



# Memorandum

Date . JUL - 3 1997

From Director, Office of Device Evaluation (HFZ-400)  
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Telectronics Pacing Systems, Inc.,  
Guardian™ ATP II Model 4211 Implantable Cardioverter/Defibrillator  
System - ACTION

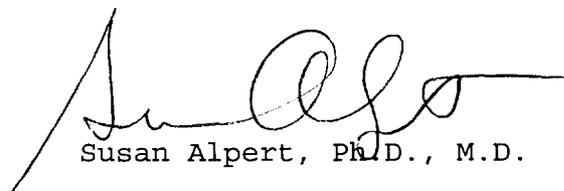
To The Director, CDRH  
ORA \_\_\_\_\_

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

- (1) a premarket approval order for the above referenced medical device (Tab B); and
- (2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

  
Susan Alpert, Ph.D., M.D.

Attachments  
Tab A - Notice  
Tab B - Order  
Tab C - S & E Summary

DECISION

Approved \_\_\_\_\_ Disapproved \_\_\_\_\_ Date \_\_\_\_\_

Prepared by Doris Terry, CDRH, HFZ-450, June 10, 1996, 443-8609

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**DRAFT**

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[DOCKET NO. \_\_\_\_\_]

Telectronics Pacing Systems, Inc.; Premarket Approval of  
Telectronics Guardian™ ATP II Model 4211 Implantable  
Cardioverter Defibrillator System

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing  
its approval of the application by Telectronics Pacing  
Systems, Inc., Englewood, CO, for premarket approval, under  
section 515 of the Federal Food, Drug, and Cosmetic Act (the  
act), of the Guardian™ ATP II Model 4211 Implantable  
Cardioverter Defibrillator System.

DATE: Petitions for administrative review by (insert date 30  
days after date of publication in the FEDERAL REGISTER).

ADDRESS: Written requests for copies of the summary of safety  
and effectiveness data and petitions for administrative review  
to the Dockets Management Branch (HFA-305), Food and Drug  
Administration, 12420 Drive, rm. 1-23, Rockville, MD 20857.

## FOR FURTHER INFORMATION CONTACT:

Doris Terry,  
Center for Devices and Radiological Health (HFZ-450),  
Food and Drug Administration,  
9200 Corporate Blvd.,  
Rockville, MD 20850,  
(301) 443-8609.

SUPPLEMENTARY INFORMATION: On July 8, 1994, Telectronics Pacing Systems, Inc., Englewood, CO 80112, submitted to CDRH an application for premarket approval of the Guardian™ ATP II Model 4211 Implantable Cardioverter Defibrillator System. The Guardian™ ATP II Model 4211 Implantable Cardioverter Defibrillator System is indicated for use in patients who are at high risk of sudden death due to ventricular fibrillation and/or ventricular tachyarrhythmias and who have experienced one of the following situations:

- survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyarrhythmia
- recurrent, poorly tolerated sustained ventricular tachycardia (VT).

Note: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies have not been conducted.

In accordance with the provisions of section 515(c)(2) of the act (21 U.S.C. 360e(c)(2)) as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel of the Medical Devices Advisory Committee, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

On July 3, 1997, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

#### Opportunity for Administrative Review

Section 515(d)(3) of the act authorizes any interested person to petition, under section 515(g) of the act (21 U.S.C. 360e(g)), for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory

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committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: \_\_\_\_\_.

\_\_\_\_\_

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Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

JUL -3 1997

Michael J. Andrews, Ph.D.  
Director, Regulatory Affairs  
Telectronics Pacing System  
7400 South Tucson Way  
Englewood, Colorado 80112

Re: P940024  
Guardian™ ATP II Model 4211 Implantable Cardioverter/  
Defibrillator System  
Filed: July 8, 1994  
Amended: September 12, 1994; May 30, August 24, September 29,  
and December 26, 1995; January 11, March 14, April 2,  
July 16 and 30, August 5, October 23, November 4,  
December 4, 20, and 31, 1996 and February 4 and  
June 12, 1997

Dear Dr. Andrews:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Guardian™ ATP II Model 4211 Implantable Cardioverter/Defibrillator System. The Guardian™ ATP II Model 4211 Implantable Cardioverter Defibrillator hereafter referred to as the 4211 implantable Cardioverter Defibrillator System consists of the following: the Guardian™ ATP II Model 4211 Implantable Cardioverter Defibrillator; Implantable Defibrillator Patch Lead Models 040-105, 040-106, 040-107, 040-128, 040-129 and 040-130; Model 4510 Implant Support Device; Generic 4211 Personality Module; and System Accessories (Adapter Models 040-051, 040-052, 040-047, 040-055, 033-330 and 033-320, Model 042-018 Patient Interface Module, Model 040-021, Stylet Kit and Cable Models 042-010, 042-011, 042-015, 042-238 and 042-017). The 4211 System is indicated for use in patients who are at high risk of sudden death due to ventricular fibrillation and/or ventricular tachyrythmias and who have experienced one of the following situations:

- survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyrythmia

- recurrent, poorly tolerated sustained ventricular tachycardia (VT).

Note: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies have not been conducted.

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval for Implantable Defibrillators and Programmers" (enclosed).

You have informed FDA in your letter dated October 22, 1996, that you will no longer manufacture the GUARDIAN™ ATP II Model 4211 Implantable Cardioverter/Defibrillator at the Lane Cove, New South Wales, Australia facility. In addition, you are not intending to market the device identified above in the United States. Should you want to market the above device or a modification of the above device under a supplement to this PMA, you will be subject to an FDA inspection. The inspection must confirm that the manufacturing facilities, methods and controls are in compliance with the applicable device Good Manufacturing Practice (GMP) regulations (21 CFR Part 820) prior to market introduction.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Expiration dating for this device has been established and approved at 3 years.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.



Page 3 - Michael J. Andrews, Ph.D.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

Should you decide to market this device you are reminded that as soon as possible, and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Boulevard  
Rockville, Maryland 20850

In addition under section 522(a) of the act, manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted device as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

At that time you should submit five (5) copies to:

Postmarket Studies Document Center  
1350 Piccard Drive (HFZ-544)  
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

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Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522.

In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the act (21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3)), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA.

If you have any questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639.

