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## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### 1 GENERAL INFORMATION

Device Generic Name: Cardiac Resynchronization Therapy – Pacemaker (CRT-P) System  
Device Trade Name: CONTAK® RENEWAL® TR Models H120 and H125\*  
Applicant's Name and Address: GUIDANT Corporation, Cardiac Rhythm Management  
4100 Hamline Avenue North  
St. Paul, Minnesota 55112-5798

Premarket Approval Number: P030005  
Date of Panel Recommendation: None  
Date of Notice of Approval to Applicant: January 26, 2004

\* Hereto forward, CONTAK RENEWAL TR will be referred to as RENEWAL TR.

### 2 INDICATIONS FOR USE

The RENEWAL TR pulse generator is indicated for 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 (as defined in the clinical trials section).

The device provides atrial-ventricular tracking modes to help preserve AV synchrony, and adaptive-rate pacing for patients who would benefit from adjusted pacing rates concurrent with physical activity.

### 3 CONTRAINDICATIONS

- This device is contraindicated in patients who have a separate implanted cardioverter-defibrillator (ICD)
- Single-chamber atrial pacing is contraindicated in patients with impaired AV nodal conduction.

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- Atrial tracking modes are contraindicated for patients with chronic refractory atrial tachyarrhythmias (atrial fibrillation or flutter), which might trigger ventricular pacing.
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  - Asynchronous pacing is contraindicated in the presence (or likelihood) of competition between paced and intrinsic rhythms.

#### **4 WARNINGS AND PRECAUTIONS**

See device labeling.

#### **5 DEVICE DESCRIPTION**

The Guidant RENEWAL TR pulse generator Models H125 and H120 CRT-P devices are designed to provide cardiac resynchronization therapy by providing biventricular electrical stimulation to synchronize the right and left ventricular contractions. The device also provides adaptive-rate bradycardia therapy. The pulse generator has independent, programmable outputs for the atrium, right ventricle, and left ventricle, featuring LV-1 and/or IS-1 lead ports<sup>1</sup>. The leads along with the device constitute the implantable portion of the RENEWAL TR system. The device's small, physiologic shape minimizes pocket size and may minimize device migration.

The ZOOM Programming System, which includes the Model 2920 Programmer/ Recorder/ Monitor (PRM), the Model 2865 CONSULT Software Application, and an accessory telemetry wand, constitutes the external portion of the RENEWAL TR system. The external components allow interrogation and programming of the pulse generator as well as access to the device's diagnostic features. The RENEWAL TR system can be programmed to provide a variety of therapy options. It also can provide noninvasive diagnostic testing and therapy history data.

#### **6 ALTERNATE PRACTICES AND PROCEDURES**

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

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<sup>1</sup> LV-1 refers to the Guidant LV, proprietary connector. IS-1 refers to the international standard ISO 5841.3:1992.

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## **7 MARKETING HISTORY**

The RENEWAL TR devices are currently available for commercial distribution in the European Economic Area. No RENEWAL TR devices have been withdrawn from the market in any country for any reason related to safety or effectiveness.

## **8 POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

### **8.1 OBSERVED ADVERSE EVENTS**

Guidant conducted an Exercise Performance Sub-Study in the COMPANION trial to demonstrate the safety and effectiveness of a CRT-P pacing system and to demonstrate, with reasonable assurance, the safety and effectiveness of biventricular stimulation, or cardiac resynchronization therapy (CRT), using the Guidant Model 1241 CONTAK TR CRT-P along with the EASYTRAK (Models 4510/4511/4512/4513) coronary venous steroid-eluting single-electrode pace/sense lead. The Exercise Performance Substudy in COMPANION was a prospective, randomized, controlled, multicenter study conducted at 67 sites in the United States and enrolled 448 patients.

Guidant's RENEWAL TR and CONTAK TR devices provide the same cardiac resynchronization therapy (biventricular pacing). Therefore, the CONTAK TR clinical trial data is applicable to RENEWAL TR. The primary difference between CONTAK TR and RENEWAL TR is that CONTAK TR utilizes an electrically common RV and LV sensing/pacing circuit whereas RENEWAL TR incorporates an independent RV and LV sensing/pacing circuit.

Table 0-1 provides information on adverse events reported in patients randomized to a CONTAK TR for a six-month period beginning from randomization.

**Table 0-1: Adverse Events Through Six Months**

(CONTAK TR Performance sub-study Patients, N=185)

	<b>Total Number Of Events (Number of Patients)</b>	<b>% Comps (Patients) N=185 Patients</b>	<b>N Comps/ 100 Device Months 4008 Months</b>	<b>% Obs (Patients) N=185 Patients</b>	<b>N Obs/ 100 Device Months 4008 Months</b>
<b>Total Device Related Adverse Events</b>	<b>194 (103)</b>	<b>23.2 (43)</b>	<b>1.5 (59)</b>	<b>45.4 (84)</b>	<b>3.4 (135)</b>
<b>LV Lead Related Events</b>					
Brady capture - LV	44 (32)	13.5 (25)	0.7 (28)	7.6 (14)	0.4 (16)
CPI PG anomaly related to event	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Inappropriate shock above rate cutoff	3 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.1 (3)
Insulation breach observed	2 (2)	1.1 (2)	0.0 (2)	0.0 (0)	0.0 (0)
Multiple counting - brady	9 (8)	0.0 (0)	0.0 (0)	4.3 (8)	0.2 (9)
Multiple counting - tachy	3 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.1 (3)
Phrenic nerve/diaphragm stimulation	17 (14)	1.1 (2)	0.0 (2)	6.5 (12)	0.4 (15)
<b>PG Related Events</b>					
Migration of device	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Pacemaker-mediated tachycardia (PMT)	4 (4)	0.0 (0)	0.0 (0)	2.2 (4)	0.1 (4)
Pocket erosion/extrusion	3 (2)	1.1 (2)	0.1 (3)	0.0 (0)	0.0 (0)
Pocket infection	6 (5)	0.5 (1)	0.0 (1)	2.2 (4)	0.1 (5)
Rate response too aggressive - brady	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Set screw, stripped	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
<b>Procedure Related Events</b>					
Allergic reaction	9 (7)	0.0 (0)	0.0 (0)	3.8 (7)	0.2 (9)
Cardiac tamponade	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Dissection, coronary sinus	4 (4)	0.0 (0)	0.0 (0)	2.2 (4)	0.1 (4)
Hematoma	11 (10)	1.1 (2)	0.0 (2)	4.3 (8)	0.2 (9)
Hemorrhage	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Hypotension	5 (5)	0.0 (0)	0.0 (0)	2.7 (5)	0.1 (5)
Perforation, cardiac	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Perforation, coronary venous	7 (7)	0.0 (0)	0.0 (0)	3.8 (7)	0.2 (7)
Pericardial effusion	5 (3)	1.1 (2)	0.1 (3)	1.1 (2)	0.0 (2)
Pericarditis	2 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.0 (2)
Physiological reaction	2 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.0 (2)
Pneumothorax	5 (5)	2.2 (4)	0.1 (4)	0.5 (1)	0.0 (1)
Post-surgical wound discomfort	21 (21)	0.0 (0)	0.0 (0)	11.4 (21)	0.5 (21)
Renal failure	2 (2)	0.5 (1)	0.0 (1)	0.5 (1)	0.0 (1)
Transient heart block	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Ventricular fibrillation	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Ventricular tachycardia	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
<b>RA Lead Related Events</b>					
Brady capture - atrium	6 (6)	2.2 (4)	0.1 (4)	1.1 (2)	0.0 (2)
Intermittent sensing - atrium rate	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Oversensing - atrium pace sense	2 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.0 (2)
Oversensing - atrium rate sense - brady	2 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (2)
Undersensing - atrium pace sense - brady	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Undersensing - atrium rate sense - brady	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
<b>RV Lead Related Events</b>					
Brady capture - RV	3 (3)	1.1 (2)	0.0 (2)	0.5 (1)	0.0 (1)
High DFTs - tachy	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Materials unretrieved in body	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Oversensing - ventricle pace sense	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Phantom shock	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)

