62.5)	136 (57.6)	181 (58.8)
	Non-Ischemic	27 (37.5)	100 (42.4)	127 (41.2)
Medications	ACE Inhibitor or Angiotensin II [N (%)]	45 (62.5)	167 (70.8)	212 (68.8)
	Beta Blocker [N (%)]	36 (50.0)	168 (71.2)	204 (66.2)
	Digoxin [N (%)]	48 (66.7)	159 (67.4)	207 (67.2)
	Amiodarone, Sotalol and/or Dofetilide [N (%)]	19 (26.4)	8 (3.4)	27 (8.8)
	History of Valve Disease [N (%)]	1 (1.4)	10 (4.2)	11 (3.6)
	History of Diabetes [N (%)]	27 (37.5)	111 (47.0)	138 (44.8)
	History of Renal Disease [N (%)]	19 (26.4)	51 (21.6)	70 (22.7)
	History of Pulmonary Hypertension [N (%)]	12 (16.7)	41 (17.4)	53 (17.2)
	History of Carotid Artery Disease [N (%)]	9 (12.5)	36 (15.3)	45 (14.6)
LVEF (%)	Mean +/- SD	22.3 +/- 6.9	23.0 +/- 7.3	22.8 +/- 7.2
PR Interval	Mean +/- SD	210 +/- 36	199 +/- 34	202 +/- 34.5
QRS Width	Mean +/- SD	160 +/- 24	155 +/- 24	156 +/- 24.3
Body Mass Index	Mean +/- SD	27 +/- 5	29 +/- 6	28.5 +/- 6.2

2. Effectiveness Analysis

2.1 CRT-AA Results – Did patients with a history of AA receive benefit from CRT?

Tables 20 and 21 show the improvement from baseline to six months in Peak VO₂, 6 Minute Walk, QOL, and NYHA class for the CRT-AA subgroup.

Table 20: Baseline to Six-Month Improvement in CRT-AA Subgroup

Measure	Clinically Meaningful Change	N	Mean (95% Confidence Interval)*
Peak VO ₂ (ml/kg/min)	1.0 ml/kg/min	60	0.94 (0.15, 1.72)
6 Minute Walk (m)	25 meters	194	34.3 (20.0, 48.5)
QOL	-5 points	233	-20.9 (-24.1, -17.7)

*Means and confidence intervals calculated using likelihood based mixed model

Table 21: Baseline to Six-Month Improvement in NYHA for the CRT-AA Subgroup

Measure	N	Probability of Improvement (95% CI)*
NYHA	246	54.0 % (36.2, 70.9)

*Probability of improvement and 95% confidence interval calculated using weighted GEE methods

As shown in Table 20 there were clinically meaningful improvements in QOL and 6 Minute Walk for CRT-AA patients. The data suggests that 54% of CRT-AA patients would improve at least one NYHA class through 6 months, as shown in Table 21. The results suggest that heart failure patients with a history of AA received benefit from CRT.

2.2 CRT-AA and OPT-AA Comparison – Among patients with a history of AA, did CRT improve patient outcomes more than OPT alone?

This analysis shows the effect of CRT therapy on baseline to six-month improvement for Peak VO₂, QOL, 6 Minute Walk, and NYHA and compared to OPT alone among AA patients.

Table 22: Baseline to Six Month Improvement: CRT-AA vs. OPT-AA

Measure	CRT-AA		OPT-AA	
	N	Mean (95% CI)*	N	Mean (95% CI)*
Peak VO ₂ (ml/kg/min)	60	0.94 (0.15, 1.72)	11	1.35(-0.45, 3.16)
6 Minute Walk (m)	194	34.3 (20.0, 48.5)	42	9.7 (-20.9, 40.3)
QOL	233	-20.9 (-24.1, -17.7)	55	-13.0 (-19.6, -6.4)

*Means and confidence intervals calculated using likelihood based mixed model

Table 23: NYHA Change for CRT-AA and OPT-AA

Measure	CRT-AA		OPT-AA	
	N	Probability of Improvement (95% CI)*	N	Probability of Improvement (95% CI)*
NYHA	246	54.0 % (36.2, 70.9)	55	51.3 % (28.4, 73.6)

*Probability of improvement and 95% confidence interval calculated using weighted GEE methods

The results suggest that, for patients with a history of AA, CRT improved the patient outcomes of QOL and 6 Minute Walk more than OPT alone. The results do not suggest the same improvement for Peak VO₂ and NYHA.