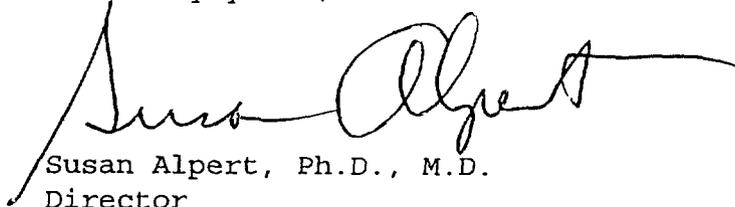
Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your device is a device that is subject to tracking because it is a permanent implant whose failure would be reasonably likely to have serious adverse consequences.

FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR § 821.20(b) and the devices that FDA has designated for tracking at 21 CFR § 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993)).

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If you have questions concerning this approval order, please contact Doris Terry at (301) 443-8609.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Susan Alpert", with a long horizontal flourish extending to the right.

Susan Alpert, Ph.D., M.D.  
Director

Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosures

## CONDITIONS OF APPROVAL

**APPROVED LABELING.** As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

**ADVERTISEMENT.** No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

**PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT.** Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

- (1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
- (2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
  - (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and
  - (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

**ADVERSE REACTION AND DEVICE DEFECT REPORTING.** As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

- (1) A mixup of the device or its labeling with another article.
- (2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and
  - (a) has not been addressed by the device's labeling or
  - (b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.
- (3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

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REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including *in vitro* diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

- (1) may have caused or contributed to a death or serious injury or
- (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)  
Center for Devices and Radiological Health  
Food and Drug Administration  
1350 Piccard Drive, Room 240  
Rockville, Maryland 20850  
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)  
Center for Devices and Radiological Health  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

## SUMMARY OF SAFETY AND EFFECTIVENESS

### I. GENERAL INFORMATION

Device Generic Name: Automatic Implantable Cardioverter Defibrillator System

Device Trade Name: GUARDIAN™ ATP II Model 4211 Implantable  
Cardioverter Defibrillator System

Applicant Name and  
Address: Teletronics Pacing Systems  
TPLC, Inc.  
7400 South Tucson Way  
Englewood, Colorado 80112

PMA Number: P940024

Date of Panel  
Recommendation: Not Applicable

Date of Notice of  
Approval to Applicant: JUL - 3 1997

### II. Indications for Use

The GUARDIAN™ ATP II Model 4211 System is indicated for patients who are at high risk of sudden death due to ventricular fibrillation and/or ventricular tachyrythmias and who have experienced one of the following situations:

- survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyrythmia
- recurrent, poorly tolerated sustained ventricular tachycardia (VT)

Note: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies have not been conducted.

### III. Device Description

The GUARDIAN™ ATP II Model 4211 system (hereafter referred to as the Model 4211) consists of the GUARDIAN™ ATP II Model 4211 Implantable Cardioverter Defibrillator, Implantable Defibrillator Patches, the Implant Support Device, and the Generic 4211 Personality Module.

System accessories include High Voltage Defibrillation Adaptors, Sense/Pace Lead Adaptors, Patient Interface Module (PIM), Spare Stylet Kits, Pacing/Defibrillation Cable, Fibrillation Cable, Diagnostic Cable, Cutaneous Patch Cable, and Subcutaneous Patch Cable.

A. GUARDIAN™ ATP II Model 4211 Implantable Cardioverter/Defibrillator

The 4211 pulse generator is an implantable cardioverter defibrillator with integral bradycardia and tachycardia pacing. It is designed to provide automatic monitoring, detection, and treatment of ventricular tachycardia (VT), ventricular fibrillation (VF), and bradycardia.

The 4211 automatically detects ventricular arrhythmias using a range of detection criteria. Upon detection and classification of an arrhythmia, the 4211 delivers appropriate therapy. If a tachyarrhythmia is detected and meets the programmed criteria, the 4211 delivers biphasic or monophasic defibrillation shock therapy, cardioversion therapy, and/or antitachycardia pacing therapy. The voltage and pulse widths of the shocks for cardioversion and defibrillation are programmable and, when possible, are synchronized with sensed events.

The 4211 also provides bradycardia support pacing in the VVI mode. The device provides backup bradycardia pacing as well as independently programmable post-shock bradycardia pacing. This allows for the device to be programmed to deliver higher energy pacing pulses after a defibrillation or cardioversion shock.

B. Implantable Defibrillator Patches (Models 040-105, 040-106, 040-107, 040-128, 040-129, and 040-130)

The Telectronics Pacing Systems Implantable Defibrillator Patch Leads are available in three sizes: Small, Models 040-105 and 040-128 (15 cm<sup>2</sup>), Standard, Models 040-106 and 040-129 (28 cm<sup>2</sup>), and Large, Models 040-107 and 040-130 (40 cm<sup>2</sup>).

Models 040-105, 040-106 and 040-107 have a 3.2 mm HV unipolar connector, and the Models 040-128, 040-129 and 040-130 have a DF-1 unipolar connector.

All models comprise a low resistance conductor, insulated by three layers, an intimate Teflon® coating, a polyurethane sleeve and a silicone sleeve. The conductor is welded to titanium mesh which is embedded in a Dacron®-reinforced silicone elastomer sheet, forming a flexible, conductive patch.

The patches can be sutured to either the pericardium or the epicardium or can

be placed submuscularly or subcutaneously, allowing the delivery of high energy shocks to defibrillate the heart. The patches may be used independently or as part of an endocardial defibrillation lead system.

C. Model 4510 Implant Support Device

The 4510 Implant Support Device, hereafter referred to as the 4510, is an external device used during ICD implant procedures. The 4510 consists of bradycardia support pacing in VVI mode; synchronized low energy cardioversion shocks; synchronized high energy defibrillation shocks; and extensive diagnostic features to monitor cardiac activity.

The 4510 is designed for use during a Telectronics ICD implant procedure. The 4510 combines features of a pacing system analyzer, a fibrillator, and a cardioverter/defibrillator.

D. Generic 4211 Personality Module

The Personality Module is used in conjunction with the 9600 Network Programmer to interface between the programmer and the 4211. The Personality Module is comprised of the software required for this interface.

E. System Accessories

The bifurcated High Voltage Defibrillation Adaptor, Model 040-051, may be used to connect two 3.2 mm HV leads to one 3.2 mm HV defibrillator connector aperture, such as those found on the 4211. The adaptor consists of a 3.2 mm HV terminal, polyurethane body, and two bifurcated legs with receptacles for Implantable Defibrillator Patch Leads. The conductor is a titanium rope insulated by outer polyurethane over inner silicone sleeving. The adaptor block and terminal pin are also titanium with an outer covering of molded silicone elastomer.

