

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

1 GENERAL INFORMATION

Device Generic Name:	Automatic Implantable Cardiac Defibrillator
Device Trade Name:	Guidant VENTAK PRIZM AVT AICD System including the: <ul style="list-style-type: none">• VENTAK PRIZM AVT pulse generator, Model 1900• Programmer Software Application, Model 2849 (Version 2.4)• PERIMETER Coronary Sinus Defibrillation Lead, Models 0202/0203/0204• System accessories:<ul style="list-style-type: none">• PARTNER RHYTHM ASSISTANT, Model 2930• Stylet Accessory Kits, Models 6321, 6322, 6323, 6324, 6325, 6236, 6327, 6328, 6329
Applicant's Name and Address:	GUIDANT Corporation, Cardiac Rhythm Management 4100 Hamline Avenue North St. Paul, Minnesota 55112-5798
Premarket Approval Application (PMA) Number:	P960040/S028
Date of Notice of Approval to Applicant:	March 27, 2003

2 INDICATIONS FOR USE

2.1 VENTAK PRIZM AVT AICD

The VENTAK PRIZM AVT AICD System is indicated for use in patients who are ICD indicated and who have atrial tachyarrhythmias or who are at risk of developing atrial tachyarrhythmias.

Patient populations who are indicated for a Guidant ICD include those who have had spontaneous and/or inducible life-threatening ventricular arrhythmias and those who are at high risk of developing such arrhythmias; or, patients who may benefit from prophylactic treatment due to a prior myocardial infarction and an ejection fraction $\leq 30\%$ (as defined in the MADIT II Clinical Study appendix).

2.2 PERIMETER CS LEAD

The PERIMETER Coronary Sinus (CS) lead, Models 0202/0203/0204 is intended for use only as an optional component of the VENTAK PRIZM AVT AICD System with the A-TRIAD[®] electrode configuration for defibrillation energy delivery if desired.

3 DEVICE DESCRIPTION

GUIDANT'S VENTAK PRIZM AVT AICD (Model 1900, PRIZM AVT) builds on the features of the VENTAK PRIZM. It is a ventricular defibrillator with dual chamber, rate-adaptive pacemaker/DDDR capabilities, plus incremental features for the treatment of atrial arrhythmias. VENTAK PRIZM AVT is designed to detect and terminate ventricular arrhythmias (ventricular tachycardia and fibrillation), atrial arrhythmias (supraventricular tachycardias, atrial flutter and atrial fibrillation (AFib)), and provide bradycardia therapy (atrial and ventricular pacing). Atrial and ventricular tachyarrhythmia therapy may include both low and high-energy shocks and/or antitachycardia pacing (ATP).

3.1 VENTAK PRIZM AVT PULSE GENERATOR

The VENTAK PRIZM AVT pulse generator, Model 1900 external case is constructed of titanium with a premolded polyurethane lead connector assembly. The inner assembly (hermetically sealed in the titanium case) contains an inner structure of discrete electrical components, a hybrid circuit assembly, batteries (two, lithium-silver vanadium oxide, and two high-voltage capacitors). The VENTAK PRIZM AVT device has the standard AICD connections including two DF-1 defibrillation lead ports, one IS-1 ventricular lead port, and one IS-1 atrial lead port. There is an additional DF-1 lead port in the header to allow connection of an optional second defibrillation/cardioversion lead in the coronary sinus to provide "A-TRIAD[™]" defibrillation therapy for atrial arrhythmias.

Sensing and Ventricular Detection: Rate is the primary detection criteria with a programmable range of 90-250 bpm in conjunction with programmed duration (1-60 seconds). The VENTAK PRIZM AVT pulse generator uses automatic gain control circuitry (AGC) in the atrium and the ventricle to sense tachyarrhythmias and bradyarrhythmias.

Each arrhythmia is classified into a programmed rate zone defined by a lower ventricular rate boundary. The pulse generator can be programmed in a one-zone, two-zone, or a three-zone configuration. The VENTAK PRIZM AVT pulse generator also provides a series of detection enhancements: Onset, AFib Rate Threshold, Stability, V Rate>A Rate, and Sustained Rate Duration (SRD). Detection enhancements are designed to increase the

specificity of the rate detection algorithm and can be used to distinguish between different types of arrhythmias within a single rate zone.

In addition, like other members of the legally marketed VENTAK family, the VENTAK PRIZM AVT incorporates atrial rate information obtained from the atrial lead into the detection enhancement features. Detection enhancements are designed to increase the specificity of the rate detection algorithm and can be used to distinguish between different types of arrhythmias in the lower zone(s) of a multi-zone configuration.

Atrial Detection: Incremental to the VENTAK PRIZM AVT from VENTAK PRIZM DR/VR is the ability to detect atrial tachyarrhythmias. Similar to the initial detection criteria for a ventricular tachyarrhythmia episode where a ventricular arrhythmia is initially declared when 8 of 10 fast ventricular beats are detected, an atrial arrhythmia is initially declared when 32 of 40 fast atrial beats are detected. Because of the extended period of atrial detection, the device will always first look to determine that an arrhythmia is NOT ventricular in origin (did not meet the ventricular detection criteria) before considering the episode for declaration of an atrial event. If at any time during the atrial detection period, the ventricular criteria become fulfilled, the device will abort any activity related to atrial therapy and address the ventricular event in the same manner as a VENTAK PRIZM DR device.

Similar in function to the ventricular detection zones, two atrial rate detection zones are available in VENTAK PRIZM AVT that allow physicians to program therapy based on the rate of the atrial arrhythmia identified. In addition, Atrial Rhythm Classification (ARC) is an algorithm available as an option to an AFIB zone, when the device is programmed in a two-zone configuration. ARC can be used in place of rate to distinguish between supraventricular tachycardias (SVT) and atrial fibrillation (AFIB) based on a combination of criteria including rate, range and standard deviation.

Ventricular Therapy: The VENTAK PRIZM AVT ventricular tachyarrhythmia therapy features are identical to the VENTAK PRIZM DR/VR.

A tachyarrhythmia that falls into the programmed heart rate range (VT-1, VT, or VF) will be treated by the ventricular therapy programmed for that range. The initial therapy is invoked when the criteria for detection is satisfied. Ventricular tachyarrhythmia therapy, which includes one or two ATP schemes and nominally up to five shocks, may be delivered to the ventricle. The first two defibrillation or cardioversion shocks range from 0.1 to 31 joules (J) stored energy. Three (3) additional shocks are available at 31 J in all zones with up to three auxiliary shocks available in the VF Zone.

For both ventricular and atrial therapy, the type and polarity of the shock waveform is programmable. If multiple therapies are required, the hierarchy of therapy is a progression from pacing to shock, with shock energies always equal to or greater than the previous

shocks within the same episode. Following shock therapy, separately programmable redetection parameters are available for a specified time period to discriminate post-shock rhythms.

Atrial Therapy: Incremental to the VENTAK PRIZM AVT from the VENTAK PRIZM DR is the ability to treat atrial arrhythmias with detection initiated atrial anti-tachycardia pacing or atrial cardioversion/defibrillation shocks.

Atrial antitachycardia pacing (ATP) ATP schemes available consist of bursts of pacing pulses delivered between the atrial pace-sense electrodes. The four types of ATP therapy schemes available include: burst, ramp, scan and ramp/scan.

Atrial Shock Therapy is provided when atrial detection criteria have been met and R-wave synchronization has been performed to determine an appropriate R-wave sequence on which to deliver the shock. The two shock vectors available to treat atrial arrhythmias in the VENTAK PRIZM AVT are the V-TRIAD and A-TRIAD (represents atrial TRIAD) vectors. The V-TRIAD shock vector is the nominal therapy vector and is the same configuration used to treat ventricular tachyarrhythmias. The A-TRIAD vector is an optional vector that is available when the VENTAK PRIZM AVT is used with a PERIMETER Coronary Sinus (CS) lead. In this configuration the pulse generator also acts as an electrode in conjunction with the upper SVC electrode of the ENDOTAK defibrillation lead and the electrode of the CS lead, forming the A-TRIAD (three-electrode) system.

In addition, VENTAK PRIZM AVT also offers Patient Controlled Atrial Shock Therapy, an option, which allows either the physician or patient to request atrial shock therapy with the Model 2930 RHYTHM ASSISTANT Patient Activator. In Patient Controlled mode, when the patient or physician places the activator over the device, the device will confirm that an atrial arrhythmia is present. Therapy is then provided ONLY if the atrial shocks are programmed, atrial detection criteria have been met and R-wave synchronization has been performed to determine an appropriate R-wave sequence on which to deliver the shock.

Bradycardia Pacing Features: The VENTAK PRIZM AVT device includes the standard brady pacing features from the VENTAK PRIZM family of devices for the atrium and ventricle in normal, temporary and post-shock modes. Incremental bradycardia pacing therapies are Post A Therapy pacing, Atrial Pacing Preference (APP) and ProACT. Post A Therapy (ATP and shock) pacing capabilities are separately programmable to ensure capture immediately following atrial therapy. APP and ProACT are two rate enhancements designed to promote atrial pacing by increasing the pacing rate.

Memory and Diagnostics: Programmed parameters as well as model number, serial number, episode count, shock lead impedance, shocks delivered and diverted, and battery

status are stored in the pulse generator's memory consistent with the VENTAK PRIZM family of devices.