	<b>Total Number Of Events (Number of Patients)</b>	<b>% Comps (Patients) N=185 Patients</b>	<b>N Comps/ 100 Device Months 4008 Months</b>	<b>% Obs (Patients) N=185 Patients</b>	<b>N Obs/ 100 Device Months 4008 Months</b>
<b>Total Patient Related Adverse Events</b>	<b>1146 (173)</b>	<b>47.6 (88)</b>	<b>4.0 (161)</b>	<b>90.3 (167)</b>	<b>24.6 (985)</b>
<b>Cardiovascular Related Events</b>					
AV Block - heart block, complete	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Air embolism	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Aneurysm	2 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.0 (2)
Arrhythmia - atrial fibrillation	43 (31)	2.7 (5)	0.1 (5)	15.1 (28)	0.9 (38)
Arrhythmia - atrial flutter	9 (7)	1.1 (2)	0.0 (2)	3.2 (6)	0.2 (7)
Arrhythmia - sinus tachycardia	3 (3)	0.0 (0)	0.0 (0)	1.6 (3)	0.1 (3)
Cardiac arrest	8 (7)	3.8 (7)	0.2 (8)	0.0 (0)	0.0 (0)
Change in arrhythmia - SVT	13 (12)	0.0 (0)	0.0 (0)	6.5 (12)	0.3 (13)
Change in arrhythmia - brady	16 (16)	1.1 (2)	0.0 (2)	7.6 (14)	0.3 (14)
Change in arrhythmia - junctional	3 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.1 (3)
Chest pain	70 (40)	3.8 (7)	0.3 (13)	20.5 (38)	1.4 (57)
Claudication	4 (3)	0.5 (1)	0.0 (1)	1.6 (3)	0.1 (3)
Coagulopathy	3 (3)	0.5 (1)	0.0 (1)	1.1 (2)	0.0 (2)
Congestive heart failure	118 (68)	9.2 (17)	0.4 (18)	33.5 (62)	2.5 (100)
Dizziness, cause undetermined	40 (33)	0.5 (1)	0.0 (1)	17.3 (32)	1.0 (39)
Dyspnea (shortness of breath)	66 (36)	1.1 (2)	0.0 (2)	18.4 (34)	1.6 (64)
Fatigue	22 (21)	0.0 (0)	0.0 (0)	11.4 (21)	0.5 (22)
Hypertension	8 (7)	0.0 (0)	0.0 (0)	3.8 (7)	0.2 (8)
Hypotension	29 (25)	0.0 (0)	0.0 (0)	13.5 (25)	0.7 (29)
Intracranial hemorrhage	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Ischemia	8 (6)	3.2 (6)	0.2 (8)	0.0 (0)	0.0 (0)
Myocardial infarction	6 (5)	2.7 (5)	0.1 (6)	0.0 (0)	0.0 (0)
Pacemaker syndrome	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Palpitations	13 (12)	0.0 (0)	0.0 (0)	6.5 (12)	0.3 (13)
Pulmonary edema	3 (3)	0.5 (1)	0.0 (1)	1.1 (2)	0.0 (2)
Shock	1 (1)	0.5 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Stroke syndrome or CVA	1 (1)	0.0 (0)	0.0 (0)	0.5 (1)	0.0 (1)
Syncope	8 (7)	0.5 (1)	0.0 (1)	3.8 (7)	0.2 (7)
Thrombosis	2 (2)	1.1 (2)	0.0 (2)	0.0 (0)	0.0 (0)
Transient ischemic attack (TIA)	2 (2)	0.0 (0)	0.0 (0)	1.1 (2)	0.0 (2)
Vascular related	11 (11)	2.7 (5)	0.1 (5)	3.2 (6)	0.1 (6)
Ventricular fibrillation	3 (3)	1.6 (3)	0.1 (3)	0.0 (0)	0.0 (0)
Ventricular tachycardia	39 (29)	7.6 (14)	0.4 (15)	9.2 (17)	0.6 (24)
<b>Non-cardiovascular Related Events</b>	<b>588 (147)</b>	<b>23.8 (44)</b>	<b>1.6 (66)</b>	<b>77.8 (144)</b>	<b>13.0 (522)</b>

A total of 18 deaths occurred in the Exercise Performance sub-study. These are presented in Table 1-2 stratified by treatment group and cause of death (as adjudicated by an independent events committee).

**Table 0-2: Deaths in the Exercise Performance Sub-study (0-6 months)**

<b>Cause of Death</b>	<b>CONTAK TR (N=185)</b>	<b>OPT (N=87)</b>
Cardiac: Cardiac procedure*	4 (2%)	0 (0%)
Cardiac: Pump failure	4 (2%)	3 (3%)
Cardiac: Sudden, unexpected	6 (3%)	1 (1%)
<b>Total Deaths</b>	<b>14 (8%)</b>	<b>4 (5%)</b>

\* Defined as any death that occurs within 30 days of the device implant procedure

## 8.2 POSSIBLE ADVERSE EVENTS

Based on the literature and pulse generator implant experience, the following alphabetical list includes possible adverse events associated with implantation of a cardiac resynchronization therapy system:

- Acceleration of arrhythmias
- Bleeding
- Cardiac tamponade
- Death
- Dehydration
- Embolism, thrombolytic and air
- Erosion
- Fibrillation or other arrhythmias
- Fluid accumulation
- Heart block
- Hematoma/seroma
- Inability to pace
- Inappropriate pacing
- Infection
- Lead abrasion
- Lead displacement/dislodgment
- Lead fracture, insulation break
- Lead tip deformation and/or breakage

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- Migration of pulse generator
  - Muscle or nerve stimulation
  - Myocardial trauma (eg, cardiac perforation, irritability, injury)
  - Myopotential sensing
  - Nerve damage
  - Pacemaker mediated tachycardia
  - Pericardial rub
  - Pneumothorax
  - Random component failures
  - Rejection phenomena (local tissue reaction, allergic reaction, fibrotic tissue formation, keloid formation)
  - Threshold elevation
  - Thrombosis
  - Valve damage
  - Venous occlusion
  - Venous trauma (eg, perforation, dissection, erosion)

In addition to the implantation of a cardiac resynchronization therapy 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

## **9 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 on the RENEWAL TR System. 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 RENEWAL TR device, and device system met the requirements set by these standards (sections that apply, as outlined in the

following tables), and Guidant's specifications. The following tables provide brief descriptions of the verification and validation tests conducted on the RENEWAL TR system.