Model 040-052 is a high voltage (HV) lead adaptor used to connect two Cardiac Pacemakers, Inc. (CPI) 6 mm unipolar terminal connectors to a Telectronics Pacing Systems 3.2 mm HV defibrillator connector aperture. The adaptor consists of a 3.2 mm HV terminal, polyurethane body, and two bifurcated legs with receptacles for the 6 mm terminals of CPI patch defibrillator leads. The conductor is a titanium rope insulated by outer polyurethane over inner silicone sleeving. The adaptor block and terminal pin are also titanium with an outer covering of molded silicone elastomer.

Model 040-047 is a high voltage adaptor which allows the connection of a CPI 6 mm unipolar defibrillation patch lead to the GUARDIAN® Implantable

Defibrillator 3.2 mm HV cavity. The adaptor consists of a 3.2 mm HV terminal pin, silicone body and a 6 mm unipolar HV receptacle to accommodate the CPI defibrillation patch lead. The conductor is a DBS wire coated with Teflon®, and insulated by outer silicone over inner polyurethane sleeving. The terminal pin and receptacle are titanium insulated with silicone.

Model 040-055 is a high voltage adaptor which allows the connection of a Medtronic 3.2 mm unipolar HV patch to a GUARDIAN® Implantable Defibrillator 3.2 mm (HV) cavity. The adaptor consists of a 3.2 mm HV terminal pin, silicone body, and a 3.2 mm unipolar HV receptacle to accommodate the Medtronic 3.2 mm unipolar patch lead. The conductor is a DBS wire coated with Teflon®, and insulated by outer silicone over inner polyurethane sleeving. The terminal pin and receptacle are titanium insulated with silicone.

The Models 033-330 and 033-320 sense/pace lead adaptors are designed to connect various sense/pace lead systems to the Teletronics ICD header. Model 033-320 implantable bradycardia lead adaptor connects two unipolar 3.2 mm pacing leads to one bipolar IS-1 (3.2 mm) pulse generator connector assembly. Model 033-330 implantable bradycardia lead adaptor connects two unipolar 5 mm (4.75) pacing leads to one bipolar IS-1 (3.2 mm) pulse generator connector terminal.

The Patient Interface Module (PIM) Model 042-018 consists of a passive, non-powered, switching network which allows the investigator to adapt a 4510 ISD to test a variety of shock configurations without manually reconfiguring the lead connections during implant. The PIM switching network is contained in a gray plastic box and consists of four 3-position rotary switches, one for each high voltage electrode, and one for the fibrillation path. The PIM adapts the 4510 ISD to a variety of lead configurations to be used for both fibrillating the patient as well as delivering therapy to treat the tachyarrhythmia.

The Accessory Stylet Kit, Model 040-121, contains two 100 cm standard stylets, two 100 cm stiff stylets, and two split suture sleeves. These stylets are intended for use with 100 cm ventricular defibrillation leads. The Accessory Kit, Model 040-060, contains two 90 cm standard stylets and two split suture sleeves. These stylets are intended for use with 90 cm atrial defibrillation leads.

The Pacing/Defibrillation Cable (Model 042-010) is used to connect the 4510 ISD to sense/pace and defibrillation leads during the implant procedure. The cable enables the 4510 to deliver pacing pulses and defibrillation shocks to the patient and to sense intrinsic activity.

The fibrillation cable (Model 042-011) is used with the 4510 Implant Support Device to deliver the fibrillation signal to the patient. The patient end of the fibrillation lead is fitted with two alligator connectors, and the other end of the cable is fitted with a Lemo connector which plugs into the FIB socket on the 4510 ISD control panel. The cable is 3.2m long and is autoclavable.

The Diagnostic Output Cable (Model 042-015) connects the 4510 ISD to an ECG monitor. This cable is terminated by a female BNC connector, and is supplied with adaptors to suit 3.5mm and 6.5mm phono sockets. The cable is 1.8m long.

The Cutaneous Patch Cable (Model 042-038) is used to connect the PIM to a cutaneous pad or patch. It has an HV banana plug to connect to the PIM, and an insulated alligator clip to connect to a pad or patch. The cable is 3m long and is autoclavable.

The Subcutaneous Patch Cable (Model 042-017) is used to connect the PIM to a subcutaneous defibrillation lead. It has a high voltage (HV) banana plug to connect to the PIM, and a molded connector block with a screw-down terminal to accept the connector from a variety of defibrillation patch leads. The cable is 3 m long and is autoclavable.

#### F. Commercially Available Devices

As part of the 4211 system, the commercially available devices used include the following: the Model 9600 Network Programmer, the 9600 Diagnostic output Cable (Model 042-068), the 9600 Auxiliary Instrument cable (Model 042-034), and commercially available sense/pace leads, including those of Teletronics as well as those distributed by other manufacturers.

#### IV. Contraindications

- Patients in whom ventricular arrhythmia is drug induced
- Patients in whom ventricular arrhythmia is due to electrolyte imbalance
- Patients with incessant VT or VF.
- Patients with myocardial ischemia/infarction who have not been stabilized for an adequate period and whose tachyarrhythmia is due to ongoing ischemia.

#### V. Warnings

- Always connect the patient to an ECG monitor and ensure that an external

defibrillator is present during Electrophysiological (EP) testing, as such testing involves the induction of potentially hazardous arrhythmias.

- During the implant procedure, and at any subsequent surgical procedures including explant or post-mortem procedures, ensure that the GUARDIAN™ ATP II is programmed to System Off before handling the device as the GUARDIAN ATP II can deliver a potentially hazardous shock if you touch the defibrillation terminals while the device is charged.
- Never incinerate a GUARDIAN™ ATP II or any other pulse generator, due to the potential for explosion. The GUARDIAN ATP II must be explanted before cremation.