2.3 CRT-AA and CRT-no AA Comparison – Among patients receiving CRT, did the presence of AA reduce the benefit of CRT?

It is conceivable that atrial arrhythmias could reduce or preclude the benefits of CRT. This analysis provided a comparison of baseline to six-month improvements for CRT-AA versus CRT-no AA patients for Peak VO₂, 6 Minute Walk, QOL, and NYHA.

Table 24: Baseline to Six Month Improvement: CRT-AA vs. CRT-no AA

Measure	CRT-AA		CRT-no AA	
	N	Mean (95% CI)*	N	Mean (95% CI)*
Peak VO ₂ (ml/kg/min)	60	0.94 (0.15, 1.72)	273	1.37 (1.00, 1.73)
6 Minute Walk (m)	194	34.3 (20.0, 48.5)	737	54.0 (46.5, 61.5)
QOL	233	-20.9 (-24.1, -17.7)	843	-25.8 (-27.5, -24.1)

*Means and confidence intervals calculated using likelihood based mixed model

Table 25: NYHA Changes for CRT-AA and CRT-no AA

Measure	CRT-AA		CRT-no AA	
	N	Probability of Improvement (95% CI)*	N	Probability of Improvement (95% CI)*
NYHA	246	54.0 % (36.2, 70.9)	879	60.3 % (43.8, 74.7)

*Probability of improvement and 95% confidence interval calculated using weighted GEE methods

Improvements were seen among patients receiving CRT, however the results suggest the presence of AA may reduce the benefit of CRT.

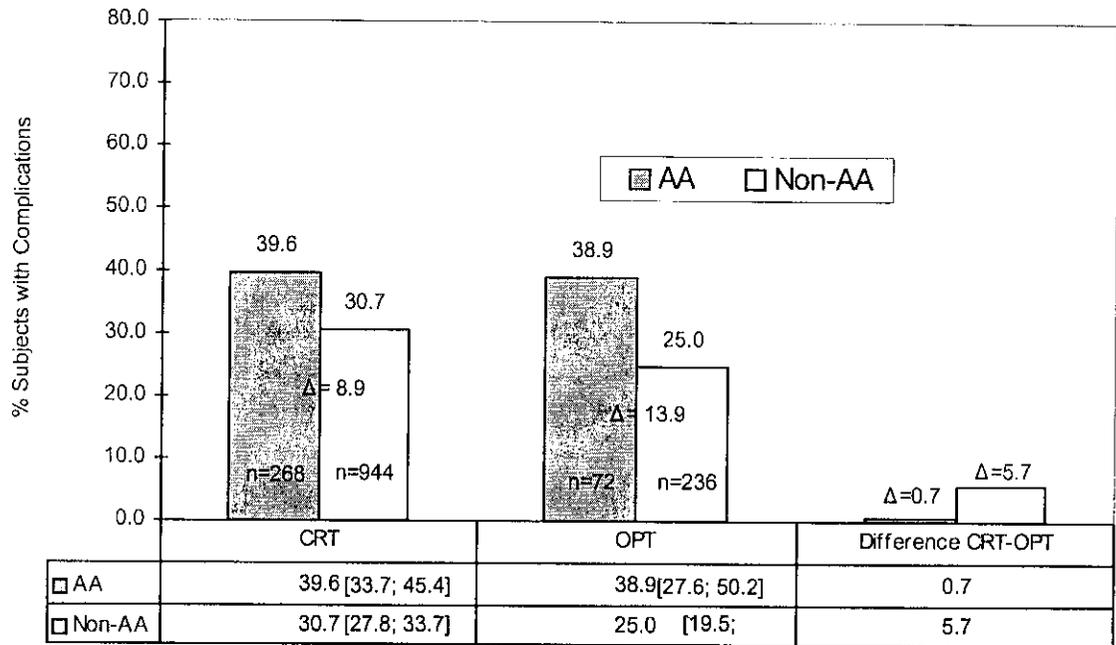
2.4 Effectiveness Analysis Summary

The effectiveness analyses suggest that the improvement within the CRT-AA group was consistent across all measures. These improvements appear to be reduced from CRT-no AA for all measures, but enhanced over OPT-AA for 6 Minute Walk and QOL.