### 9.1 DESIGN VERIFICATION TESTING (DVT)

The design verification testing of the RENEWAL TR 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, as described below:

**Table 0-3: Component Testing**

Many of the components used in the RENEWAL TR pulse generator are the same components used in other Guidant pulse generators. The new components for the RENEWAL TR were tested and passed.

Summary of Component Testing*	Sample Size	Test Results (Pass/Fail)
<b>Header*:</b> Temperature challenge, visual inspection, dimensional analysis, mechanical/materials test, moisture/humidity test.	10 to 16	Pass
<b>External Case*:</b> Visual inspection, dimensional analysis	3	Pass
<b>Feedthru:</b> Electrical test/properties, temperature challenge, visual inspection, dimensional analysis, destructive analysis, hermeticity, mechanical/materials test, ionic contamination.	3 to 32	Pass
<b>Hybrid Assembly:</b> Electrical test, life test, temperature challenge, visual inspection, dimensional analysis.	3 to 53	Pass
<b>Battery:</b> Electrical test/properties, temperature challenge, visual inspection, dimensional analysis, destructive analysis, hermeticity.	4 to 41	Pass
*Materials used in these components were previously tested and met the requirements of ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing (1997)		

**Table 0-4: Electronic and Mechanical Testing**

Summary of Pulse Generator DVT	Sample Size	Test Results (Pass/Fail)
<b>Electronic Design Verification Testing</b>		
Tests were conducted in the following functional areas: Telemetry operation, sensing, pacing, standards testing, magnet, electrograms, device clock, and faults/error handling.	3	Pass
<b>Mechanical Design Verification Testing</b>		
Tests were conducted in the main functional areas: mechanical requirements, environmental tests, and package and shipping tests. Such tests included internal atmosphere and hermeticity, connector assembly, lead and adapter compatibility, thermal and mechanical shock, vibration, and dimensional analysis. The IS-1 connector assembly met requirements of ISO 5841-3: 1992(E).	1 to 15	Pass
Packaging and Shipping tests were done to ensure that the device remains damage free and that the package remains functional while in transit and	1 to 6	Pass

Summary of Pulse Generator DVT	Sample Size	Test Results (Pass/Fail)
storage mode prior to implant. Labeling must remain legible.		

**Table 0-5: Electromagnetic Compatibility (EMC) Testing**

Testing was based on prEN45502 Active Implantable Medical Devices, Part 2-1 Requirements for active implantable medical devices intended to treat bradyarrhythmia (cardiac pacemakers) March 1998, AAMI PC69 (1<sup>st</sup> edition 2000) and the AAMI Pacemaker Standard, August 1975 (Table 1-5).

Summary of Electromagnetic Compatibility (EMC) Testing	Sample Size	Test Results (Pass/Fail)
RENEWAL TR pulse generator performance was evaluated when subjected to the following:	3	Pass*
• Conducted frequency as defined in the CEN/ CENELEC European Standard.		
• Radiated radio frequency; pulsed and continuous wave		
• High voltage external defibrillation shocks.		
• Exposure to electrostatic discharge pulses.		
• Exposure to electrocautery		
• Exposure to static magnetic fields up to 10 mT		
• RF Near-Field Evaluation per AAMI PC69.		
• RF Ablation Energy Interference Immunity Evaluation		
• Exposure to Electronic Article Surveillance (EAS) Systems per Georgia Technical Institute EAS test protocol for Implantable Medical Devices.		
• Diagnostic Ultrasound Immunity Evaluation		
• Radio & Telecommunications Terminal Equipment (RTTE) Evaluation		

\*Guidant reported that there were no instances of memory errors, parameter changes, or damage from any tests. Additionally, the devices delivered appropriate pacing therapy per the system requirements. Finally, the telemetry scheme was shown to meet the European RTTE Directive.

**Table 0-6: Battery Reserve Capacity Testing**

Summary of Battery Capacity Testing	Sample Size	Test Results (Pass/Fail)
The Battery 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.	4	Pass

**Table 0-7: 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) to ensure proper function, timing, and data exchange. The firmware version number is 1.0.00.	PG Software	Pass with 2 anomalies*

\*1) When the Brady mode is VDDR, pace impedance and R-wave amplitude test measurements are made on all left ventricular events. 2) The events in the data point legend on the Trending screen will be classified as Paced and/or Sensed depending on mode. These anomalies have no effect on therapy or patient safety.

**Table 0-8: Model 2865 Software Application DVT**

Summary of Model 2865 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 1.8 for use with the Model 2920 PRM.	PRM Software	Pass

## 9.2 DESIGN VERIFICATION AND VALIDATION TESTING FOR THE RENEWAL TR SYSTEM

**Table 0-9: System Design Verification and Validation Testing**

System Design Verification and Validation Testing	Sample Size	Test Results (Pass/Fail)
<b>System Features Tests:</b> Tests were conducted to exercise all features of the RENEWAL TR system. Feature groups tested included device family, programmer support, lead support, bradycardia modes, bradycardia therapy, diagnostics, and faults/error handling.	1 system (pulse generator and programmer software)	Pass
<b>Simulated Use Test:</b> From a field user perspective, Guidant evaluated the performance of the RENEWAL TR. Clinical scenarios were simulated using the pulse generator, programmer (PRM), PRM software, and a cardiac signal simulator.	5 users performed tests.	Pass
<b>Animal Study:</b> The study verified that the components of the CRT-P System were compatible and performed safely in an <i>in-vivo</i> canine model.	1 animal, 2 devices	Pass

## 9.3 ANIMAL STUDY

This acute study was designed to evaluate the safety and performance of the RENEWAL TR in an *in-vivo* canine model. The study objective focused on the compatibility of the system components, their ease of use and their operation in the expected clinical environment. Two devices were tested in one canine model. In conclusion, the RENEWAL TR device, with the final representative firmware and software versions, functioned as expected as a system. All devices sensed heart rhythms and delivered therapy according to programmed parameters. Features tested operated per design intent. When subjected to environmental stresses expected during clinical use, the system performed and reacted appropriately.

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## **9.4 SAFETY AND RISK ANALYSIS**

The safety and risk analysis of the RENEWAL TR 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).

### **9.4.1 BIOCOMPATIBILITY EVALUATION**

The biocompatibility of the tissue contacting materials used in the RENEWAL TR pulse generator was established in previous PMA applications (D970003/S12 and P010012/S2), and meet the requirements of ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing (1997). Pulse generator materials include: polyurethane, titanium, stainless steel, and silicone rubber that are all currently used in Guidant's commercially available pacemaker devices.

### **9.4.2 STERILIZATION VALIDATION**

Sterilization assessments were performed and validated that the RENEWAL TR pulse generator can be effectively sterilized with the Oxyfume 2000<sup>®</sup> or the 100% ethylene oxide (EtO) sterilization process.