## VI. Precautions

- Changes to the patient's drug regimen or underlying cardiovascular status, may change the heart's electrophysiologic characteristics. Any such changes should be assessed by further EP studies to ensure that the programming of the GUARDIAN™ ATP II is appropriate for the patient.
- Do not implant the GUARDIAN™ ATP II if the patient has a fixed unipolar pacemaker, or a pacemaker which may revert to unipolar pacing under some conditions.
- Ensure that the defibrillation lead impedance is greater than 20 ohms. An impedance below 20 ohms could damage the Guardian™ ATP II.
- If the patient develops an arrhythmia while the episode log is being read, break the telemetry link to allow the GUARDIAN™ ATP II to detect the arrhythmia and deliver therapy according to the programmed parameters.
- If an external stimulator is used to induce tachyarrhythmia, use the therapy assessment procedure to suspend automatic operation, and remove the external induction connections before delivering therapy.
- Electrical interference from intense electromagnetic fields or from directly conducted alternating current (AC) or MRI may affect the operation of the GUARDIAN™ ATP II.
- Low levels of alternating current (AC) - for example from poorly grounded electrical equipment- may affect the operation of the Guardian™ ATP II.
- Keep cellular phones at least 15 cm (6 inches) away from the pulse generator. For phones with an output power above 3W, maintain a minimum distance of 30 cm

(12 inches).

- Do not carry a cellular phone in the Listen or Standby mode in a breast pocket or on a belt within 15 cm (6 inches) of the pulse generator.
- Program the Guardian™ ATP II to System Off before any electrosurgical procedure, and interrogate the device afterwards to confirm that it is functioning appropriately.
- Patients with implanted defibrillators should not be subjected to MRI, lithotripsy, electrocautery or RF ablation.
- When it is necessary to perform external defibrillation, Telectronics recommends the following procedure:
  - Program the GUARDIAN™ ATP II to System Off before applying external defibrillation.
  - Place external defibrillation paddles at least 10 cm away from the GUARDIAN ATP II and such that the GUARDIAN ATP II, the sense/pace and shock electrodes are not in line with the current flow. Do not use internal defibrillation paddles if the GUARDIAN™ ATP II is connected to the lead system.
  - Interrogate the GUARDIAN™ ATP II after external defibrillation to confirm that it is functioning appropriately.
- Avoid ionizing radiation. If the patient must receive high dose radiotherapy, take the following precautions:
  - Program the GUARDIAN ATP II to System Off and disable bradycardia support pacing for the duration of radiotherapy treatment.
  - Protect the GUARDIAN™ ATP II from direct exposure.
  - Provide temporary pacemaker backup if the patient requires bradycardia support pacing.
  - Interrogate the GUARDIAN™ ATP II after the treatment to confirm that it is functioning appropriately.
  - Interpret any changes in the operation of the GUARDIAN™ ATP II as radiation damage and take immediate remedial action.
- Do not use diathermy directly over the implanted system.

## VII. Alternative Practices and Procedures

Cardioversion and defibrillation are accepted treatments for the indications described

*JD*

in Section II. The most reliable method for increasing the survival of persons at high risk of sudden cardiac death is the prompt treatment of ventricular fibrillation and hemodynamically unstable ventricular tachycardias by the application of a high energy electrical discharge to the heart.

The most widespread alternative chronic treatment is the suppression of ventricular tachyarrhythmias with antiarrhythmic drug therapy. Other commercially available automatic implantable pacer cardioverter defibrillator systems, may also meet the needs of the patients with the indications previously described.

### VIII. Marketing History

A total of three hundred and thirteen 4211 systems have been implanted outside the United States as of March 17, 1995.

The 4211 system is commercially released in 20 countries (Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Liechtenstein, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden and the United Kingdom) and in clinical trial in Australia. Approval for implant of the 4211 system in the European Union was granted with CE mark approval in December, 1993. There were no reported instances where the device was withdrawn from the marketplace due to safety and effectiveness concerns.

### IX. Adverse Events

The Guardian ATP II clinical study involved 88 devices implanted in 85 patients for a cumulative period of 1785.36 implant months (mean implant duration = 21.0 +/- 7.9 months, range 5 days to 35.1 months ). Adverse events reported from the clinical study included 14 observations and 18 complications. Eleven patients died during the course of the study. None of the deaths were judged to be related to the device. In addition, 5 devices which were not part of the Guardian ATP II clinical study exhibited a high current drain leading to battery depletion. There were no deaths or injuries associated with these failures. The implant durations for these devices ranged from 17 to 33 months. The high current drain was due to the failure of a transistor resulting from contamination during testing conducted by the component's manufacturer.

Observations and complications which occurred during the study, and are reported for more than one patient are listed by frequency of occurrence in Table 1.

**Table 1** Incidence of Reported Adverse Events

	No. of patients	% of patients	No. of events	Events/patient month
*Observations	13	15.3%	14	0.008
Shocks for fibrillation	2	2.4%	3	0.002
Environmental noise	3	3.5%	3	0.002
Increased pacing threshold	2	2.4%	2	0.001
**Complications (total)	3	21.2%	18	0.010
Lead dislodgment	5	5.9%	5	0.003
Infection	5	5.9%	5	0.003
Other lead complications	4	4.7%	3	0.002

\*Observations can be corrected by non-invasive measures such as reprogramming.  
Note: 6 of the 13 patients had one event each

\*\*Complications can only be corrected by invasive measures such as surgical intervention.  
Note: 1 patient had one event.

Five devices which were not part of the Guardian™ ATP II clinical study exhibited a high current drain leading to battery depletion. There were no deaths or injuries associated with these failures. The implant durations for these devices ranged from 17 to 33 months. The high current drain was due to the failure of a transistor resulting from contamination during testing conducted by the component's manufacturer.

## X. Summary of Studies

### A. Component Testing

Component testing was performed on the following critical components in the 4211: integrated circuits, special transistors, transformers, printed circuit boards, crystal, high voltage capacitor, power cell, and terminal assemblies. Fifteen to 45 components of each, depending on tests, were tested.

### B. Device Testing

The results of device testing demonstrated that the 4211 was comprehensively validated. Specifically the combination of hardware, software, and system testing performed on the 4211 showed the device met the design specifications. The device testing is described below.

### C. Hardware Testing

The device testing and assessment of the hardware of the 4211 consisted of electrical validation (5 devices), mechanical validation (11 functional units and 4 non-functional units), reliability testing, FMECA (Failure modes, effects, and criticality analysis) and testing to assure that 4211 header connections were compatible with Teletronics DF-1 leads. Validation testing of the 4211 encompassed the original design and all subsequent modifications, such as the addition of a current limiting circuit.

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#### D. Implant Software Testing

Implant software testing on 2 units encompassed three major areas, Module Testing, Integration Testing, and Release. Module testing provided verification that individual modules met their own design specifications. Integration Testing verified that the integrated modules met the system functional specification. The release testing demonstrated that the implant software was performing according to specification.