The VENTAK PRIZM AVT pulse generator provides the following diagnostic features (also previously available in VENTAK PRIZM DR):

- Real-time electrograms and event markers which assist in evaluating system response;
- Non-invasive methods for inducing arrhythmias, including Shock on T induction
- Automatic battery voltage evaluation;
- Automatic capacitor reformation every 90 days;
- Pacing lead impedance, which can be used as a relative indicator of lead status over time;
- Battery status indicator displayed as one of three levels: Beginning of Life (BOL), Elective Replacement Indicator (ERI), and End of Life (EOL);
- Programmable audible tones (beeper function) which can be used to assist with system evaluation such as pulse generator batter status, capacitor charging, and ventricular rate sensing;
- Magnet control which can be programmed OFF to ensure the tachy mode will not be changed in the presence of a magnetic field, or programmed ON to allow the tachy mode of the pulse generator to be changed from OFF (inactive) or Monitor Only mode to Monitor + Therapy mode or from Monitor + Therapy to OFF mode; and
- The magnet can also divert or inhibit therapy, and activate the beeper when Enable Magnet Use is programmed ON.

The VENTAK PRIZM AVT has also enhanced the diagnostic features to include information related to the new atrial therapy as listed below:

- Added real time event markers for new features: Atrial detection, Atrial therapy (ATP and shock), Atrial Pacing Preference (APP)/ ProACt and Ventricular Rate Regulation (VRR).
- Reorganized EP test screen into separate Atrial and Ventricular EP test screens to better differentiate between atrial and ventricular arrhythmia induction methods.
- Added atrial information to System Summary Screen.
- Provided additional counters for atrial event, episode and therapy.
- Added Atrial Shock Lead Integrity Test to provide data on optional coronary sinus lead.
- Added information identifying concomitant atrial and ventricular episodes.

3.2 THE PROGRAMMING SYSTEM AND MODEL 2849 SOFTWARE APPLICATION

A legally marketed programming system (Model 2920 PRM and its accessories) provides communication between the physician and the pulse generator via radio frequency (RF) telemetry. This allows identification of the implanted pulse generator. The Model 2849 Software Application contains the software code specifically required to interface with the Guidant VENTAK PRIZM AVT pulse generator. The software allows the user to interrogate, program and command certain functions such as, parameter programming codes, intracardiac electrograms, and event markers.

3.3 PERIMETER CS LEAD

The PERIMETER Coronary Sinus (CS) lead, Models 0202, 0203, and 0204, is an implantable atrial defibrillation transvenous lead designed for use with the Guidant VENTAK PRIZM AVT AICD. The PERIMETER CS lead is an optional unipolar lead for use in patient's requiring lowered atrial defibrillation thresholds.

The PERIMETER CS lead, a Guidant ENDOTAK® lead, and the metallic housing of the VENTAK PRIZM AVT AICD use the Guidant A-TRIAD electrode system for defibrillation energy delivery. Appropriately positioned in the heart, the shock electrodes of the PERIMETER CS lead, an ENDOTAK lead proximal coil, and the pulse generator case are intended to form a bi-directional vector for effective delivery of defibrillation pulses to the atria of the heart.

3.4 THE RHYTHM ASSISTANT

The RHYTHM ASSISTANT offers a user-friendly interface for patients to interact with their implanted AICD via RF telemetry. The RHYTHM ASSISTANT features easy to use buttons, intuitive visual symbols and clear voice feedback that allows patients to inquire the status of their implanted device, activate therapy if appropriate, divert therapy if necessary and record electrograms if desired. The PARTNER Rhythm Assistant is an optional, battery-powered, telemetry device used in conjunction with the implanted PRIZM AVT Model 1900 device for determination of atrial rhythm and self-activation of programmed patient atrial shocks. When the Model 1900 device is programmed to Patient Controlled Mode (Atrial tachy mode), a patient can use the Model 2930, PARTNER Rhythm Assistant to inquire about the status of their atrial rhythm, and if an arrhythmia is present, deliver programmed atrial shock therapy. In this mode it can also be used to trigger storage of an electrogram. When the PRIZM AVT device is programmed to Automatic or Monitor Only Mode, a patient

can use the PARTNER Rhythm Assistant to inquire about the status of their atrial rhythm, but is unable to affect delivery of atrial shock therapy.

The PARTNER Rhythm Assistant is designed to give a patient audible and visual feedback, in the form of voice commands and/or simple lighted symbols. It has two buttons, a Status button which will communicate with the PRIZM AVT Model 1900 device to retrieve information about rhythm status, and a Therapy button which when pressed, will request atrial shock therapy.

4 CONTRAINDICATIONS

The VENTAK PRIZM AVT AICD is contraindicated in:

- Patients whose ventricular tachyarrhythmias may have a reversible cause, such as 1) digitalis intoxication, 2) electrolyte imbalance, 3) hypoxia, or 4) sepsis, or whose ventricular tachyarrhythmias have a transient cause, such as 1) acute myocardial infarction, 2) electrocution, or 3) drowning
- Patients who have a unipolar pacemaker
- Patients who exhibit permanent (chronic) AFib, which is refractory to all therapies

5 WARNINGS AND PRECAUTIONS

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

6 ALTERNATIVE PRACTICES AND PROCEDURES

Alternative therapies include the use of antiarrhythmic medication, electrical ablation and cardiac surgery, and other legally marketed implantable cardioverter defibrillators.

7 MARKETING HISTORY

The VENTAK PRIZM AVT (Model 1900) and the PERIMETER CS lead (Models 0202/0203/0204) are distributed commercially outside the United States. These devices are approved for sale in Europe and Hong Kong.

The METRIX System was commercially distributed outside the United States after receiving CE mark June 4, 1997. Distribution has since been ceased due to a lack of product availability and the subsequent approval of Guidant's VENTAK PRIZM AVT System.

Neither the VENTAK PRIZM AVT, the METRIX, nor the PERIMETER CS leads, have been withdrawn from market in any country for any reason related to the safety and effectiveness.

8 ADVERSE EVENTS

The VENTAK PRIZM AVT/PERIMETER CS Study (hereafter referred to as the PRIZM AVT Study) was a prospective, multi-center, randomized within patient, clinical evaluation conducted at 25 sites in the United States and enrolled a total of 110 patients to document appropriate system performance of the VENTAK PRIZM AVT in humans.

Table 1 provides information on all adverse events reported since the date of implant in patients attempted or implanted with the VENTAK PRIZM AVT AICD System in the United States study. During this period, a total of 78 events were reported in 43 patients. Of these, 21 were classified as complications, and 57 were classified as observations.

Table 1: Adverse Events

(78 Events in 43 patients implanted or attempted with the VENTAK PRIZM AVT/PERIMETER CS Lead, 349 total device months)

	Total Number Of Events (Number of Patients)	% Complications (Patients) N=96 Patients	Complications per 100 Device Months (Events) 349 Months	% Observations (Patients) N=96 Patients	Observations per 100 Device Months (Events) 349 Months
Total Adverse Events	78 (43)	15.6 (15)	6.0 (21)	39.6 (38)	16.3 (57)
CS Lead-Related Events					
Lead dislodgment – Coronary Sinus	1 (1)	1.0 (1)	0.3 (1)	0.0 (0)	0.0 (0)
PG-Related Events					
Pectoral muscle stimulation	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
RA Lead-Related Events					
Intermittent sensing - atrium rate - brady	1 (1)	1.0 (1)	0.3 (1)	0.0 (0)	0.0 (0)
Lead dislodgment – right atrium	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Oversensing-atrium pace sense-brady	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Undersensing-atrium pace sense-brady	2 (2)	0.0 (0)	0.0 (0)	2.1 (2)	0.6 (2)
RV Lead-Related Events					
Brady capture - RV	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Brady capture - ventricle	2 (1)	1.0 (1)	0.3 (1)	1.0 (1)	0.3 (1)
Inappropriate shock due to oversensing	2 (2)	0.0 (0)	0.0 (0)	2.1 (2)	0.6 (2)
Oversensing - ventricle rate - tachy	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Phantom shock	2 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.6 (2)
Threshold Difficulty	3 (2)	1.0 (1)	0.3 (1)	2.1 (2)	0.6 (2)
Undersensing - ventricle rate sense-tachy	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Subtotal Device-Related Events	19 (14)	4.2 (4)	1.1 (4)	12.5 (12)	4.3 (15)

	Total Number Of Events (Number of Patients)	% Complications (Patients) N=96 Patients	Complications per 100 Device Months (Events) 349 Months	% Observations (Patients) N=96 Patients	Observations per 100 Device Months (Events) 349 Months
Procedure-Related Events					
Hematoma	4 (2)	2.1 (2)	0.9 (3)	1.0 (1)	0.3 (1)
Post surgical wound discomfort	4 (4)	0.0 (0)	0.0 (0)	4.2 (4)	1.1 (4)
Subtotal Procedure Related Events	8 (6)	2.1 (2)	0.9 (3)	5.2 (5)	1.4 (5)
Cardiovascular Related Events					
Arrhythmia - SVT	3 (3)	1.0 (1)	0.3 (1)	2.1 (2)	0.6 (2)
Arrhythmia - VT	2 (2)	1.0 (1)	0.3 (1)	1.0 (1)	0.3 (1)
Bradycardia	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Change in arrhythmia	2 (2)	0.0 (0)	0.0 (0)	2.1 (2)	0.6 (2)
Chest pain	2 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.6 (2)
Congestive heart failure	8 (8)	4.2 (4)	1.1 (4)	4.2 (4)	1.1 (4)
Death	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Dizziness	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Dyspnea (shortness of breath)	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Fatigue	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Hypotension	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Pseudoaneurysm	1 (1)	1.0 (1)	0.3 (1)	0.0 (0)	0.0 (0)
Shortness of breath	3 (3)	0.0 (0)	0.0 (0)	3.1 (3)	0.9 (3)
Syncope	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Thrombus	1 (1)	1.0 (1)	0.3 (1)	0.0 (0)	0.0 (0)
Ventricular fibrillation	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Ventricular tachycardia	1 (1)	0.0 (0)	0.0 (0)	1.0 (1)	0.3 (1)
Subtotal Cardiovascular Related Events	31 (20)	6.3 (6)	2.3 (8)	15.6 (15)	6.6 (23)
Total Non-cardiovascular Related Events	20 (17)	6.3 (6)	1.7 (6)	11.5 (11)	4.0 (14)

A total of 4 deaths occurred during the study as shown in Table 2. One death was preoperative. An independent events committee adjudicated three of the four deaths. One death has a pending review.