### **9.4.3 SHELF LIFE FOR PMA DEVICES**

Expiration dating for this device has been established at 2 years from the battery-attach date.

## **10 SUMMARY OF CLINICAL STUDIES**

Guidant conducted an Exercise Performance Sub-Study in the COMPANION trial (CONTAK TR Clinical Study) to demonstrate the safety and effectiveness of a CRT-P pacing system and to demonstrate, with reasonable assurance, the safety and effectiveness of biventricular stimulation, or cardiac resynchronization therapy (CRT), using the Guidant Model 1241 CONTAK TR CRT-P along with the EASYTRAK (Models 4510/4511/4512/4513) coronary venous steroid-eluting single-electrode pace/sense lead.

Guidant's CONTAK TR and RENEWAL TR devices provide the same cardiac resynchronization therapy (biventricular pacing). Therefore, the CONTAK TR Clinical Study data also applies to RENEWAL TR. The primary difference between the two devices is that CONTAK TR utilizes an electrically common RV and LV sensing/pacing circuit whereas RENEWAL TR incorporates an independent RV and LV sensing/pacing circuit.

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Guidant also conducted the CONTAK RENEWAL Holter Study, which verified that the enhancements made to the delivery of biventricular pacing do not interfere with the therapy the patient receives. These enhancements, i.e., independent sensing inputs and pacing outputs, were incorporated into both the CONTAK RENEWAL and the RENEWAL TR design to allow greater diagnostic and system evaluation, while still providing continuous appropriate biventricular pacing. Because both devices incorporate the same independent sensing/pacing design, the CONTAK RENEWAL Holter Study data applies to RENEWAL TR.

## **10.1 CONTAK TR CLINICAL STUDY**

### **10.1.1 STUDY DESIGN**

This was a multi-center, prospective, clinical investigation (conducted at 67 sites in the United States with 448 patients enrolled), evaluating CRT as a treatment modality combined with optimal pharmacological therapy in patients with chronic heart failure by measuring improvement in exercise performance. Exercise performance was measured via peak VO<sub>2</sub> and 6MW in patients who had a qualifying baseline visit. These patients were then randomized on a 1:2:2 basis to optimal pharmacological therapy alone or CRT (CONTAK TR CRT-P or CONTAK CD CRT-D) combined with optimal pharmacological therapy. All device recipients were implanted with the commercially available EASYTRAK coronary venous pace/sense lead and commercially available right ventricular and atrial pace/sense leads.

The effectiveness data was pooled for the CRT arm using patients that were implanted with either a CONTAK TR or CONTAK CD device. Patients underwent repeat exercise performance testing at 3 and 6 months of follow up. Effectiveness data was collected from patients (OPT and CRT) who had a qualifying baseline peak VO<sub>2</sub> (< 22 ml/kg/min) and 6MW (150 meters ≤ six-minute walk distance ≤ 425 meters) test and went on to complete a qualifying (maximal effort) peak VO<sub>2</sub> and/or 6MW at the 3 and/or 6 month follow up. Device safety data were reported on all patients in the Exercise Performance sub-study who were randomized to a CONTAK TR device and had a qualifying baseline peak VO<sub>2</sub> and 6MW test.

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### 10.1.1.1 Inclusion/Exclusion Criteria

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

- Moderate or severe heart failure, defined as symptomatic heart failure for at least six months with NYHA class III or IV symptoms at the time of enrollment, and at least one of the following events in the previous 12 months:
  - Hospitalization for heart failure management
  - Outpatient visit in which intravenous (IV) inotropes or vasoactive infusion were administered continuously for at least 4 hours
  - Emergency room visit of at least twelve hours duration in which IV heart failure medications were administered (including diuretics)
- $QRS \geq 120$  ms and PR interval  $> 150$  ms from any two leads of a 12 lead ECG
- Left ventricular ejection fraction  $\leq 35\%$
- Left ventricular end diastolic dimension  $\geq 60$  mm (required only if LVEF measured by echo) or  $> 3.0$  cm/m<sup>2</sup> [The cm/m<sup>2</sup> is calculated by LVEDD (in cm) divided by BSA (body surface area)]
- Age  $\geq 18$  years
- Optimal pharmacologic therapy for heart failure (beta-blocker, ACE inhibitor, Diuretic, and Spironolactone)

Additional eligibility criteria for the Exercise Performance sub-study:

- Understand the nature of the sub-study and provide informed consent
- Have been enrolled at a participating sub-study investigational center
- Have no neuromuscular or vascular disability that prevents normal walking (e.g., intermittent claudication, arthritis, residual stroke weakness)
- Have no history of angina during previous exercise testing
- Have no cardiac disabilities that would ordinarily contraindicate exercise testing:
  - changing pattern on the ECG
  - changing pattern of chest discomfort
  - decompensated heart failure
  - uncontrolled arrhythmias
- $FEV_1/FVC \geq 50\%$
- $150 \text{ m} \leq \text{Six minute walk distance} \leq 425 \text{ m}$
- Baseline Peak  $VO_2 < 22$  ml/kg/min

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

- Unable or unwilling to undergo device implant and follow-up testing
- Meet the general indications for an implantable cardioverter defibrillator
- Meet the general indications for antibradycardia pacing
- Expected to receive a heart transplant in the next six months
- Chronic, medically refractory atrial tachyarrhythmias
- Unexplained syncope
- Myocardial infarction within 60 days of randomization
- History of non-compliance with oral heart failure therapy
- Progressive or unstable angina
- Uncontrolled blood pressure: Systolic BP > 160 mm Hg or < 85 mm Hg or diastolic BP > 90 mm Hg
- Patients with a hypersensitivity to 0.7 mg nominal dose of dexamethasone acetate
- Surgically uncorrected primary valvular disease
- Coronary artery disease (CAD) in which surgical or percutaneous correction is recent (within 60 days of randomization)
- Women who are pregnant or not using medically acceptable birth control
- Hypertrophic obstructive cardiomyopathy
- Amyloid disease
- Hospitalization for heart failure or IV inotropic or vasoactive therapy in excess of 4 hours in the 30 days prior to enrollment
- Involved in any other investigational studies
- Life expectancy < 6 months due to any other medical conditions

#### 10.1.1.2 *Follow-up schedule*

Enrollment	Initial assessment of patient eligibility; taking of patient history.
Baseline Screening	Special testing*
Randomization	Randomization status (OPT, CRT-P or CRT-D) was assigned.
Implant (CRT-P or CRT-D arm)	Implant of investigational devices and acute device testing for those randomized to a CRT therapy arm.
Routine Follow-up	Routine evaluation of device function and patient condition at pre-discharge, one week, and one month
Three- and six-month Visits	Evaluation of randomized therapy with Special Testing* and device function at three- and six-months after the Post-Recovery Visit.
Quarterly Visits	After the six-month visit, patients were seen for routine evaluation of device function and patient condition.

\* Special Testing included a Symptom-Limited Treadmill Test with measurement of oxygen uptake (Peak VO<sub>2</sub>), a Six-Minute Walk, Quality of Life (QOL) questionnaire and New York Heart Association Classification.