#### E. System Qualification

Major System qualification tested one 4211 device in conjunction with the 9600 Network Programmer and the 4211 Personality Module software. This testing was successfully completed.

#### F. System Hazards Analysis

The System Hazards Analysis identifies the hazards that the system can present to the patient, the fault conditions that can cause each hazard, and the strategies used to mitigate each fault. These hazards are similar to those present for other implantable cardioverter defibrillator devices.

#### G. EMI Testing

Five 4211 devices were subjected to EMI (electromagnetic interference) testing. The results of this testing demonstrated susceptibility to power frequency signals above 0.05mV rms. However, when considering EMI susceptibility at 50 and 60 Hz power frequencies, it was noted that an external electric field of greater than 8kV/m (0.10mV) is required to induce an inappropriate shock. As the typical electric field strength expected to be encountered within the patient's normal environment is in the order of 100V/m, the probability of a patient with an implanted 4211 being subjected to EMI of sufficient field strength to provoke inappropriate shocks is remote. The above testing shows that the 4211 complies to specification and is not adversely effected by EMI. The device is therefore considered qualified and fit for purpose.

#### H. Implantable Defibrillator Patches

Extensive pre-clinical validation testing was performed on the Implantable Defibrillator Patches, Models 040-105, 040-106 and 040-107 to qualify patch performance electrically, mechanically, and biologically suitable for human implant (8-30 patch leads were tested depending on the test performed). Acute animal studies were initiated to separately evaluate the condition of cardiac tissue which had undergone defibrillation shock, delivered by the patch/tissue contact, independently from any effects that may occur due to the physical presence of the patches themselves. Chronic animal studies were initiated to clinically evaluate patch performance over time. The results of the in-vivo and in-

vitro tests demonstrated that the Implantable Defibrillator Patch Leads were suitable for human use.

#### I. 4510 Implant Support Device

Four 4510 units which includes the ISD hardware were tested electrically and mechanically, and the software was validated to demonstrate that the 4510 ISD meets specifications.

#### J. Generic 4211 Personality Module

Both manual and automatic validation testing was performed on the software comprising the 4211 personality module. As a result of that validation, the software was assessed to meet specifications and fit for release.

#### K. Accessories

Four high voltage defibrillation adaptors, Models 040-047 (8 units), 040-055 (6 units), 040-051 (14) and 040-052 (7 units) have been developed to interface between the 4211 and Teletronics Implantable Defibrillator Patch Leads. Laboratory testing was conducted to verify their electrical and mechanical suitability for use in implantable defibrillation systems.

The adaptors were subjected to aging, either in a dry oven at 80°C for 260 hours or in 0.9% saline at 80°C for 550 hour, and then tested for insertion and withdrawal forces, inspected for corrosion or other damage, measured for electrical leakage, electrical resistance, contact electrical resistance, corrosion/shock testing and ultimate tensile/pull strength. All units passed all tests.

The adaptor/lead assemblies were flexed for one million cycles and shocked, between pulses, at 10 minute intervals in a 37°C saline tank. At the end of the testing, all samples were within specified physical and electrical values, with no insulation degradation noted. Based on these data, it was concluded that the design and manufacturing process changes were validated and could be implemented.

Two bradycardia adaptors, Models 033-320 (15 units) and 033-330 (15 units) can be utilized to interface between two unipolar sense/pace leads and the bipolar IS-1 (3.2 mm) aperture of the 4211 header. Adaptors of each model were subjected to validation testing with various lead models to ensure proper functional, mechanical and electrical stability. All 033-320 and 033-330 adaptors passed the test criteria. Based on the successful results of validation testing, the adaptors were considered appropriate for their intended use.

Tests were performed on the connector in accordance with the requirements of the IS-1

standard No. ISO 5841-3. All leads passed the test criteria, with the exception of one unipolar lead which was eliminated after being damaged during a test setup. Based on these data, it was concluded that the design and the manufacturing processes of lead connectors are considered to comply with IS-1 standard.

Mechanical and electrical qualification testing, consisting of functionality and high voltage breakdown testing followed by environmental testing. All units passed all test. All mechanical and electrical requirements to validate the design and performance of the Patient Interface Module (PIM) were satisfied.

The Model 042-010 Pacing/Defibrillation Cable, Model 042-011 Fibrillation Cable, Model 042-015 Diagnostic Cable, Model 042-038 Cutaneous Patch Cable, and Model 042-017 Subcutaneous Patch Cable underwent successful mechanical and electrical testing. Several of the named models were tested.

#### L. Biocompatibility Testing

Biocompatibility testing was performed on materials in the 4211 and the Teletronics Implantable Defibrillator patch leads which contact human tissue. The results of the biocompatibility testing demonstrate that the materials in the 4211 and leads are in compliance with the Tripartite guidelines. All materials in contact with human tissue have been tested for biocompatibility and have been shown to be safe and reliable for long-term human implantation.

#### M. Animal Testing

Animal testing was performed to analyze the performance of the 4211 system in vivo under conditions simulating actual clinical use. In some cases, acute and chronic animal tests were performed. In other cases, human ECG signals were recorded, stored, and used to determine the response of devices to actual recorded signals. These demonstrated that the 4211 system was fit for release into a human clinical study.

The 4211 is manufactured from a similar hardware and software platform as the GUARDIAN® ATP 4210. Due to the similarity with the GUARDIAN® ATP 4210, pre-clinical validation of the 4211 combined the results of pre-clinical validation on the 4210. pre-clinical testing on the 4211 to validate the therapy enhancements (Biphasic Shock Therapy, Automatic Sensitivity Tracking, Detection and Confirmation Modifications, Antitachycardia Pacing Enhancements, and Therapy Sequencing Enhancements).

The acute human testing of the 4210 consisted of bench testing using recorded signals. ECG signals were recorded during electrophysiology studies and used to test the functionality of the 4210. These validation tests showed that the 4210 functioned according to specification in the human model. The 4210 was determined to be fit for human use.

The enhancements to the 4211 were validated in a human antitachycardia pacing trial, a human Automatic Sensitivity Tracking trial, and a bench trial of the 4211. The human antitachycardia pacing trial was carried out with a total of 9 patients. ATP was applied to 36 episodes of VT with cycle lengths ranging from 228 ms to 400 ms. The trial concluded that the Ramp (AutoD) algorithm is an effective treatment for sustained ventricular tachycardia with an increased risk of acceleration at cycle lengths less than 270ms.