Table 2: Deaths that Occurred During the Study

Death Classification	Center Reported (N)	Events Committee (N)	Pending review
Unknown	1	0	1
Sudden Cardiac	1	1	0
Non-sudden Cardiac	0	1	0
Non-cardiac	2	1	0
All-Cause Deaths	4	3	1

9 POTENTIAL ADVERSE EVENTS

Based on the literature and ICD implant experience, the following alphabetical list includes possible adverse events associated with implantation of an ICD system:

• Acceleration of arrhythmias	• Keloid formation
• Air embolism	• Lead abrasion
• Allergic reaction	• Lead discontinuity
• Bleeding	• Lead fracture, insulation break
• Cardiac perforation	• Lead tip deformation and/or breakage
• Chronic nerve damage	• Lead migration/dislodgement
• Defibrillation-induced ventricular proarrhythmia	• Local tissue reaction
• Early recurrent atrial fibrillation	• Myocardial damage, injury, irritability
• Erosion	• Pneumothorax
• Excessive fibrotic tissue growth	• Post-shock disturbances
• Extrusion	• Potential mortality due to defibrillate or pace, or other non-device-related causes
• Fluid accumulation (seroma)	• Random device component failure
• Formation of hematomas or cysts	• Shunting current or insulating myocardium during defibrillation with internal or external paddles
• Incomplete connection with pulse generator	• Thromboemboli
• Infection	• Transvenous lead-related thrombosis
• Inappropriate shocks	• Venous occlusion/perforation

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

• Dependency	• Fear of shocking while conscious
• Depression	• Fear that shocking capability may be lost
• Imagined shocking	• Fear of premature battery depletion

10 SUMMARY OF STUDIES

10.1 NONCLINICAL LABORATORY TESTING

Prior to initiation of clinical studies, Guidant conducted the following bench testing (i.e., components, assemblies, device system and software tests), biocompatibility evaluation, sterilization validation on the VENTAK PRIZM AVT 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 VENTAK PRIZM

AVT device, PERIMETER CS lead and the entire VENTAK PRIZM AVT 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 VENTAK PRIZM AVT and lead system.

10.1.1 PULSE GENERATOR: DESIGN VERIFICATION TESTING (DVT)

The design verification testing of the VENTAK PRIZM 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 as described below:

10.1.1.1 **COMPONENT TESTING:** The major components for the VENTAK PRIZM AVT are identical to the legally marketed VENTAK PRIZM (PMA P960040). The header was modified to include an additional DF-1 port. The new header was tested and passed (Table 3).

Table 3: Component Testing

Summary of Component Testing	Sample Size	Test Results (Pass/Fail)
Header: Visual inspection, dimensional analysis, retainer ring weld strength, thermal shock, high temp/high humidity storage, methylenedianiline (MDA), cytotoxicity, pyrogenicity, material analysis.	1 to 35	Pass

10.1.1.2 **ELECTRONIC AND MECHANICAL DESIGN VERIFICATION TESTS:** Design verification testing was done to demonstrate that all device level requirements were met. Mechanical design verification testing was performed on VENTAK PRIZM AVT devices that were exposed to a representative manufacturing process, including sterilization cycles and vibration tests (Table 4).

Table 4: Electrical and Mechanical Design Verification Testing

Summary of Pulse Generator DVT	Sample Size	Test Results (Pass/Fail)
Electronic Design Verification Testing		
The tests were conducted on the VENTAK PRIZM AVT at four different stages of the pulse generator 1) the welded pulse generator assembly, 2) pulse generators with external battery connections, 3) the hybrid system board, and 4) the system test board. Tests were conducted in the following functional areas: Telemetry operation, Sensing, Pacing, Shocking, Magnet, Beeper, Electrograms, Device Clock, Battery Status, Faults/Error handling. The VENTAK PRIZM AVT met electrical design specifications	6-13	Pass
Mechanical Design Verification Testing		

Summary of Pulse Generator DVT	Sample Size	Test Results (Pass/Fail)
<p>Tests were conducted on the VENTAK PRIZM AVT in the main functional areas: mechanical requirements, environmental tests, and package and shipping tests. Such tests included internal atmosphere, connector assembly lead adaptor compatibility, X-ray identification, thermal shock and cycling, mechanical shock, vibration, etc. The VENTAK PRIZM AVT met mechanical device specifications.</p> <p>The IS-1/DF-1 connector assembly met requirements of ISO 5841-3: 1992(E) and ISO 11318: 1993(E).</p>	1-12	Pass
<p>Packaging and Shipping tests were done to ensure that the device remains damage free and that the package remains functional while in transit and storage mode prior to implant. Labeling must remain legible.</p>	8	Pass

10.1.1.3 ELECTROMAGNETIC COMPATIBILITY (EMC) EVALUATION: The VENTAK PRIZM AVT pulse generator was evaluated to ensure that the device will operate safely in the presence of commonly encountered electromagnetic interference (EMI) such as cellular phones, cordless phones, electronic article surveillance systems (EASS), and radios designed for the home (provided labeled guidances are adhered to). Testing was based on prEN45502 Active Implantable Medical Devices, Part 2-1 Requirements for active implantable medical devices intended to treat bradyarrhythmia (cardiac pacemakers) Version 9.0, draft Nov. 1996 and the Association for the Advancement Medical Instrumentation (AAMI) Pacemaker Standard, August 1975.

Table 5: Electromagnetic Compatibility (EMC) Testing

Summary of Electromagnetic Compatibility (EMC) Testing	Sample Size	Test Results (Pass/Fail)
<p>VENTAK PRIZM AVT pulse generator performance was evaluated when subjected to the following:</p> <ul style="list-style-type: none"> • Radiated Interference: radio frequencies at 27 MHz and 72 MHz, both pulsed and continuous, at amplitudes up to 200 V/m field strength as defined in the AAMI PC 69 standard, • Conducted frequency from 16.6 Hz to 50 MHz as defined in prEN45502 Active Implantable Medical Devices. Part 2-1 Requirements for active implantable medical devices intended to treat bradyarrhythmia (cardiac pacemakers). Version 9.0. • High voltage external defibrillation shocks • Exposure to electrostatic discharge pulses • Exposure to RF Ablation Energy • Exposure to Diagnostic Ultrasound • Exposure to Electronic Article Surveillance Systems (EASS) per Georgia Technical Institute EASS test protocol for Implantable Medical Devices, Version 2.0. • Exposure to electrocautery 	4	Pass*

Summary of Electromagnetic Compatibility (EMC) Testing	Sample Size	Test Results (Pass/Fail)
• Exposure to static magnetic fields up to 10mT (the reed switch is activated/deactivated when the field is maintained at >1.0mT.)		
Summary of Cellular Telephone Testing for VENTAK PRIZM AVT		
Resistance to Interference from Cellular Telephones (450 MHz to 3000 MHz) as defined in the AAMI PC69 standard	4	Pass

10.1.1.4 **BATTERY CAPACITY TEST:** The VENTAK PRIZM AVT battery is identical to the VENTAK PRIZM battery; therefore, the VENTAK PRIZM battery testing applies to the VENTAK PRIZM AVT and was not repeated. However, a Battery Capacity Test was performed for the VENTAK PRIZM AVT device to establish the usable capacity of the cell (battery) and the reserve capacity between ERI (Elective Replacement Indicator) and EOL (End Of Life) when used with the pulse generator's electronics (Table 6).

Table 6: Battery 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. The battery met Guidant specification.	3	Pass

10.1.1.5 **PULSE GENERATOR SOFTWARE DESIGN VERIFICATION TEST:** Design verification testing of the software in the VENTAK PRIZM AVT pulse generators (also known as firmware) is listed below in Table 7.

Table 7: Pulse Generator Software Design Verification Test

Summary of Pulse Generator Software Design Verification Test: (from VENTAK PRIZM AVT)	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 1.5.00.	PG Software	Pass with 10 anomalies* that have no effect on patient safety or device effectiveness

*1) In one test case, the recorded pre therapy cardiac cycle interval averages were inaccurate. 2) In one test case, it is possible for the delivery of atrial shock to be delayed by one cardiac cycle. 3) In one different test case, it is possible to deliver an atrial shock one cardiac cycle early. 4) In one test case, although delivery of pacing occurs properly, labeling of one pace event for APP or ProAct could occur one cardiac cycle early. 5) In one test case, although delivery of pacing occurs properly, labeling of one pace event for Up Rate Smoothing could occur one cardiac cycle early. 6) This anomaly is a result of a test function that is not enabled in a clinical setting. 7) This anomaly is a result of a test function that is not enabled in a clinical setting. 8) In one test case, an atrial therapy counter is incorrectly incremented. 9) In one test case, after autocapacitor reform caused end of battery life, atrial tachy mode is turned off and the the battery condition improves

to Elective Replacement Indication, it is possible for the physician to change change to mode setting to on but indication is off. 10) In one test case a brief delay in completion of atrial anti-tachy pacing occurred. These anomalies have no effect on patient safety or device effectiveness.