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### 10.1.1.3 Endpoints

The Exercise Performance Substudy consisted of:

#### **CRT Effectiveness:**

*Primary:* Co-primary endpoint consisting of Peak VO<sub>2</sub> derived from a symptom-limited exercise test and Six-Minute Walk, with CRT results pooled from the CONTAK TR and CONTAK CD arms.

Effectiveness was determined by assessing both Peak VO<sub>2</sub> and Six-minute walk distance improvements with CRT compared to OPT. Prospectively, success was defined as occurring if 1) Peak VO<sub>2</sub> improved  $\geq 0.7$  ml/kg/min ( $p < 0.05$ ) and 6 MWD improvement resulted in  $p < 0.10$ , or 2) Peak VO<sub>2</sub> improved  $\geq 0.5$  ml/kg/min ( $p < 0.10$ ) and 6 MWD improvement resulted in  $p < 0.05$ .

*Additional:* Quality of Life as measured by the Minnesota Living with Heart Failure Questionnaire<sup>®</sup> and NYHA Class.

#### **Safety:**

*Primary:* System-related complication-free rate

*Primary:* Incidence of lead-related adverse events.

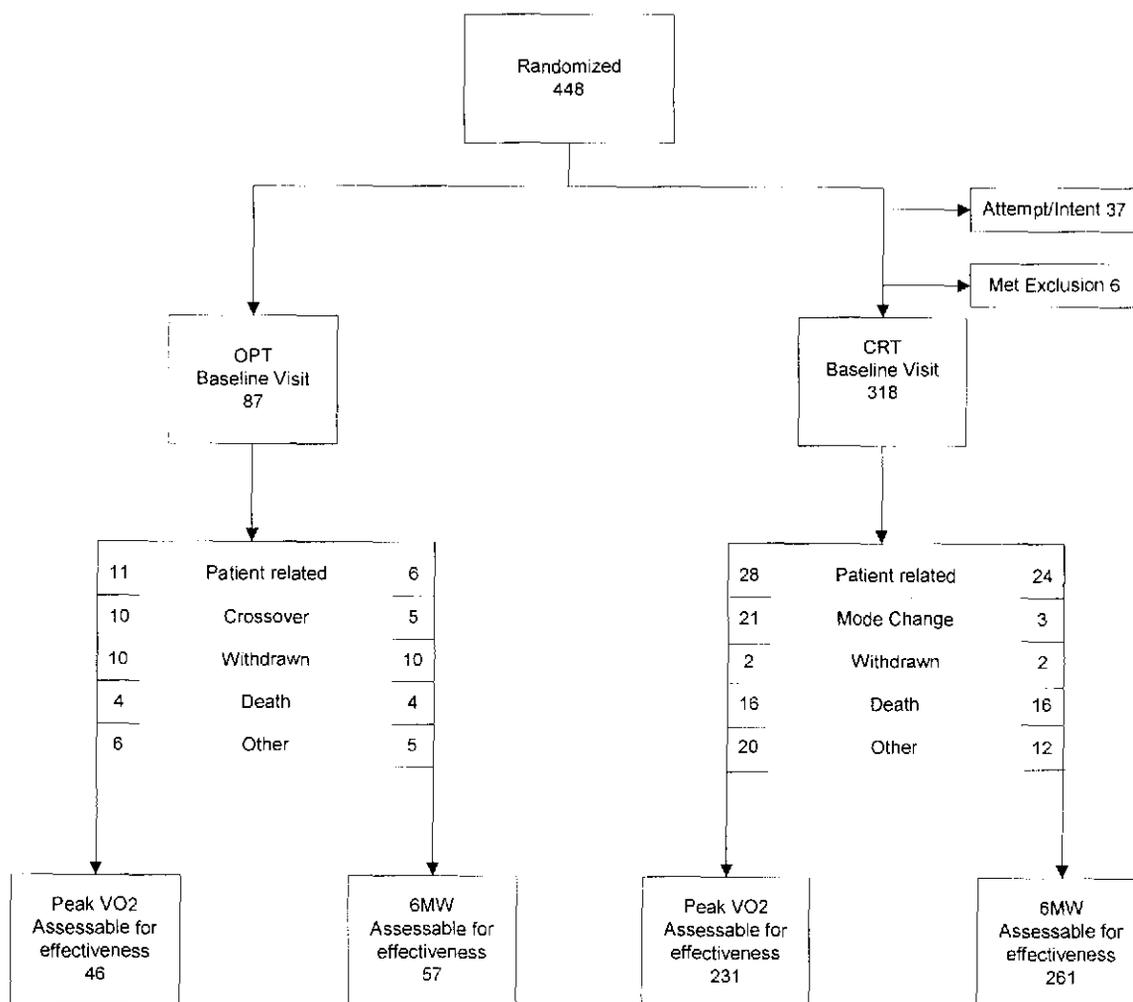
#### **Lead Effectiveness:**

*Secondary:* Left ventricular pacing thresholds, biventricular sensing, and biventricular lead impedance.

*Note that during the course of the COMPANION trial, the EASYTRAK Coronary Venous pace/sense lead was established as safe and effective in a separate clinical study and was approved for commercial distribution (P010012, 05/02/02). Refer to the commercially available EASYTRAK Coronary Venous pace/sense lead labeling for clinical safety and performance characteristics.*

**10.1.1.4 Study Results**

**10.1.1.4.1 Patient Accountability**





Food and Drug Administration  
 9200 Corporate Boulevard  
 Rockville MD 20850

10.1.1.4.2 Baseline Characteristics

Table 0-10: Characteristics of Patient Population

Characteristic		CRT (N=318)	OPT (N=87)	P-value*
Age (years)	Mean +/- SD	62.1 +/- 11.8	63.1 +/- 10.6	0.48
	Range	32.0 - 86.0	27.0 - 85.0	
Gender [N (%)]	Female	109 (34.3)	24 (27.6)	0.24
	Male	209 (65.7)	63 (72.4)	
NYHA Classification [N (%)]	Class III	294 (92.5)	79 (90.8)	0.61
	Class IV	24 (7.5)	8 (9.2)	
Ischemic Etiology	Ischemic	141 (44.3)	42 (48.3)	0.51
	Non-schemic	177 (55.7)	45 (51.7)	
LVEF (%)	Mean +/- SD	22.5 +/- 6.9	22.2 +/- 8.0	0.79
	Range	5.0 - 35.0	5.0 - 35.0	
Resting Heart Rate (bpm)	Mean +/- SD	73.1 +/- 12.8	73.5 +/- 11.5	0.78
	Range	46.0 - 122.0	54.0 - 103.0	
QRS Width(ms)	Mean +/- SD	159.2 +/- 25.0	155.7 +/- 25.8	0.26
	Range	120.0 - 276.0	120.0 - 224.0	
LBBB/NSIVCD (%)	LBBB	230 (72.3)	62 (71.3)	0.60
	Non-specific	54 (17.0)	18 (20.7)	
	RBBB	34 (10.7)	7 ( 8.0)	
Peak VO2 (ml/kg/min)	Mean +/- SD	12.7 +/- 3.3	12.4 +/- 3.3	0.42
	Range	3.0 - 21.2	4.8 - 21.5	
Six Minute Walk Distance (m)	Mean +/- SD	292.4 +/- 65.5	291.6 +/- 70.5	0.92
	Range	152.0 - 411.5	162.4 - 414.0	
Quality of Life Score (points)	Mean +/- SD	59.8 +/- 23.1	55.4 +/- 23.3	0.12
	Range	0.0 - 105.0	0.0 - 97.0	
Heart Failure Medications [N (%)]	Diuretic	300 (94.3)	82 (94.3)	0.98
	ACE inhibitor or ARB	286 (89.9)	82 (94.3)	0.22
	Beta Blockers	240 (75.5)	60 (69.0)	0.22
	Aldosterone Antagonist	178 (56.0)	51 (58.6)	0.66
	Digoxin	239 (75.2)	65 (74.7)	0.93