The human Automatic Sensitivity Tracking (AST) trial was divided into 2 studies. The first study was an investigation of the efficacy of the AST algorithm during bradycardia pacing in which 11 patients participated. The second study was conducted to demonstrate sensing and detection of tachyarrhythmias. Twelve patients participated in this study. The trial demonstrated that the 4211 was safe and effective in sensing (and detecting) both normal rhythms and tachyarrhythmias in the clinical environment.

The bench trial of the 4211 was performed to evaluate Automatic Sensitivity Tracking, Therapy Sequencing (All therapies) and Therapy Sequencing (Pre-Shock confirmation). The testing included the use of signals gathered during an endocardial defibrillation lead trial. Thirty-four patient files were presented to 2 devices in each study. The trial showed that the 4211 can detect, confirm, and treat human arrhythmias appropriately. The devices functioned according to specifications.

In conclusion, the acute human testing demonstrated that the main differences between the 4210 and the 4211 have been validated by the trials listed above. The studies also examined the overall functionality of the device and showed that the GUARDIAN® ATP II 4211 is suitable for use in chronic human trials.

#### N. Clinical Studies

The Guardian ATP II clinical study involved 88 devices implanted in 85 patients for a cumulative total of 1785.36 implant months (mean implant duration - 21.0+/- 7.9 months, range 5 days to 35.1 months).

The patients had a mean age of 64 years (range 37 to 79 years) and a mean ejection fraction of 33 +/- 12 percent. Eleven patients (13 percent) were females. Inclusion and exclusion criteria were chosen to avoid gender bias. The preponderance of male patients reflects both the gender referral pattern for cardiac disease and the severity of disease in the centers involved. Separate analyses of safety and effectiveness data for both male and female groups indicated no difference between the genders. The data reported are representative for both men and women.

The primary objective of the study was to determine the total cumulative survival of patients implanted with the Guardian ATP II system compared to historical controls.



The following Table is a distribution of patients by indication:

**Table 2**

Description	Patients
VT or VF where the efficacy of other therapies cannot be accurately predicted	19%
VT or VF despite drug therapy	54%
VT or VF with intolerance or noncompliance with drug therapy	8%
VT or VF with inducible tachyarrhythmias	19%

The following table summarizes the characteristics of the patient population.

**Table 3**

Description	Patients
Percent Male	88%
Mean Age	64 years
Mean Left Ventricular Ejection Fraction	33%
NYHA Classification II	54%
History of Coronary Artery Disease	73%
Antiarrhythmic Drug Therapy at Implant	47%
Concomitant Surgery at Implant	28%
Previous Implantable Defibrillator	47%

The clinical study demonstrated the efficacy of the Guardian ATP II regarding sensing and therapy delivery. There were no reports of failure to sense or detect a spontaneous arrhythmia out of a total of 10,526 recorded episodes. Only two sensing errors were reported in response to induced arrhythmias; both of these occurred at the Prior to Discharge electrophysiology study.

Data obtained from the Guardian ATP II episode log showed an overall reversion rate for all ventricular arrhythmias of 97.8 percent (97.4 percent for VT, 100 percent for VF). Arrhythmias were reverted using all three levels of therapy provided by the Guardian ATP II: ATP, cardioversion shocks and defibrillation shocks. These data are summarized in Table 4.

**Table 4**

	Result	95% CI
Overall reversion (VT&VF)	97.8%	96.0%, 99.0%
Overall reversion (VT only)	97.4%	96.2%, 98.7%
Overall reversion (VF only)	100%	95.4%
ATP reversion VT	83.6%	83.1%, 85.7%
ATP acceleration rate	2.6%	1.7%, 3.7%
Cardioversion reversion VT	95.3%	86.9%, 99.0%
Cardioversion acceleration rate	4.7%	1.0%, 13.1%
Defibrillation reversion VT	99.2%	95.4%, -
Defibrillation reversion VF	100%	

There have been twelve 4211 devices explanted. Eight devices were explanted due to patient deaths. Three devices were explanted because of infection, one of which was re-implanted after the infection cleared. One device was explanted at the time of heart transplant. There have been no devices explanted due to End-of-Life. Events arising during the implant procedure resulted in two devices not being implanted. Excluding device explant due to patient death, there were four explants (4.7%) in the population. This rate is consistent with those reported for the historical control groups.

Patient survival was calculated using the Kaplan-Meier product-limit method. A total of 11 patients died during the clinical study; Two sudden cardiac deaths (SCDs) were reported at 410 and 462 days post implant. Four non-sudden cardiac deaths and five non-cardiac deaths also occurred; one of these was a perioperative death (within 30 days of implant). SCD and total survival results are shown in Table 5 with 95% confidence intervals (CI).

**Table 5**

	Result	95% CI
SCD Survival at 12 months	100%	-
Total Survival at 12 months	94.0%	88.9%, 99.1%
Mean Implant duration (days)	638	-

**XI. Conclusions Drawn from the Studies**

The 4211 system has met the primary study objective by exhibiting a total cumulative survival rate at one year of 94.0% for the 4211 population. It has also been shown to be

an effective therapy for episodes of Sudden Cardiac Death as the 1 year cumulative SCD survival is 100 % for 4211 patients.

The therapies delivered by the device have all proven to be effective in treating spontaneous episodes of ventricular arrhythmias. The antitachycardia pacing facility has exhibited an 83.6% efficacy rate in the 4211 population. Cardioversion therapy showed a similarly high efficacy rate of 95.3%.

This study has met the objectives outlined in the protocol, has demonstrated that the device and its lead systems are safe and effective when used according to device labeling.

#### XII. Panel Recommendation

Pursuant to section 515(c)(2) of the Food Drug and Cosmetic Act (the Act) as amended by the Safe Medical Devices Act of 1990, the PMA application was not referred to the Circulatory System Devices panel, an FDA advisory panel, for review and recommendation because the information in the PMA application substantially duplicates information previously reviewed by this panel.

#### XIII. FDA Decision

FDA found Telectronics Pacing Systems's facilities in compliance with the Device Good Manufacturing Practices regulation (21 CFR part 820).

The review and subsequent approval of the PMA application was interrupted, and thus delayed, due to system modifications and reports which warranted FDA reviews. After review of the data contained within the PMA application, amendments and additional information reported for the Telectronics Guardian™ ATP Model 4211 Implantable Defibrillator System, FDA recommended approval of the application.

#### XIV. Approval Specifications

The post approval recommendations are discussed in Section XIII.