10.1.2 PROGRAMMER SOFTWARE APPLICATION: DESIGN VERIFICATION TESTING

The design verification testing of the Model 2849 Programmer Software Application (the PRM Software) included a pulse generator software verification test and arrhythmia scenario test.

10.1.2.1 **PROGRAMMER SOFTWARE DVT:** The Programmer Software Design Verification Test was performed to ensure that the software meets the functional software requirements specifications. Testing was conducted with either a VENTAK PRIZM AVT system including a pulse generator software verification test and arrhythmia scenario test. VENTAK PRIZM AVT pulse generator, a Model 2930 RHYTHM ASSISTANT and a Model 2920 PRM (Programmer, Recorder, Monitor) with the Model 2909 Multiple Application Utility (MAU) and Model 2849 Software Application installed on it, or the same system with a pulse generator simulator replacing the VENTAK PRIZM AVT pulse generator (Table 8).

Table 8: Model 2848 Software Application DVT

Summary of Model 2848 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 2.4 for use with the Model 2920 PRM.	PG Software	Pass

10.1.2.2 **ARRHYTHMIA SCENARIO TEST:** GUIDANT performed an Arrhythmia Scenario Evaluation Test to verify that the pulse generators in this submission appropriately sense heart signals. Applied signals are taken from a library of real human arrhythmia tape recordings. In addition, the ability of the pulse generators to transmit electrogram signals was tested.

Table 9: Arrhythmia Scenario Test

Summary of Pulse Generator Software Design Verification Test: (from VENTAK PRIZM AVT)	Sample Size	Test Results (Pass/Fail)
Test input data included the following waveforms: 1) Normal Sinus Rhythms Test 2) Monomorphic Ventricular Tachycardia Rhythms Test, 3) Polymorphic Ventricular 4) Tachycardia (VT) Rhythms Test and 5) Atrial and Ventricular Scenario Rhythms Test 6) Electrograms Equivalence Test. In addition, because of additional new features specific only to the VENTAK PRIZM AVT, the Arrhythmia Scenario Evaluation Test also included evaluation of R-wave synchronization, and Atrial Rhythm Classification (ARC).	PG Software	Pass

10.1.3 PERIMETER CS LEAD: DESIGN VERIFICATION TESTING

Electrical and mechanical integrity of the PERIMETER CS lead were performed to demonstrate conformance to a battery of lead tests and are summarized below. All leads were preconditioned with temperature cycling, and shipping test conditions prior to functional testing.

Table 10: PERIMETER CS Lead DVT

Summary of PERIMETER CS Lead DVT	Sample Size	Test Results (Pass/Fail)
Full Lead Testing:		
<u>Packaging visual</u> verified that the packaging met the requirements of the sterile pack and final pack engineering documents.	8	Pass
<u>Lead Introducer</u> testing verified that the PERIMETER CS Lead will pass through a 7-French introducer with no damage to the lead.	8	Pass
<u>Sylet Insertion/Withdrawal</u> testing verified that force required to insert and withdraw a 0.017" diameter stylet is less than 7 oz.	8	Pass
<u>Electrical Resistance</u> : DC Resistance was required to be less than 5 ohms.	8	Pass
<u>Pressure Decay</u> testing verified the integrity of the insulation and bonds. Leads were pressurized to 14 ± 2 PSI with dry nitrogen; leads must not exhibit evidence of nitrogen leakage.	8	Pass
<u>Axial Load</u> testing verified that the lead can withstand implant forces and demonstrated compliance to the requirements defined by prEN 45502-2-2, section 23.3. (draft Nov. 96).	8	Pass
<u>Defibrillation Tank</u> : testing confirmed the energy waveform delivery capability of the lead by applying extensive monophasic and biphasic pulses after soaking in a saline solution.	8	Pass
DF-1 Terminal Testing:		
<u>DF-1 Insertion/Withdrawal Force/Set-Screw Deformation</u> : this test verified that the DF-1 terminal meets maximum insertion/withdrawal requirements per ISO 11318:section 4.1.22.	8	Pass
<u>DF-1 Terminal Insertion/Withdrawal Durability</u> : this test verified the durability of the connector when it is subjected to repeated insertions and withdrawal cycles using a pulse generator DF-1 lead port	8	Pass
<u>DF-1 High Voltage Seal Integrity</u> : this test verified that the DF-1 terminal subassembly could be electrically isolated from the external environment under high voltage conditions.	8	Pass
<u>DF-1 CEN/CENELEC Connector Flex Fatigue Test</u> : this test verified that the DF-1 terminal subassembly conforms to the prEN 45502-2-2 connector flex fatigue test.	8	Pass
Flex Fatigue Testing:		
<u>Bell Mouth Flex Fatigue Test of Lead Conductor</u> verified compliance of the lead conductor with the requirements of prEN 45502.	8	Pass
<u>Fixation Bias Fatigue</u> testing verified that the spiral fixation bias region of the PERIMETER CS lead can withstand cyclic fatigue associated with intracardiac	12	Pass

Summary of PERIMETER CS Lead DVT	Sample Size	Test Results (Pass/Fail)
coronary vein placement.		
Manufacturing Process Validation for Bond/Weld/Strength Testing:		
All welded electro-mechanical connections must withstand a minimum assembly joint pull force. All load-bearing molded and bonded connections must have a minimum dry pull strength.	15-60	Pass

10.1.4 PRIZM AVT SYSTEM TESTING

10.1.4.1 DESIGN VALIDATION TESTING

Design validation testing that was conducted on the VENTAK PRIZM AVT system included system features tests and a simulated use test (field study).

Table 11: System Design Validation Testing

System Design Validation Testing	Sample Size	Test Results (Pass/Fail)
System Features Tests: Tests were conducted to exercise major features of the VENTAK PRIZM AVT system. Each test demonstrated the functionality of a given feature and verified that the programmer had properly loaded parameters into the pulse generator. Feature groups tested included programmer support, lead support, tachy modes, tachyarrhythmia detection, tachyarrhythmia therapy, bradycardia modes, bradycardia therapy, diagnostics, and faults/error handling. The system performed as expected based on the specifications.	Systems consisting of VENTAK PRIZM AVT PG and programmer software.	Pass
Simulated Use Test: From a field user perspective, Guidant field clinical engineers evaluated the performance of the VENTAK PRIZM AVT/PERIMETER CS system and verified that the labeling/manuals were easily understood and the entire VENTAK PRIZM AVT /PERIMETER CS system performed as expected during clinical use. Clinical scenarios were simulated using the pulse generator, programmer (PRM), PRM software, a cardiac signal simulator, and the PERIMETER CS lead and accessories (stylets).	3 users performed tests.	Pass

10.1.4.2 SAFETY AND RISK ANALYSIS

The safety and risk analysis of the VENTAK PRIZM AVT system was conducted to identify potential hazards and their causes, and to take appropriate actions to minimize patient and user risk. Analysis included the following:

Hazard Analysis: Hazard Analysis identified potential hazards with using the system devices and documented the response taken to control the probability of occurrence or to

minimize the risk. Potential hazards were peer reviewed for adequacy of the mitigation; residual risk was deemed acceptable.

Failure Modes and Effects Criticality Analysis (FMECA): FMECA identified potential design, test, or process inadequacies that could adversely affect the safety and performance of the device and recommended corrective actions to eliminate or minimize these inadequacies. Three recommendations were identified and were incorporated into device testing scheme.

Reliability Prediction Analysis: The Reliability Prediction Analysis was performed using field performance failure rates of similar pulse generators along with the “Parts Stress Analysis Prediction” procedure in MIL-HDBK-217F in the absence of field performance data. The analysis resulted in an expected field performance of 0.147% failures/month.

10.1.4.3 STERILIZATION VALIDATION

Sterilization assessments were performed and validated that the VENTAK PRIZM AVT pulse generator, PERIMETER CS leads, and system accessories can be effectively sterilized with the Getinge Oxyfume 2000® or the 100% ethylene oxide (EtO) sterilization process. These processes are identical to those used for Guidant’s commercially available ICD pulse generators and leads.

For the VENTAK PRIZM AVT pulse generator, the sterility assurance level (SAL) was estimated to be 10⁻²². For the PERIMETER CS lead, the SAL was estimated to be 10⁻²¹.

10.1.4.4 SHELF LIFE FOR PMA DEVICES

Included in Table 12: Device Shelf Life is the expiration dating for all devices included in this sPMA submission.

Table 12: Device Shelf Life

Device	Shelf Life
VENTAK PRIZM AVT, Model 1900	Expiration dating for this device has been established and approved at 1 year from the battery-attach date.
PERIMETER CS Lead, 0202, 0203, 0204	Expiration dating for this device has been established and approved at 4 years from the date of sterilization.
RHYTHM ASSISTANT	Expiration dating for this device has been established and approved at 6 years from the battery-attach date.

Device	Shelf Life
Accessories: <ul style="list-style-type: none"> • Stylet kits, Model 6321, 6322, 6323, 6324, 6325, 6236, 6327, 6328, 6329 	Expiration dating for these devices has been established and approved at 4 years from the date of sterilization.