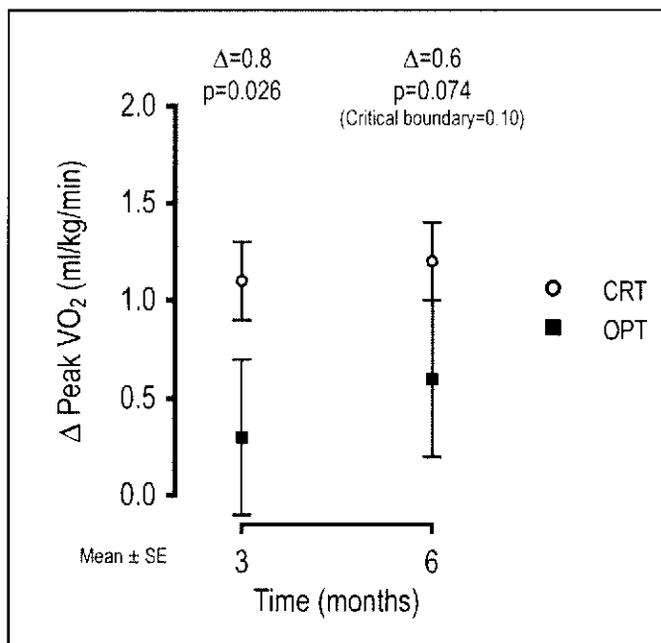
\*Continuous data were analyzed using a two-tailed t-test procedure, and categorical data were analyzed using a two-tailed chi-square procedure. A p-value < 0.05 is considered significant.

**10.1.1.5 CRT EFFECTIVENESS**

**10.1.1.5.1 Primary Effectiveness Endpoint 1: Maximal Oxygen Consumption (Peak VO<sub>2</sub>)**

Peak VO<sub>2</sub> was determined from a standardized protocol for exercise testing as a means of measuring a patient’s capacity for performing physical activity.

**Figure 1: Maximal Oxygen Consumption Results**



**Table 1-11: Maximal Oxygen Consumption Results**

Peak VO <sub>2</sub> (ml/kg/min)	CRT		OPT		p-value*
	N	Mean $\pm$ S.E.	N	Mean $\pm$ S.E.	
$\Delta$ at 3 months	247	1.1 $\pm$ 0.2	52	0.3 $\pm$ 0.4	0.026
$\Delta$ at 6 months	230	1.2 $\pm$ 0.2	46	0.6 $\pm$ 0.4	0.074

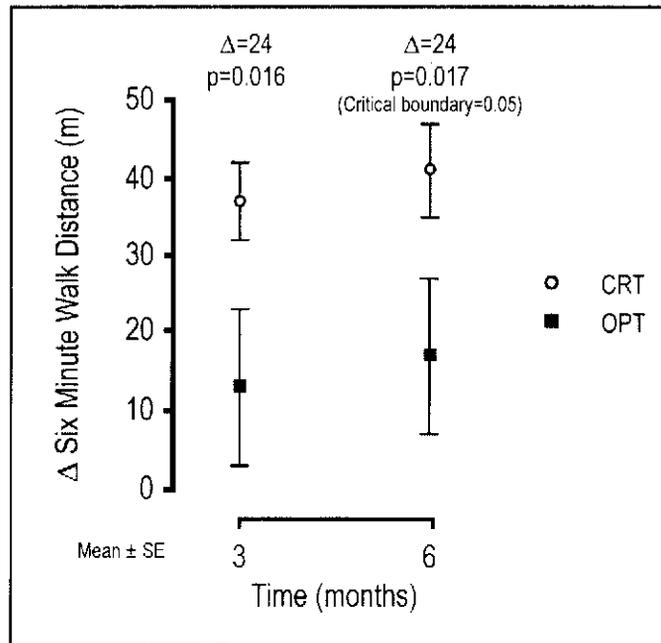
\* P-values obtained using one-tailed longitudinal analysis methods.

*The longitudinal analysis is performed on all available data. The percentage of missing data at the six month endpoints for Peak VO<sub>2</sub> and 6 minute walk were 36% and 28% for the CRT arm and 47% and 34% for the OPT arm. The longitudinal analysis performed is most appropriate when missing data occurs at the percentages found in this trial.*

**10.1.1.5.2 Primary Effectiveness Endpoint 2: Six-Minute Walk Distance**

The Six-Minute Walk test is a measure of a patient’s ability to sustain exercise during an activity similar to that which a patient may typically perform on a daily basis. For this test, patients are instructed to walk as far as possible in 6 minutes in a level corridor.

**Figure 2: Change in 6 Minute Walk**



**Table 1-12: Change in 6 Minute Walk**

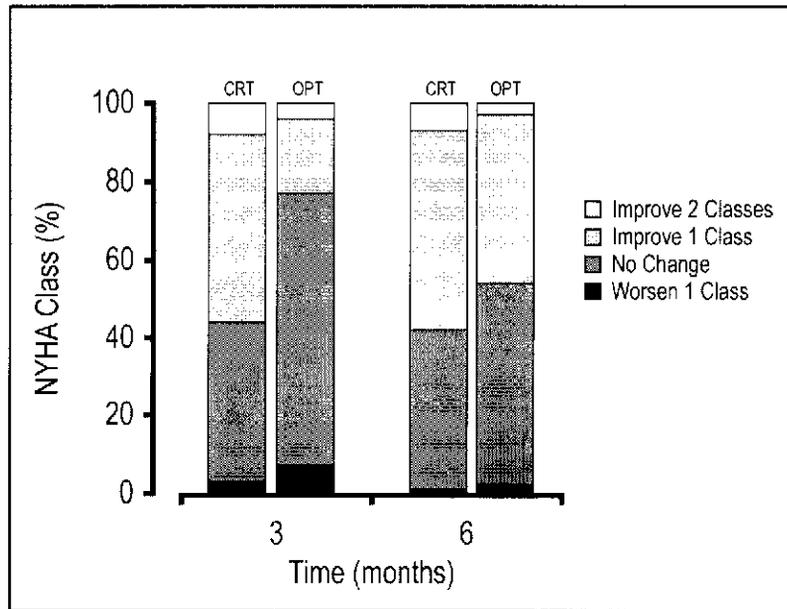
Six Minute Walk (m)	CRT		OPT		p-value*
	N	Mean ± S.E.	N	Mean ± S.E.	
Δ at 3 months	274	37 ± 5	63	13 ± 10	0.016
Δ at 6 months	260	41 ± 5	57	17 ± 10	<b>0.017</b>

\* P-values obtained using one-tailed longitudinal analysis methods.