# GUARDIAN™ ATP II 4211

## Physician's Manual

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Pacing Systems

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## **PREFACE**

This manual describes the prescription, use and operation of the GUARDIAN ATP II, a third-generation implantable cardioverter/defibrillator (ICD) incorporating antitachycardia and bradycardia support pacing. The GUARDIAN ATP II is designed to automatically detect and deliver therapy to treat ventricular tachycardia (VT), ventricular fibrillation (VF) and bradycardia, and forms part of an integrated system together with a lead system, a 9600-series programmer with compatible software and a 4510 Implant Support Device.

All people responsible for the implant procedure, postoperative care, and patient follow-up should be familiar with the information provided in this manual, as well as with the general clinical use of third generation ICDs. Separate Physician's Manuals for the programmer, lead system and implant support device give further details about those devices.

This manual is organized into three parts.

- Part 1 contains information intended to assist the physician in prescribing the GUARDIAN ATP II for a particular patient. This includes indications and contraindications, a summary of potential adverse effects, and details of precautions to be observed by clinical staff and by the patient. A summary of the clinical study performed to demonstrate the safety and efficacy of the GUARDIAN ATP II is also included in Part 1.
- Part 2 contains instructions for the use of the GUARDIAN ATP II. These instructions cover the implant procedure and subsequent follow up. A troubleshooting chapter is also included to assist clinical staff to determine the cause of unexpected behavior.
- Part 3 contains a detailed description of the operation of the GUARDIAN ATP II, including programmable parameters and other specifications.

A comprehensive index is included at the end of the manual.

Contact Telectronics at the address on the back cover of this manual if you have any other questions concerning the operation of the GUARDIAN ATP II.



**PART 1**  
**PRESCRIBING THE GUARDIAN ATP II**

<b>Chapter 1</b>	<b>Description of the GUARDIAN ATP II</b>	<b>Page 4</b>
	Indications and contraindications for the use of the GUARDIAN ATP II.	
<b>Chapter 2</b>	<b>Warnings</b>	<b>Page 5</b>
	A summary of warnings relating to potential safety hazards for the patient or clinical staff.	
<b>Chapter 3</b>	<b>Precautions</b>	<b>Page 6</b>
	A summary of precautions to be observed by clinical staff or by the patient.	
<b>Chapter 4</b>	<b>Adverse Effects</b>	<b>Page 8</b>
	A summary of potential adverse effects that could occur with use of the GUARDIAN ATP II.	
<b>Chapter 5</b>	<b>Clinical Study</b>	<b>Page 11</b>
	A summary of the clinical study performed to demonstrate the safety and efficacy of the GUARDIAN ATP II.	

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## DESCRIPTION OF THE GUARDIAN ATP II

The GUARDIAN ATP II implantable cardioverter/defibrillator (ICD) incorporates antitachycardia pacing, cardioversion and defibrillation shock therapy and VVI bradycardia support pacing. It is designed to automatically detect and deliver therapy to terminate treatable ventricular tachycardia (VT), ventricular fibrillation (VF) and bradycardia through an implanted lead system.

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**Caution:**

*Federal Law restricts this device to sale by or on the order of a physician (or properly licensed practitioner).*

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### Indications

The GUARDIAN ATP II Model 4211 Implantable Cardioverter Defibrillator System is indicated for use in patients who are at high risk of sudden death due to ventricular fibrillation and/or ventricular tachyarrhythmias and who have experienced one of the following situations:

- survival of at least one episode of cardiac arrest manifested by a loss of consciousness) due to a ventricular tachyarrhythmia
- recurrent, poorly tolerated sustained ventricular tachycardia (VT)

Note: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies have not been conducted.

### Contraindications

The implantation of the GUARDIAN ATP II is contraindicated in:

- patients in whom ventricular arrhythmia is drug induced or is due to electrolyte imbalance
- patients in incessant VT or VF
- patients with myocardial ischemia/infarction who have not been stabilized for an adequate period and whose tachyarrhythmia is due to ongoing ischemia.

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## WARNINGS

### Electrophysiological Testing

- Always connect the patient to an ECG monitor and ensure that an external defibrillator is present during Electrophysiological (EP) testing, as such testing involves the induction of potentially hazardous arrhythmias.

### Handling

- During the implant procedure, and at any subsequent surgical procedures including explant or post-mortem procedures, ensure that the GUARDIAN ATP II is programmed to System Off before handling the device as the GUARDIAN ATP II can deliver a potentially hazardous shock if you touch the defibrillation terminals while the device is charged.
- Never incinerate a GUARDIAN ATP II as the pulse generator could explode. The GUARDIAN ATP II must be explanted before cremation.

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## PRECAUTIONS

### Changes to the Patient's Status or Drug Regime

- Changes to the patient's drug regimen or underlying cardiovascular status may change the heart's electrophysiologic characteristics. Any such changes should be assessed by further EP studies to ensure that the programming of the GUARDIAN ATP II is appropriate for the patient.

### Implantation

- Do not implant the GUARDIAN ATP II if the patient has a fixed unipolar pacemaker, or a pacemaker which may revert to unipolar pacing under some conditions.
- Ensure that the defibrillation lead impedance is greater than 20  $\Omega$ . An impedance below 20  $\Omega$  could damage the GUARDIAN ATP II.

### Using the Programmer

- If the patient develops an arrhythmia while the episode log is being read, remove the programming wand to break the telemetry link and allow the GUARDIAN ATP II to detect the arrhythmia and deliver therapy according to the programmed parameters.
- If an external stimulator is used to induce tachyarrhythmia, use the therapy assessment procedure to suspend automatic operation, and remove the external induction connections before delivering therapy.

### Environmental Hazards

- Electrical interference from intense electromagnetic fields may affect the operation of the GUARDIAN ATP II.
- Low levels of alternating current (AC) - for example from poorly grounded electrical equipment - may affect the operation of the GUARDIAN ATP II.

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## Cellular Phones

Recent studies have indicated there may be a potential interaction between cellular phones and ICD operation. Potential effects may be due to either the radio frequency signal or the magnet within the phone and could include inhibition or possible discharge of the ICD when the phone is within close proximity (within 6 inches or 15 centimeters) to the implanted device.

Based on testing to date, effects resulting from an interaction between cellular phones and the implanted ICD have been temporary. Simply moving the phone away from the implanted device will return it to its previous state of operation. Because of the great variety of cellular phones and the wide variance in patient physiology, an absolute recommendation to cover all patients cannot be made.