3. Safety Analysis – Among patients with a history of AA, does CRT therapy increase the risk of complications?

Complications of all types, whether of procedural, therapy, patient or device origin, were included. The observed complication rates over a six-month period in the AA and non-AA subgroups are presented in Figure 2 below. The reported rates represent the percentages of patients experiencing at least one complication.

Figure 2: All Type Complications



As shown in Figure 2, the subgroup of patients with AA had a higher rate of complications in both the CRT and OPT populations. However, comparing the difference of CRT-AA to OPT-AA (0.7%) suggests that receiving CRT comes at no observable increase in risk.

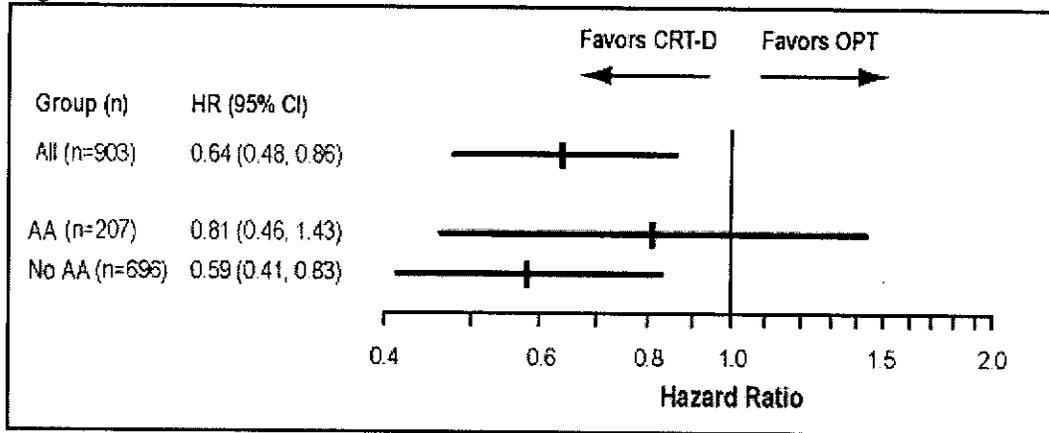
The results suggest that among patients with AA, CRT therapy does not increase the risk of complications compared to those receiving standard OPT therapy.

4. Mortality Analysis – Among patients with a history of AA, does CRT-D provide a mortality benefit?

The analysis compared patients randomized to CRT-D and OPT in the AA population. A prior history of AA was reported in 135/595 (22%) CRT-D patients and 72/308 (23%) OPT patients.

CRT-D patients with a history of AA had a 19% reduction in the risk of all-cause mortality, while those with no history of AA were associated with a 41% reduction in all-cause mortality compared to OPT patients (Figure 3).

Figure 3: Hazard Ratio Table



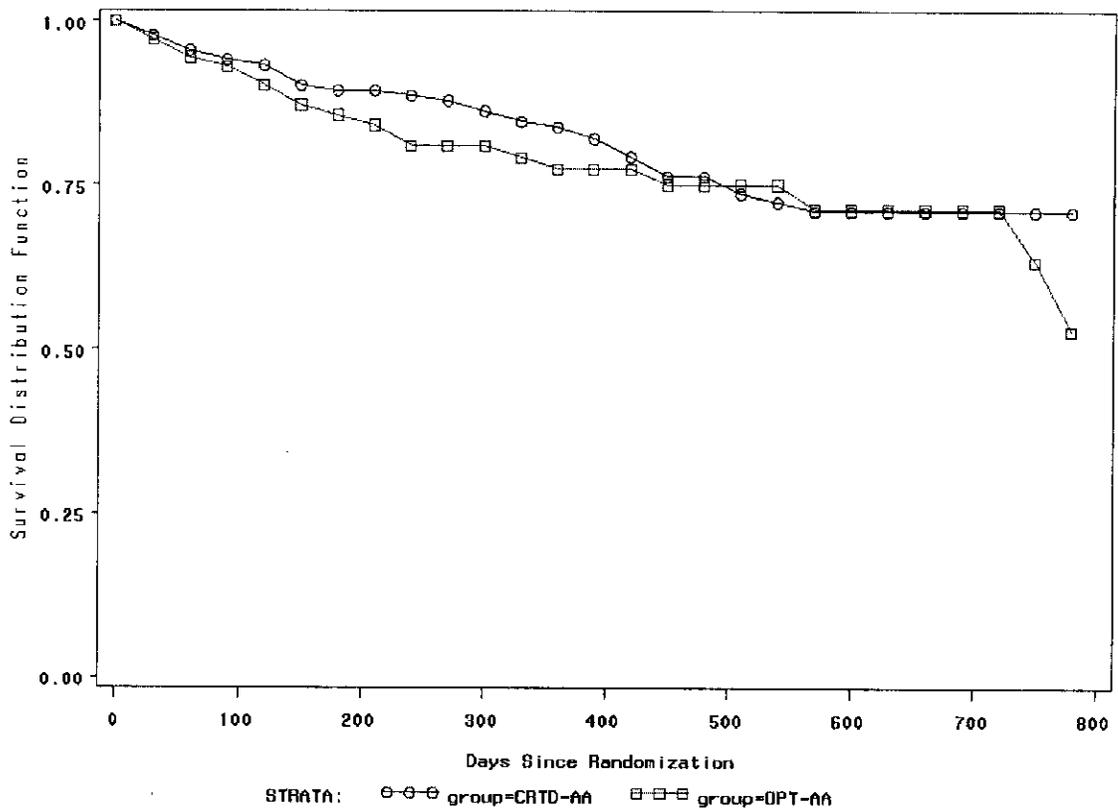
In addition to the hazard ratio, relative risk ratios at 12 months were also calculated with consistent results.