10.2 BIOCOMPATIBILITY EVALUATION

The biocompatibility of the tissue contacting materials used in the VENTAK PRIZM AVT pulse generator, and the PERIMETER CS lead and lead accessories was established in previous PMA applications (P890061, P910077, P960040, P010012 and P910073, P950001, P960060, P010012 respectively). Pulse generator materials include: polyurethane, titanium, and silicone rubber that are all currently used in Guidant's commercially available ICD devices.

Materials used in the PERIMETER CS lead that have direct long-term tissue or blood contact include: titanium, platinum iridium, silicone rubber (including silicone rubber with titanium oxide pigment), stainless steel and polyurethane. The biocompatibility of titanium, platinum, polyurethane and silicone rubber (including silicone rubber with titanium oxide pigment) has been established in previous PMA applications (P910073, P950001, P960060, and P010012). Guidant performed biocompatibility testing on these materials and all were determined to be biocompatible. There were numerous tests done for the various materials as reported in M00027/M003. Tests included, but were not limited to, cytotoxicity, hemolysis, Ames Mutagenicity, and acute and chronic system toxicity.

10.3 ANIMAL STUDIES

Guidant conducted an animal study in compliance with Good Laboratory Practice (GLP) regulations (21 CFR § 58) with the VENTAK PRIZM AVT system in an *in-vivo* canine model to demonstrate that the system meets user needs and intended uses. The animal study also addressed the compatibility of the system components and verified that the components of the VENTAK PRIZM AVT system were compatible, and the system performed safely for its intended use. In addition to the system study described above, Guidant conducted an animal study that verified the PERIMETER CS lead DFT levels were unaffected by medical adhesive backfill.

11 SUMMARY OF CLINICAL STUDIES

Guidant conducted the VENTAK PRIZM AVT Clinical Study to demonstrate the safety and effectiveness of the PRIZM AVT atrial and ventricular defibrillator (Model 1900), the

PERIMETER CS Lead (Models 0202, 0203, 0204), and the RHYTHM ASSISTANT Therapy Activator (Model 2930).

11.1 VENTAK PRIZM AVT STUDY

11.1.1 SOURCES OF SAFETY AND EFFECTIVENESS DATA

The VENTAK PRIZM AVT System includes the VENTAK PRIZM AVT pulse generator, Model 1900, the Programmer Software Application, Model 2849 (Version 2.4), and the PERIMETER Coronary Sinus Defibrillation Lead, Models 0202/0203/0204. To support the safety and effectiveness of the VENTAK PRIZM AVT System, Guidant used two sources of clinical data, the VENTAK PRIZM AVT Clinical Study (IDE G010103) and the InControl METRIX Clinical Study (IDE G960033). The InControl METRIX Clinical Study included the METRIX Atrial Defibrillator, the Perimeter RA Model 7205 Right Atrial Defibrillation lead, and a PERIMETER CS Model 7109 Coronary Sinus Defibrillation lead. Guidant acquired InControl and continued to monitor the METRIX trial, which enrolled a total of 111 patients at 26 study centers. All safety and effectiveness study objectives were met, as was presented in the final closeout report June 25, 2002. Due to limitations in manufacturability and the pursuit of Guidant's VENTAK PRIZM AVT System, these InControl products were never pursued for US market release. The data from the METRIX trial was used to support approval of the Guidant PERIMETER CS lead, Models 0202/0203/0204 as is described further in Section 11.1.5.7.

11.1.2 VENTAK PRIZM AVT STUDY DESIGN

The VENTAK PRIZM AVT study was a prospective multi-center, randomized within patient, clinical evaluation conducted at 25 sites in the United States and enrolled a total of 110 patients. All patients received two randomization assignments prior to implantation. Randomization A affected the programming for VF conversion testing done at implant. All patients were randomized (1:1) to having Atrial Rhythm Classification(ARC) and atrial pacing features (APP, Post Atrial Therapy APP; ProACT), programmed either "ON" or "OFF," and then were crossed over to the other group after the first successful VF induction. Once VF was appropriately induced, both with features "ON" and "OFF," subsequent VF inductions were programmed per the physician's discretion. Following all implant testing, Randomization B determined the chronic programming for each patient. Patients were randomly assigned (1:1) to having atrial pacing features (APP, Post Atrial Therapy APP and ProACT) either "ON" or "OFF" for a 3 month duration and then crossed over to the opposite programming for a subsequent 3 month duration. For this chronic programming, VRR and ARC were always programmed "ON". Patients remained programmed in the assigned mode

between discharge and the 3-month follow-up visit when they were crossed over to the opposite programming mode.

11.1.3 INCLUSION/EXCLUSION CRITERIA

To be included, patients had to be:

- Geographically stable residents available for follow-up
- Willing and capable of participating in all testing associated with the clinical investigation
- Age 18 or above, or of legal age to give informed consent specific to state and national law
- Able to provide documented* evidence of one or more episodes of AFib/AT within 12 months of implantation

NOTE: *Source documentation included one or more of the following: 12-Lead ECG, Telemetered rhythm strips, Holter and Event monitor recordings and/or reports.

Patients fulfilling any of the following would be excluded:

- Life expectancy of less than 6 months due to other medical conditions
- Patients with a unipolar pacemaker that will not to be removed/capped
- Concurrent participation in any other clinical investigation, including drug investigations
- Ventricular tachyarrhythmias associated with a reversible cause, e.g., digitalis toxicity, hypoxia, sepsis, transient electrolyte imbalance, acute myocardial infarction, electrocution, or drowning
- Known pregnancy
- History of permanent (chronic) AFib that is refractory to all therapies
- Cardiovascular surgery within three months of implantation
- NYHA Class IV heart failure
- Prosthetic mechanical tricuspid heart valve
- A Cerebral Vascular Event/ Transient Ischemic Attack within 12 months of implantation.
- Patients with an occurrence of AFib for ≥ 48 Hours within 6 weeks of implantation and
- Who are not therapeutically anticoagulated to an INR= 2.0-3.0*, or,
- Who have been determined, by a routine transesophageal echocardiogram (TEE) to have intracavitary “smoke” or thrombus within 6 weeks of implantation.

*Appropriate anticoagulation should be available from time of episode or patient should have a TEE

11.1.4 ENDPOINTS

11.1.4.1 PRIMARY SAFETY OBJECTIVES

Endpoint 1: System Complication-Free Rate. Defined as the percentage of implanted patients who have not experienced any adverse clinical events (Type I, II, III complications) through the 6-month follow-up period.

Endpoint 2: Ventricular Fibrillation (VF) Detection Time. To verify that new atrial features (Atrial Rhythm Classification (ARC), APP, Post Atrial Therapy APP and ProACT) had no adverse effect on normal AICD sensing and detection, patients had VF detection times measured with these features “ON” and “OFF”. The order of testing was determined by randomization.

11.1.4.2 PRIMARY EFFICACY OBJECTIVES:

Endpoint 1: Appropriate Detection and Classification of Atrial Arrhythmias. To determine the effectiveness of PRIZM AVT to correctly detect and classify atrial arrhythmias from all other rhythms, appropriate detection and classification was determined from induced atrial episodes at implant or pre-discharge. Episodes were documented by surface electrocardiogram.

Endpoint 2: AFib Shock Conversion Rate. To demonstrate the effectiveness of the PRIZM AVT in terminating induced and spontaneous episodes of AFib, shock conversion efficacy was calculated by determining the number of successful shock-treated atrial episodes divided by the total number of shock-treated episodes. Successful conversion was defined as a minimum of two normal sinus rhythm or paced beats in 10 seconds post atrial shock (maximum three shocks per episodes).

11.1.4.3 SECONDARY STUDY OBJECTIVES

The secondary objectives of the study were identified as observational data and as such had no statistically driven sample size. The secondary objectives of the PRIZM AVT study were:

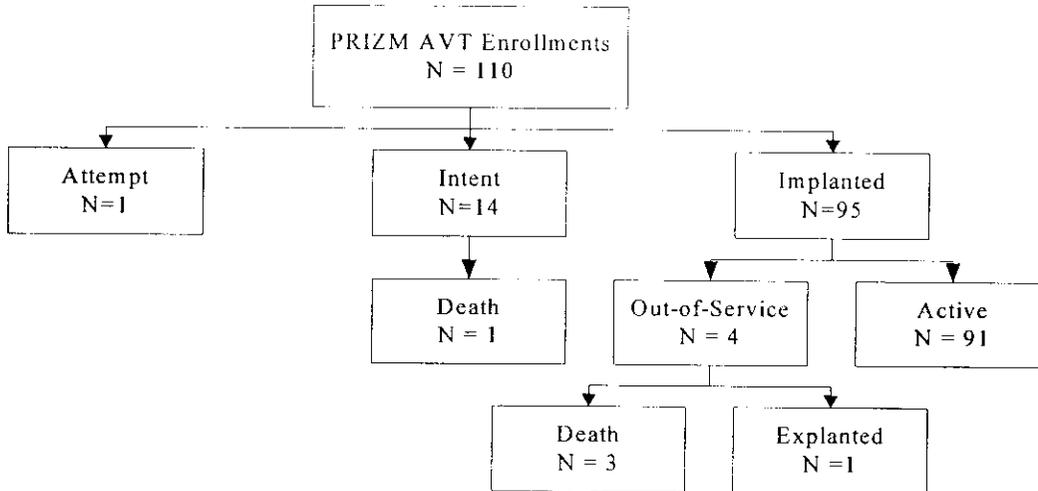
- Effect of atrial pacing features (Atrial Pacing Preference (APP) Post Atrial Therapy APP and ProACT) on:
 - Observation 1: Frequency of AFib or Atrial Tachycardia (AT)
 - Observation 2: Time to First AFib or AT Event
 - Observation 3: Percentage Time in AFib/AT (burden of AFib/AT)
- Appropriate Delivery of Atrial Shock Therapy