**10.1.1.5.3 Ancillary Effectiveness: New York Heart Association Class (NYHA)**

The determination for New York Heart Association (NYHA) Class is based on mutual assessment, by the patient and physician, of the patient’s heart failure symptoms both at rest and while performing ordinary physical activity.

**Figure 3: Change in NYHA**



**Table 1-13: Change in NYHA**

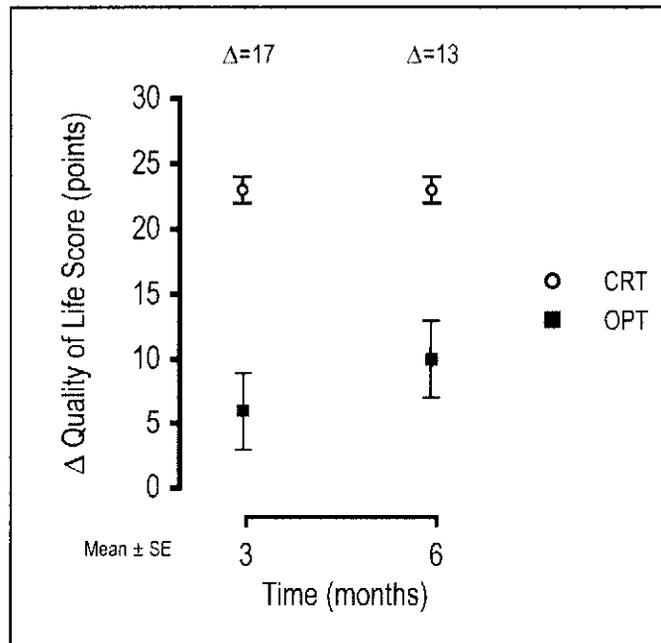
NYHA Classification	Change	CRT		OPT		p-value*
		N	Patients	N	Patients	
Three Months	Improve 2 Classes	N=294	22 (7.5%)	N=69	3 (4.4%)	<0.01
	Improve 1 Class		142 (48.3%)		13 (18.8%)	
	No Change		122 (41.5%)		48 (69.6%)	
	Worsen 1 Class		8 (2.7%)		5 (7.3%)	
Six Months	Improve 2 Classes	N=291	20 (6.9%)	N=65	2 (3.1%)	0.032
	Improve 1 Class		149 (51.2%)		28 (43.1%)	
	No Change		118 (40.6%)		34 (52.3%)	
	Worsen 1 Class		4 (1.4%)		1 (1.5%)	

\* P values are not adjusted for multiplicity and were obtained using a one-tailed Mantel-Haenszel chi-square method.

**10.1.1.5.4 Ancillary Effectiveness: Quality of Life (QOL)**

Quality of Life (QOL) was assessed using the 21-question Minnesota Living with Heart Failure questionnaire. Each question, answered by the patient, is ranked on a scale ranging from 0 to 5. A lower total score indicates an improved quality of life.

**Figure 4: Quality of Life Score**



**Table 1-14: Quality of Life Score**

Quality of Life (points)	CRT		OPT		p-value*
	N	Mean ± S.E. [95% CI]	N	Mean ± S.E. [95% CI]	
Δ at 3 months	289	23 ± 1 [20.1, 25.7]	72	6 ± 3 [0.6, 11.3]	<0.001
Δ at 6 months	279	23 ± 1 [19.7, 25.4]	66	10 ± 3 [4.2, 15.2]	<0.001

\* P values are not adjusted for multiplicity and were obtained using one-tailed longitudinal analysis methods.

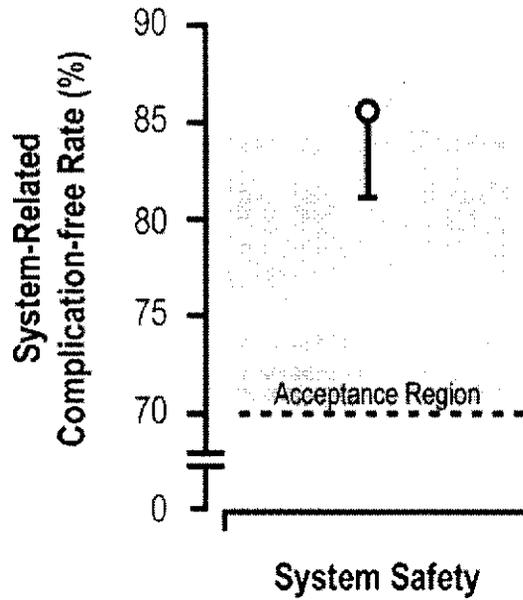
**10.1.1.6 SAFETY**

**10.1.1.6.1 Primary Safety Endpoint 1: CONTAK TR System Safety**

The system-related complication-free rate for the CRT group at the lower confidence bound was 81.1% through six months (Figure 5). This exceeds the acceptance criterion of 70% established to demonstrate safety for the CONTAK TR and EASYTRAK pace/sense lead

CRT-P system. Table 15 summarizes the system related complications documented through six months of follow-up.

**Figure 5: System-Related Complication-Free Rate**



**Table 0-15: System Related Complications by Category (0-6 months)  
(TR Exercise Performance sub-study Patients, N=185)**

	<b>Number Of Events</b>	<b>Number Of Patients</b>	<b>Complication Free Rate</b>	<b>Lower 95% Confidence Bound</b>
<b>Total System Related Adverse Events</b>	<b>34</b>	<b>27</b>	<b>85.4</b>	<b>81.1</b>
<b>LV Lead Related Events</b>				
Brady capture - LV	13	12	93.5	90.5
Insulation breach suspected	1	1	99.5	98.6
Phrenic nerve/diaphragm stimulation	2	2	98.9	97.7
<b>PG Related Events</b>				
Migration of device	1	1	99.5	98.6
Pocket erosion/extrusion	1	1	99.5	98.6
Pocket infection	1	1	99.5	98.6
<b>Procedure Related Events</b>				
Cardiac tamponade	1	1	99.5	98.6
Perforation, coronary venous	1	1	99.5	98.6
Pneumothorax	3	3	98.4	96.9
Respiratory related	2	2	98.9	97.7
<b>RA Lead Related Events</b>				
Brady capture - atrium	2	2	98.9	97.7
Intermittent sensing - atrium rate	2	2	98.9	97.7
<b>RV Lead Related Events</b>				
Brady capture - RV	2	2	98.9	97.7
Materials unretrieved in body	1	1	99.5	98.6
Oversensing - ventricle pace sense	1	1	99.5	98.6

\* Patients may have events in multiple categories.

In conclusion, the ability of the CONTAK TR system to effectively deliver CRT therapy has been demonstrated. The result of this success was improved exercise performance, as measured by Peak VO<sub>2</sub> and Six-Minute Walk distance, for those patients receiving optimal pharmacological therapy (OPT) with CRT as compared to patients receiving optimal pharmacological therapy alone. Additionally, New York Heart Association (NYHA) Class and Quality of Life test scores improved overall for those patients receiving OPT + CRT compared to the control. The incidence of system-related complications and lead-related adverse events both met study endpoint acceptance criteria.