Table 26: Relative Risks at 12 months

Group (N)	% Failure		Absolute Risk Reduction	Relative Risk Reduction
	OPT	CRT-D		
All (n=903)	19.0% (14.8%, 24.2%)	12.1% (9.7%, 15.2%)	6.9%	36.3%
AA (n=207)	22.9% (14.4%, 35.1%)	17.1 (11.6%, 24.8%)	5.8%	25.3%
No AA (n=696)	17.8% (13.2%, 23.8%)	10.6 (8.0%, 14.0%)	7.2%	40.4%

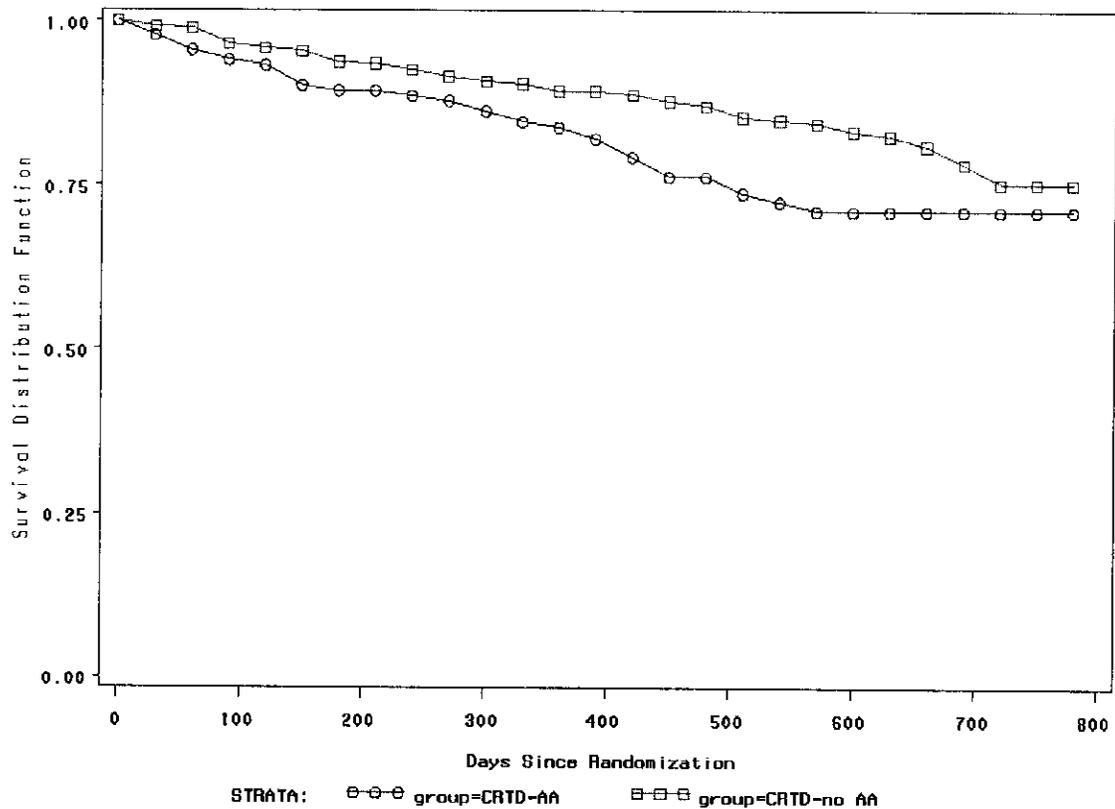
A survival curve is provided for CRT-AA and OPT-AA patients in Figure 4.