- Frequency of Ventricular Proarrhythmia

11.1.5 STUDY RESULTS

11.1.5.1 PATIENT ACCOUNTABILITY

Figure 1: Enrollment and Follow-Up of Randomized Patients



11.1.5.2 PATIENT CHARACTERISTICS

Table 13: PRIZM AVT Patient Characteristics

Characteristic	Measure	
Number of Patients Implanted		95
Number of Patients Attempted		1
Age at Implant (years)	N	96
	Mean +/- SD	68.7 ± 10.0
	Minimum	40
	Maximum	86
Gender [N (%)]	Female	23 (24%)
	Male	73 (76%)
LVEF (%)	N	90
	Mean +/- SD	33.8 ± 12.7
	Minimum	15
	Maximum	73

Characteristic	Measure	
NYHA Classification [N (%)]	Class I	16 (17%)
	Class II	52 (55.3%)
	Class III	26 (27.7%)
Implant Indications [N (%)]*	Survival of at least one episode of cardiac arrest (manifested by the loss of consciousness) due to a ventricular tachyarrhythmia	17 (15.9%)
	Recurrent poorly tolerated, sustained ventricular tachycardia (VT) and/or ventricular fibrillation (VF)	22 (20.6%)
	Prior myocardial infarction, left ventricular ejection fraction of less than or equal to 35%, and a documented episode of non-sustained VT, with an inducible ventricular tachyarrhythmia	32 (29.9%)
	Other (consistent with NASPE guidelines for ICD implantation)	36 (33.6%)
Primary Tachyarrhythmia [N (%)]	Monomorphic VT (MVT)	50 (53.2%)
	Nonsustained VT	24 (25.5%)
	Polymorphic VT (PVT)	8 (8.5%)
	Ventricular Fibrillation (VF)	6 (6.4%)
	Ventricular Flutter	1 (1.1%)
	Other	5 (5.3%)
Primary Atrial Arrhythmia [N (%)]	Atrial Fibrillation (AFib)	66 (68.8%)
	Atrial Flutter	18 (18.8%)
	Paroxysmal Atrial Fibrillation	1 (1%)
	Paroxysmal Atrial Tachycardia	5 (5.2%)
	Paroxysmal Supraventricular Tachycardia	4 (4.2%)
	Other	2 (2.1%)

*Patients may have more than one indication

11.1.5.3 STUDY RESULTS: PRIMARY ENDPOINTS

SAFETY OBJECTIVE ENDPOINT 1: SYSTEM-COMPLICATION FREE RATE

Hypothesis: Complication free rate for PRIZM AVT (p_1) is not equivalent to the PRIZM historical control rate of 89.3% (p_2), the difference is greater than or equal to 10%: $p_2 - p_1 \geq \Delta$

Results: The PRIZM AVT System, including the PERIMETER CS lead and PARTNER Rhythm Assistant, is as safe as other commercially available ICDs. The System Complication-Free Rate Endpoint was met.

A total of 22 type I, II or III complications occurred in 17 patients during the United States (US) and the Outside of United States (OUS) VENTAK PRIZM AVT clinical studies. During study design, it was determined that a sample of 86 patients followed for 6-months would be required to adequately power the System-Complication Free Rate endpoint. This endpoint was calculated from 96 patients during the US VENTAK PRIZM AVT clinical study (G010103) and 83 OUS VENTAK PRIZM AVT Field Following patients. This additional safety data has been included in order to present the most comprehensive view of device safety using all available data. During these studies, 100 patients were followed beyond a six-month visit, achieving the required sample size. In total, 179 patients were followed for 1096 months for an average experience of 6.1 months. Using survival analysis techniques, the VENTAK PRIZM AVT AICD 6-month Complication Free Rate was calculated to be 90.4%, or 1.1% greater than the 89.3% Complication Free Rate demonstrated by the historical control (VENTAK PRIZM). The 95% Lower Confidence Bound (LCB) for VENTAK PRIZM AVT's complication free rate was 86.7%, which is within 10% of the control rate (89.3%) demonstrating equivalence. Figure 2 shows the Kaplan-Meier curve while Table 14 shows details of the Kaplan-Meier Analysis.

Figure 2: Percent of Patients Free From Complications

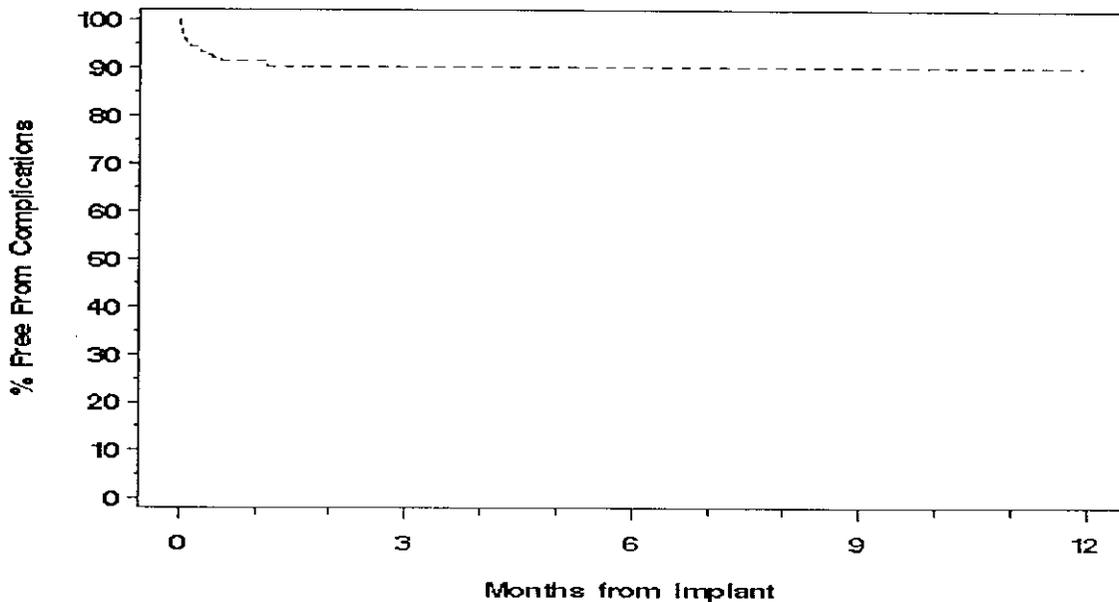


Table 14: Kaplan Meier Analysis

Statistic	Start of Interval (Months from Implant)						
	0	1	2	3	4	5	6
Number at Risk at Start of Interval	179	159	143	120	108	96	84
Number of Events in Interval	15	2	0	0	0	0	0

Statistic	Start of Interval (Months from Implant)						
	0	1	2	3	4	5	6
Cumulative Number of Events	15	17	17	17	17	17	17
Number Censored in Interval	5	14	23	12	12	12	84
Cumulative Number Censored	5	19	42	54	66	78	162
% Freedom from Event	100	90	90	90	90	90	90

SAFETY OBJECTIVE ENDPOINT 2: VF DETECTION TIME

Hypothesis: VF Detection Time for the PRIZM AVT (atrial therapy features “ON”) (t_1) is longer than the PRIZM (atrial therapy features “OFF”) (t_2) by 2 seconds; $t_1 - t_2 \geq \Delta$

Results: Addition of new atrial features (ARC; APP; Post A Therapy APP and ProACT) has no effect on the ability of the PRIZM AVT device to successfully detect ventricular fibrillation. The VF Detection Time endpoint was met.

Eighty-seven (87) paired VF episodes were successfully induced at implant with the new atrial features (ARC; APP; Post Atrial APP and ProACT) ON and OFF according to randomization. Average VF detection time with all features ON was 2.28 ± 0.81 , and with all features OFF was 2.24 ± 0.58 (see Table 15). The test for equivalence between the ON and OFF period measurements produced a statistically significant result ($p < 0.001$), demonstrating equivalence between the two groups.

Table 15: VF Detection Time

Atrial Rhythm Classification and Atrial pacing features	Mean(sec)	Std Dev(sec)
Features Programmed ON	2.28	0.81
Features Programmed OFF	2.24	0.58
<i>Difference</i>	<i>0.04</i>	<i>0.91</i>
Test For Equivalence, $p < 0.001$		

EFFICACY OBJECTIVE ENDPOINT 1: APPROPRIATE DETECTION AND CLASSIFICATION OF ATRIAL ARRHYTHMIAS

Hypothesis: Sensitivity for PRIZM AVT is not equivalent to 93%, the difference is greater than Δ ; $93\% - \text{Sensitivity} \geq \Delta$

Results: The PRIZM AVT AICD is effective at discriminating atrial arrhythmias from all other rhythms. The Appropriate Detection and Classification endpoint was met.

Two hundred and forty-six (246) (161 AFib, 68 AFlutter, 17 Other) induced atrial episodes were reviewed for appropriate detection and classification by the device. All episodes were appropriately detected and classified for 100% sensitivity. Testing for equivalence between the sensitivity of PRIZM AVT AICD and the hypothesized sensitivity of 93% shows a significant result ($p < 0.001$) demonstrating equivalence.