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## 10.1.2 CONTAK RENEWAL HOLTER STUDY

### 10.1.2.1 STUDY DESIGN

The CONTAK RENEWAL Holter Study was a prospective, multi-center, non-randomized evaluation conducted in Europe, in which 46 patients completed testing. The purpose of the study was to demonstrate continuous appropriate biventricular (BiV) pacing over a 24 hour period and during exercise using Holter monitor recordings. All patients had been implanted with a CONTAK RENEWAL for a minimum of one month at the time of the study initiation.

#### *10.1.2.1.1 Inclusion/Exclusion Criteria*

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

- Availability for 24 hours follow-up at an approved study center
- Willingness and ability to participate in all testing associated with this study
- Age 18 or above, or of legal age to give informed consent as specified by national law
- Implanted with the CONTAK RENEWAL system for at least 1 month
- Stable when programmed according to labeled recommendations for continuous BV pacing
- Sinus rhythm at follow-up
- Active atrial lead implanted

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

- Life expectancy of less than six months due to other medical conditions
- Concurrent participation in any other clinical study, including drug study
- In atrial fibrillation at follow-up
- Inability or refusal to sign the Patient Informed Consent
- Inability or refusal to comply with the follow-up schedule
- Known pregnancy

### 10.1.2.1.2 Baseline Demographics

The patient characteristics at study entry are summarized in Table 1-16.

**Table 0-16: Preimplant Characteristics of Study Patients**

Characteristics		Patient Data
N patients		46
Gender		Male: 40 (87%), Female: 6 (13%)
Age (years)		60.9 ± 9.0
NYHA at implant [N (%)]	I	0 (0%)
	II	5 (10.9%)
	III	34 (73.9%)
	IV	7 (15.2%)
NYHA current	I	9 (19.6%)
	II	25 (54.3%)
	III	11 (23.9%)
	IV	1 (2.2%)
Duration implanted (months)	Mean ± SD	8.3 ± 4.1
	Range	1.5 – 15.0
	Median	9.0

### 10.1.2.1.3 Programming Parameters

Refer to Chapter 3 of the System Guide for information about programming to maintain CRT. Programming recommendations in this study were consistent with the recommendations in Chapter 3.

## 10.1.2.2 ENDPOINTS

The study had two primary endpoints: 1) continuous appropriate BiV pacing during activities of daily living and 2) continuous appropriate BiV pacing during exercise. The mean percentage of sinus beats appropriately BiV paced was measured by a Holter monitor over a 24 hour period and during exercise. Exercise intensity was measured using the Borg rating of perceived exertion (RPE) 6-20 scale. Patients were asked to exercise to a Borg level of 15 (difficult). The exercise protocol used was left to the discretion of the physician based on the patients' functional status. The type of exercise performed, duration and intensity of exercise testing is listed in Table 1-17 and Table 1-18.

**Table 0-17: Type of Exercise Testing Performed**

Exercise Performed	Number of Patients
Bicycle Ergometry	24 (52.2%)
Hall Walk	8 (17.4%)
Stair Climbing	14 (30.4%)
Total	46

**Table 0-18: Duration and Intensity of Exercise Testing**

		Results (N = 46)
Borg RPE Rating Obtained	Mean ± SD	15 ± 1
	Median	15
	Range	7 – 18
Duration of Exercise (minutes)	Mean ± SD	6.6 ± 3.3
	Median	6.0
	Range	1 – 17
Maximum HR Obtained (bpm)	Mean ± SD	103 ± 20
	Median	105
	Range	60 – 156

**10.1.2.2.1 Study Results****10.1.2.2.1.1 Pacing during activities of daily living**

The mean percentage of appropriately continuously paced beats during daily living was calculated as  $99.6 \pm 1.3\%$  with a median of 100% and is summarized in Table 1-19. Continuous appropriate BiV pacing is defined as pacing provided between the lower rate limit and the MTR, excluding PVCs.

**Table 0-19: Activities of Daily Living: Continuous Appropriate BiV Pacing**

	Statistic	P-value <sup>a</sup>
Mean ± SD	99.6 ± 1.3	--
Range	91.4 – 100	--
Median <sup>b</sup>	100	<0.01

<sup>a</sup> The p-value is based on the sign-rank test.

<sup>b</sup> Due to the non-normality of the data a non-parametric test of the median was performed comparing the median to 90%.

### 10.1.2.2.1.2 Pacing During Exercise

The mean percentage of appropriately continuously paced beats during exercise was calculated as  $98.3 \pm 5.6\%$  with a median of 100% and is summarized in Table 1-20. Continuous appropriate BiV pacing is defined as pacing provided between the lower rate limit and the MTR, excluding PVCs.

**Table 0-20: Exercise: Continuous Appropriate BiV Pacing**

	Statistic	P-value <sup>a</sup>
Mean $\pm$ SD	$98.3 \pm 5.6$	--
Range	68.1 – 100	--
Median <sup>b</sup>	100	<0.01

a The p-value is based on the sign-rank test.

b Due to the non-normality of the data a non-parametric test of the median was performed comparing the median to 90%.

### 10.1.2.2.1.3 Device Counters

Finally, during the study CONTAK RENEWAL device counters were found to correlate highly to the data collected on the independent Holter monitors

**Table 0-21: Correlation Between Holter and Device**

	Mean $\pm$ SD	Correlation (P-value)
Holter	$97,536 \pm 13,307$	0.97 (<0.01)
Device	$100,143 \pm 13,373$	--

## 10.1.3 CONCLUSIONS DRAWN FROM THE STUDIES

### Safety

The CONTAK TR system met the primary safety endpoint. Results were within protocol specified performance criteria for system-related complications.

### Effectiveness

The effectiveness of the CONTAK TR system has been demonstrated by a six-month clinically significant improvement in peak  $VO_2$  and six-minute hall walk distance, for those patients receiving optimal pharmacological therapy (OPT) with CRT as compared to patients receiving OPT alone. Additionally, the cardiac resynchronization therapy demonstrated a statistically significant improvement in quality of life and reduction in NYHA functional class.

Guidant's CONTAK TR and RENEWAL TR devices provide the same cardiac resynchronization therapy (biventricular pacing). Therefore, the CONTAK TR Clinical Study data also applies to RENEWAL TR.

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Guidant also conducted the CONTAK RENEWAL Holter Study, which verified that the enhancements made to the delivery of biventricular pacing do not interfere with the therapy the patient receives. Because RENEWAL TR incorporates the same independent sensing/pacing design and CONTAK RENEWAL, the Holter Study data applies to RENEWAL TR.

## **11 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 the review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## **12 CDRH DECISION**

FDA issued an approval order on January 26, 2004. A post market study to evaluate the safety and effectiveness of the device was required. This decision was based on the preclinical studies and clinical study results. The conditions of Approval are those outlined in the attached Conditions of Approval for Cardiac Pacemakers and Programmers.

## **13 APPROVAL SPECIFICATIONS**

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