Figure 4: Kaplan Meier Survival Curves for CRTD-AA vs. OPT-AA



Additionally, an analysis comparing CRTD-AA and CRTD-no AA suggested that individuals with AA were found to be at greater risk of mortality [hazard ratio = 0.65, 95% CI (0.43, 0.99)]. The result is consistent with recent studies of AA in heart failure.¹³ A survival curve is provided in Figure 5.

Figure 5: Kaplan Meier Survival Curves for CRTD-AA vs. CRTD-no AA



Among patients with a history of AA, there appears to be a mortality benefit associated with CRT-D (Figure 4). However, the observed results suggest that the magnitude of this benefit may be reduced in AA patients (Figure 5).

C. SUMMARY OF COMPANION SUB-ANALYSES

The following summarizes the results of analyses performed to address the relative risks and benefits of CRT use in AA patients.

Risk Conclusion: There was no added risk of complications that appeared to be attributable to CRT use in patients with a history of AA.

Benefits Conclusion: Baseline to six-month improvements were observed in effectiveness variables associated with the use of CRT therapy in AA patients; these improvements were clinically meaningful improvements for 6 Minute Walk and QOL. However, these improvements may be somewhat reduced relative to the improvements observed in patients without atrial arrhythmias.

Risk / Benefit Conclusion: CRT pacing was associated with a benefit in QOL, 6 Minute Walk, NYHA, Peak VO_2 and mortality for HF patients with a history of atrial arrhythmias. Although these benefits may be somewhat reduced relative to HF patients

without atrial arrhythmias, safety analyses suggested that the benefits of CRT pacing come at no added risk to the patient when compared to OPT therapy alone.

XII. CONCLUSIONS DRAWN FROM THE STUDIES

The CONTAK RENEWAL 3 AVT trial, a prospective clinical study, was conducted using the CONTAK RENEWAL 3 AVT CRT-D Systems in patients with a history of atrial tachyarrhythmias (AT) and with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction ($EF \leq 35\%$), and QRS duration ≥ 120 ms. This study demonstrated safety and effectiveness of atrial therapies in a heart failure patient population, confirmed the safety of combining ICD, CRT and atrial therapies, and confirmed the delivery of CRT and ICD therapy in the presence of atrial therapies.

The COMPANION study supports safety and effectiveness of Guidant CRT-D devices, like RENEWAL 3 AVT, in patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction ($EF \leq 35\%$), and QRS duration ≥ 120 ms.

Guidant performed a retrospective sub-analysis of patients within the COMPANION study to compare patients with previously reported paroxysmal or persistent atrial arrhythmias prior to enrollment to those patients without a prior history. This retrospective sub-analysis suggested CRT provides observed effectiveness in patients with a history of atrial arrhythmias with no added risk attributable to CRT therapy and AF interaction.

The clinical studies were performed using pulse generator firmware version 1.1.00, with the Model 2920 programmer and programmer software Version 1.5. The final approved software builds are pulse generator firmware Version 1.1.00 with Patch A and programmer software Version 3.01 for use with the Model 3120 programmer. FDA has reviewed the updates and their verification and validation testing, and does not believe that additional clinical data is required for use of the updated software versions.

In summary, the CONTAK RENEWAL 3 AVT study and a retrospective sub-analysis of the COMPANION study together provide a reasonable assurance of the safety and effectiveness of the CONTAK RENEWAL 3 AVT CRT-D Systems in a patient population with heart failure and a history of atrial arrhythmias.

XIII. 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.

XIV. CDRH DECISION

FDA issued an approval order for P010012/S037 on March 13, 2008.

The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

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

Postapproval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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