EFFICACY OBJECTIVE ENDPOINT 2: AFIB SHOCK CONVERSION RATE

Hypothesis: Atrial Fibrillation Shock Conversion rate for PRIZM AVT (p_1) is not equivalent to existing conversion rates (p_2), the difference is greater than 10%: $p_2 - p_1 \geq \Delta$

Results: The PRIZM AVT is at least as effective in converting AFib using shock therapy as conventional pharmacological options and other commercially available devices. The AFib Shock Conversion Rate endpoint was met.

AFib Shock Conversion Rate was calculated from induced and spontaneous episodes classified as AFib that received verifiable shock therapy (data that could be confirmed with stored or real-time electrograms). All AFib episodes that received verifiable shock therapy were included in the analysis, even those that may not have received the three shocks allowable by the endpoint, due to programming. One hundred and sixty-five (165) AFib episodes had verifiable conversion data of which 144 were successfully converted (device conversion; defined as two normal sinus rhythm or paced beats in 10 seconds post shock, maximum of three shocks). The AFib Shock Conversion Rate was therefore calculated as 87%. Testing for equivalence between the PRIZM AVT AICD AFib Shock Conversion Rate and the existing conversion rates of 60% shows a significant result ($p < 0.001$), demonstrating equivalence.

Table 16 gives details of AFib Shock Conversion Rate, First Shock Conversion Rate and Clinical Conversion Rate (defined as sinus rhythm two minutes post shock, induced episodes only) for all 165 AFib episodes. Separate device conversion efficacies are also shown for induced AFib episodes (93%) and spontaneous episodes (77%).

Table 16: AFib Conversion Rate

	AFib Episodes (N)	Successful Conversions (N)	Conversion Rate
AFib Shock Conversion Rate - All AFib Episodes	165	144	87%
AFib Shock Conversion Rate - Induced	104	97	93%
AFib Shock Conversion Rate - Spontaneous	61	47	77%

	AFib Episodes (N)	Successful Conversions (N)	Conversion Rate
First Shock Conversion Rate	165	123	75%
Clinical Conversion Rate- Induced	103	91	88%

11.1.5.4 STUDY RESULTS: ADDITIONAL ATRIAL EPISODE ANALYSIS (POST HOC)

ALL ATRIAL EPISODE SHOCK CONVERSION RATE

A total of 4208 atrial episodes (classified as AFib, AFlutter or other) in 85 patients were recorded (induced and spontaneous) during the clinical investigation. Many spontaneous episodes were non-sustained or did not receive shock therapy specifically because of physician-determined programming of the device. Of the 255 episodes that did receive shock therapy, 244 had verifiable conversion data. Two hundred eight (208) of the 244 episodes successfully converted (device conversion; defined as two normal sinus rhythm or paced beats in 10 seconds post shock, maximum of three shocks) giving an overall atrial shock conversion rate of 85%. Table 17 shows the details of Device Conversion Rate, First Shock Conversion Rate and Clinical Conversion Rate (defined as sinus rhythm two minutes post shock) for all atrial episodes.

Table 17: Conversion Rate for All Atrial Episodes

	Atrial Episodes (N)	Successful Conversions (N)	Conversion Rate
Device Conversion Rate-all episodes	244	208	85%
First Shock Conversion Rate- all episodes	244	189	77%
Clinical Conversion Rate- all episodes*	156	140	90%

*Clinical Conversion Rate is calculated from all induced atrial episodes

11.1.5.5 STUDY RESULTS: OBSERVATIONAL OBJECTIVES

The effect of the atrial pacing features APP, Post Atrial Therapy APP and ProACt was investigated in a cross-over trial where patients were randomized to therapies either On or Off for a three month duration and then crossed over to the opposite programming for a subsequent three month duration. The results from 52 patients followed for 6 months indicated the following about the combined use of the Atrial Pacing Features:

NOTE: Two patients were identified as having unique issues unrelated to the performance of the Atrial Pacing Features. As a result the exact number of true atrial episodes could not be determined. The data in the following sections is therefore presented using two columns, one

in which all data is presented and another where these two patients were excluded from analysis.

FREQUENCY OF AFIB/AT

Details of Frequency of AF/AT episodes from patients completing the 3 Month ON, 3-Month OFF randomized cross-over, are shown in Table 18.

Table 18: Frequency of AFib/AT

Group	Number of AFib/AT Episodes (all Patients)	Number of AFib/AT Episodes (2 Patients Excluded*)
ON (n=52)	2730	1772
OFF (n=52)	2297	2148

* Excluding two patients per Note listed above

Results of the Wilcoxon signed-rank test (Table 19): for each of the 52 patients, frequency of AFib/AT episodes was calculated for each period by the number of episodes divided by the follow-up time and then standardized to 3 months. The difference between these frequencies is not significantly different from 0 (p=0.07).

Table 19: Wilcoxon Signed-Rank Test Results

Group	Number of AFib/AT Episodes (all Patients)	Number of AFib/AT Episodes (2 Patients Excluded*)
Median of the difference	0	0
Mean of the difference	-3.4	14.2
p-value	0.07	0.04

* Excluding two patients per Note listed above

Based on the results of the Wilcoxon signed-rank test, the data indicates a reduction in the number of atrial arrhythmic episodes, the ON group showing fewer episodes.

TIME TO FIRST AFIB/AT EPISODE

Details of Time to First AFib/AT Episode from patients completing the 3-Month ON, 3-Month OFF randomized cross-over, are shown in Table 20. Only patients that had episodes during either period are included in the analysis.

Table 20: Time to First AFib/AT Episode (Median days)

Group	Time to First AF/AT Episode (all Patients)	Time to First AF/AT Episode (2 Patients Excluded*)
ON	12.4 (n=24)	12.4 (n=22)
OFF	18.8 (n=21)	24.3 (n=20)

* Excluding two patients per Note listed above

Using the Wilcoxon signed-rank test, the difference in time to first AF/AT episode, the median difference was -17.2. This difference is not significantly different from 0 (p=0.24).

Note: The analysis with the two patients removed did not affect the results.

PERCENTAGE OF TIME IN AFIB/AT (BURDEN OF AFIB/AT)

Details of Percentage Time in AFib/AT from patients completing the 3-Month ON, 3-Month OFF randomized cross-over, are shown in Table 21. Only patients where the device determined that percentage time in AFib was greater than zero during either period were included in the analysis.

Table 21: Percentage of Time in AFib/AT (Median)

Group	Percentage of time in AF/AT (all Patients)	Percentage of time in AF/AT (2 Patients Excluded*)
ON	6.5% (n=14)	6.5% (n=12)
OFF	5.0% (n=13)	5.0% (n=11)

* Excluding two patients per Note listed above

Using the Wilcoxon signed-rank test, the median difference in percentage time in AF/AT was -1.0. This difference is not significantly different from 0 (p=0.77). Note: The analysis with the two patients removed did not affect the results.

PACING FEATURE-RELATED ADVERSE EVENTS

The safety of the Pacing Features was evaluated by looking at the number of associated adverse events. Of the 52 patients who completed the 3-Month ON, 3-Month OFF cross-over, there were no complications reported to be associated with these features (617 US patient months and 747 international patient months).

11.1.5.6 STUDY RESULTS: ADDITIONAL SAFETY DATA

APPROPRIATE DELIVERY OF ATRIAL SHOCK THERAPY

Two hundred seventy nine (279) atrial shocks in 72 patients, were delivered during the clinical investigation. Of these, 279 (100%) were considered appropriate.

DEFIBRILLATION-INDUCED VENTRICULAR PRO-ARRHYTHMIA

From 279 atrial shocks delivered during the clinical investigation, none (0%) induced a ventricular arrhythmia.

11.1.5.7 STUDY RESULTS: PERIMETER CS LEAD

The primary data source supporting safety of atrial defibrillation with the PERIMETER CS lead was obtained in the InControl METRIX Atrial Defibrillation System Clinical Study (IDE G960033). The Guidant PERIMETER CS lead (Models 0202/0203/0204) is nearly identical to the InControl PERIMETER CS lead (Model 7109), with minor changes implemented for purposes of manufacturability and consistency among other Guidant family leads. All safety and effectiveness study objectives were met in the METRIX Clinical Study.

PERIMETER CS LEAD SAFETY DATA

The METRIX Clinical Trial (IDE G960033) collected data on the PERIMETER CS lead and is summarized in Table 22; there were no CS lead related complications in the METRIX Clinical Trial.

Table 22: METRIX Lead Related Complications

Study	Number of CS Leads	Total Patient Months (CS Lead only)	PERIMETER CS Lead Related Complications
METRIX	111	3707	None

Additional safety data for the PERIMETER CS lead was collected during the PRIZM AVT Clinical Trial conducted in both the United States and Europe. As part of the PRIZM AVT Clinical Trial, a separate protocol was initiated to provide continued access for patients enrolled in the METRIX clinical trial. The data from this Continued Access for METRIX protocol or CAM, is also provided in the table below. Table 23 summarizes the lead safety data gathered to support approval of the PERIMETER CS Lead.

Table 23: PRIZM AVT and CAM PERIMETER CS Lead Related Complications

Study	Number of CS Leads	Total Patient Months (CS Lead only)	PERIMETER CS Lead Related Complications
PRIZM AVT	28	294	1 †
CAM	8	35	None
TOTAL	36	329	1

† One CS lead dislodged and was repositioned without further incident; cause unknown

PERIMETER CS LEAD EFFECTIVENESS DATA

Efficacy data including lead impedance measurements and A-TRIAD shock conversion efficacy, was collected during the PRIZM AVT Clinical Trial.

A. PERIMETER CS LEAD MEASUREMENTS

Table 24 below presents shock impedance data collected from the PERIMETER CS lead during the PRIZM AVT clinical investigation. This data represents impedances measured using the A-TRIAD™ configuration (CS→SVC + Can). All measured values were within acceptable ranges.

Table 24: PERIMETER CS Lead Impedance Measurements (ATRIAD)

Study	Statistic	Implant	Pre-discharge	1 Month Follow-up	3 Month Follow-up	6 Month Follow-up
PRIZM AVT	N	28	27	27	28	27
	Mean +/- SD	47 +/- 14	40 +/- 10	45 +/- 11	48 +/- 9	50 +/- 11
	Range	27 - 95	26 - 82	20 - 79	33 - 75	37 - 95
CAM	N	8	8	*	*	*
	Mean +/- SD	53 +/- 8	53 +/- 8	*	*	*
	Range	43 - 63	39 - 57	*	*	*

* The CAM Study does not have ATRIAD shock impedance follow-up data available

B. A-TRIAD SHOCK CONVERSION EFFICACY

For devices that were programmed to receive shock therapy using the ATRIAD vector (and therefore had a PERIMETER CS Lead implanted) a conversion rate for all atrial episodes was calculated and is provided below in Tables 25 and 26. All atrial episodes that received verifiable shock therapy (source documentation available) with the ATRIAD vector were included in the analysis. Successful conversion for this data was defined as two normal sinus rhythm or paced beats in 10 seconds post shock.

Table 25: ATRIAD First Shock Conversion Rates (N=36)

Clinical Study	Number of Atrial Episodes	Number of Successful Conversions	First Shock* Conversion Efficacy
PRIZM AVT	84	53	63%
CAM	59	44	75%
All Studies Combined	143	97	68%

*Defined as successful conversion after first shock attempt

Table 26: ATRIAD Shock Conversion Rates (N=36)

Clinical Study	Number of Atrial Episodes	Number of Successful Conversions	Shock** Conversion Efficacy
PRIZM AVT	84	65	77%
CAM	59	54	92%
All Studies Combined	143	119	83%

**Defined as successful conversion after a maximum of three therapy attempts per zone per episode

One hundred forty-three (143) Atrial episodes had verifiable conversion data of which one hundred nineteen (119) were successfully converted. ATRIAD Shock Conversion Rate was therefore calculated as 83%.

11.1.5.8 STUDY RESULTS: PARTNER RHYTHM ASSISTANT, MODEL 2930

Summary: From 27 patients and 34 documented uses, there have been no Type I, II or III complications associated with the PARTNER Rhythm Assistant.

USES OF THE MODEL 2930 RHYTHM ASSISTANT

Sixteen (16) patients are currently using the Model 2930, PARTNER Rhythm Assistant. Table 28 presents documented data associated with use of the PARTNER Rhythm Assistant. This data reflects data captured during patient follow-ups and does not take into account ambulatory uses of the Rhythm Assistant.

Table 28: PARTNER Rhythm Assistant Data

Detail	N
Patients Demonstrating Use	27
Documented Uses	34
Patients with Rhythm Assistant at Home	16
Shocks Initiated	2

Two (2) shocks were initiated in 2 patients using the Model 2930 Rhythm Assistant. Prior to the introduction of the Model 2930 Rhythm Assistant, 1 shock was initiated using a magnet Model 6860.

ADVERSE EVENTS ASSOCIATED WITH THE PARTNER RHYTHM ASSISTANT

There was one adverse event directly associated with use of the PARTNER Rhythm Assistant. A summary of this event is shown in Table 29. Analysis of the activator indicated that the malfunction was due to a single battery defect. This adverse event was classified as a Type I Observation and not as a Type I, II or III Complication and hence did not contribute to the overall System Complication-Free Rate. Failure to cardiovert or defibrillate was not considered an adverse event specific to the use of the PARTNER Rhythm Assistant if a shock was appropriately delivered.

Table 29: PARTNER Rhythm Assistant Observation

Type	Patient ID	Date	Category	Description	Suspected Cause	Corrective Action
I	100182922	07/12/2002	Malfunction, intermittent problem	Malfunction, intermittent problem	Activator malfunction.	Came in for activator change out and ICD interrogation.

11.1.5.9 ADDITIONAL STUDY DATA

CONCOMITANT ARRHYTHMIA TESTING

To determine the ability of the PRIZM AVT device to discriminate between atrial and ventricular arrhythmias, patients were also induced into AFib + VT/VF. There were 111 successful inductions of AFib +VF/VT at implant. One hundred and eleven (111) were appropriately declared as ventricular episodes (100%).

SPONTANEOUS VENTRICULAR EPISODES

A total of 402 spontaneous ventricular episodes were recorded during the clinical investigation in 28 patients. Fifty-eight (58) episodes received therapy (ATP and/or shocks). The remainder were non-sustained. Of the 58 episodes receiving therapy, 10 were classified as VF, 22 as ventricular tachycardia (VT) and 26 as another rhythm (e.g. rapidly conducted atrial arrhythmia). The breakdown of classification of episodes receiving therapy can be found in Table 30.

Table 30: Treated Spontaneous Ventricular Episodes

Ventricular Episode Classification	N	% of all Ventricular Episodes
VF Episodes	10	17%
VT Episodes	22	38%
Other	26	45%
Total	58	100%

Of the 10 spontaneous VF episodes, nine received shock therapy and all were successfully converted with the device, giving a VF shock conversion rate of 100%. One episode documented as VF, received ATP therapy and was successfully converted. VF and VT shock conversion efficacies are shown in Table 31.

Table 31: Shock Conversion Rate for Spontaneous Ventricular Episodes

Ventricular Episode	Number of Episodes Receiving Shock therapy	Number of Successful Conversions	Conversion Rate
VF Episodes (n=10)	9	9	100%
VT episodes (n=22)	11	10	91%

ATRIAL DEFIBRILLATION MARGIN TESTING

There was no requirement for specific atrial defibrillation testing during the clinical investigation. Seventy-eight (78) patients had shock energies determined by atrial defibrillation margin testing where the only requirement was for two shock conversions. The average first successful shock energy determined by this testing was 10.6 J in patients in the V-TRIAD configuration and 5.2 J in patients in the A-TRIAD configuration (see Table 32).

Table 32: First Shock Energies in V-TRIAD and A-TRIAD

Configuration	First Successful Shock (J)	Number of Patients
V-TRIAD (RV→SVC + Can)	10.6 ± 4.1	70
A-TRIAD (CS→SVC + Can)	5.2 ± 3.2	8

11.1.5.10 GENDER ANALYSIS

Seventy-three men (76%) and 23 women (24%) were implanted or attempted in the PRIZM AVT study. The percentage of females is consistent with similar Guidant ICD trials. Analyses showed that safety and efficacy of this study do not differ with respect to gender. Specific comparisons are provided below.

There were 67 men (91.8%) and 20 women (87.0%) free of complications in the PRIZM AVT study. The rates of complication free subjects between men and women are not different ($p=0.44$, Fisher's Exact test). No statistical difference was found between men and women regarding VF Detection Time at implant. The average difference (atrial features ON versus OFF) was 0.02 seconds for men and 0.11 seconds for women ($p=0.69$, t-test). For both males and females, all induced atrial arrhythmias were appropriately detected and classified by the device for 100% sensitivity. No statistical difference was found between men and women regarding Afib Shock Conversion Rate. The men had a conversion rate of 86% and the women a conversion rate of 91% ($p=0.57$, Fisher's Exact Test).

12 CONCLUSIONS DRAWN FROM STUDIES

The PRIZM AVT AICD introduces incremental features for the treatment of atrial arrhythmias. Bench, animal, and clinical data support the safety and effectiveness of these features when used in combination in this device. The new elements of the device include atrial detection capabilities, atrial therapies (shock and antitachycardia pacing schemes), additional atrial pacing features, enhanced diagnostics related to the new atrial therapies, a new lead (PERIMETER Coronary Sinus lead), and a new patient interface system that allows the patient to interact with their AICD and to deliver programmed atrial shock therapy (PARTNER Rhythm Assistant).

In vitro testing, consisting of component-level testing, device testing, system testing, and *in vivo* animal studies, demonstrate the proper operation of the PRIZM AVT System. This testing provides reasonable assurance that the devices are safe and perform as intended.

Clinical studies have demonstrated that the PRIZM AVT has an adequate overall safety profile; appropriately detects and classifies atrial arrhythmias; has an acceptable AFib shock conversion rate; and does not alter VF detection times with the addition of the new features. Atrial shocks were appropriately delivered and did not induce ventricular arrhythmia in this study. Additionally, the results of the clinical study suggest that the atrial pacing features, by themselves, have no effect on the safety profile of the device, the frequency of AF/AT, the time to first AF/AT episode, or the percentage of time spent in AF/AT. Finally, the clinical study demonstrated acceptable performance of the PERIMETER CS lead and the PARTNER Rhythm Assistant devices.

13 CDRH DECISION

The results of the preclinical and clinical studies demonstrated that the new design features, when used in combination in the PRIZM AVT System and when used as indicated in the labeling, are safe and effective.

FDA found Guidant's manufacturing facility to be in compliance with the Device Quality System Regulation, (21 CFR part 820).

14 APPROVAL SPECIFICATIONS

Directions for Use:

See labeling

Hazards to Health from Use of the Device:

See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the Labeling

Post-approval Requirements, Restrictions:

See approval order.