Patients having an implanted ICD who operate a cellular phone should:

- **Maintain a minimum separation of 6 inches (15 centimeters) between a hand-held personal cellular phone and the implanted device. Portable and mobile cellular phones generally transmit at higher power levels compared to hand-held models. For phones transmitting above 3 watts, maintain a minimum separation of 12 inches (30 centimeters) between the antenna and the implanted device.**
- **Patients should hold the phone to the ear opposite the side of the implanted device. Patients should not carry the phone in a breast pocket or on a belt within 6 inches (15 centimeters) of the implanted device as some phones emit signals when they are turned ON but not in use (i.e., in the listen or standby mode). Storing the phone in a location opposite the side of the implant is recommended.**

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## **Electrosurgical Procedures**

- Program the GUARDIAN ATP II to System Off before any electrosurgical procedure, and interrogate the device afterwards to confirm that it is functioning appropriately.
- Patients with implanted defibrillators should not be subjected to MRI, lithotripsy, electrocautery or RF ablation.
- When it is necessary to perform external defibrillation, take the following precautions:
  - Program the GUARDIAN ATP II to System Off before applying external defibrillation.
  - Place external defibrillation paddles at least 10 cm away from the GUARDIAN ATP II and such that the GUARDIAN ATP II, the sense/pace and shock electrodes are not in line with the current flow. Do not use internal defibrillation paddles if the GUARDIAN ATP II is connected to the lead system.
  - Interrogate the GUARDIAN ATP II after external defibrillation to confirm that it is functioning appropriately.
- Avoid ionizing radiation. If the patient must receive high dose radiotherapy, take the following precautions:
  - Program the GUARDIAN ATP II to System Off and disable bradycardia support pacing for the duration of radiotherapy treatment.
  - Protect the GUARDIAN ATP II from direct exposure.
  - Provide temporary pacemaker backup if the patient requires bradycardia support pacing.
  - Interrogate the GUARDIAN ATP II after the treatment to confirm that it is functioning appropriately.
  - Interpret any changes in the operation of the GUARDIAN ATP II as radiation damage and take immediate remedial action.
- Do not use diathermy directly over the implanted system.



## 4.

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**ADVERSE EFFECTS**
**Reported Adverse Effects**

The GUARDIAN ATP II clinical study involved 88 devices implanted in 85 patients for a cumulative total of 1785.36 implant months (mean implant duration =  $21.0 \pm 7.9$  months, range 5 days to 35.1 months). Adverse events reported from the clinical study included 14 observations and 18 complications. Eleven patients died during the course of the study. None of the deaths were judged to be related to the device.

Observations and complications reported for more than one patient are listed by frequency of occurrence in Table 1.

**Table 1:** *Incidence of reported adverse events*

	<i>No. of patients</i>	<i>% of patients</i>	<i>No. of Events</i>	<i>Events / patient month</i>	<i>Patient months between events</i>
<b>Observations<sup>1</sup> (total)</b>	13	15.3%	14	0.008	127.5
Shocks for atrial fibrillation	2	2.4%	3	0.002	595.1
Environmental noise	3	3.5%	3	0.002	595.1
Increased pacing threshold	2	2.4%	2	0.001	892.7
<b>Complications<sup>2</sup> (total)</b>	18	21.2%	18	0.010	99.2
Lead dislodgment	5	5.9%	5	0.003	357.1
Infection	5	5.9%	5	0.003	357.1
Other lead complications	4	4.7%	3	0.002	595.1

1. Observations can be corrected by non-invasive measures such as reprogramming.
2. Complications can only be corrected by invasive measures such as surgical intervention.

Five devices which were not part of the GUARDIAN ATP II clinical study exhibited a high current drain leading to battery depletion. There were no deaths or injuries associated with these failures. The implant durations for these devices ranged from 17 to 33 months. The high current drain was due to the failure of a transistor resulting from contamination during testing conducted by the component's manufacturer.

## Potential Adverse Effects

In addition to the adverse events reported in this clinical study, other potential adverse effects may occur with this type of device. This includes effects due to the GUARDIAN ATP II and all its components, the lead systems, the patient's individual response, complications of surgery and defibrillator therapy, and environmental hazards.

Potential adverse effects and complications include, but are not limited to, those listed in Table 2.

**Table 2:** *Potential adverse effects and complications*

<i>Cause</i>	<i>Possible Effects</i>
<b>Components</b>	
Premature cell depletion	Decrease in pacing output, rate or sensitivity; loss of capture or inhibition; increased pulse duration; decreased or no shock output; entry to a backup mode
Random component failure	No bradycardia pacing output; reversion to asynchronous mode; rate change; loss of capture; inappropriate or no shock discharge; entry to a backup mode; inability to reprogram the device.
<b>Electromagnetic Interference</b>	
Large power tools, industrial equipment, appliances, AC current leakage, etc. Cellular phones.	Output inhibition; reversion to asynchronous mode or slower than normal pacing rate; spurious senses; inappropriate shock discharge.
Electrocautery, RF ablation, diathermy, magnetic resonance imaging (MRI)	Output inhibition, cardiac burns, ventricular fibrillation; reversion to fixed rate pacing; inappropriate shock discharge; entry to a backup mode.
External defibrillation	No output; cardiac burns; increased defibrillation threshold; exit block; entry to a backup mode.
<b>Lead system</b>	
Dislodgment, fracture or insulation break in sense/pace lead	Intermittent or continuous loss of capture, pacing, and/or sensing; slower than normal pacing rate; quicker than expected cell depletion; oversensing or undersensing, possibly leading to inappropriate or no shock discharge.
Dislodgment, fracture or insulation break in defibrillation lead	Decreased or no shock discharge; increased defibrillation threshold; entry to a backup mode.
Setscrew not securely tightened, connector not fully inserted into terminal, or adaptors not securely applied,	Intermittent or continuous loss of capture or sensing; slower than normal pacing rate; failure to defibrillate; oversensing or undersensing, possibly leading to inappropriate or no shock discharge; entry to a backup mode.
Cardiac perforation or penetration.	Intermittent or continuous loss of capture and/or sensing; cardiac tamponade; hematoma; muscle or nerve stimulation; threshold rise or exit block.

**Table 2:** *Potential adverse effects and complications*

<b>Cause</b>	<b>Possible Effects</b>
<b>Lead system (continued)</b>	
Myocardial irritability at implant.	Ventricular tachycardia; ventricular fibrillation; PVCs or non-sustained ventricular tachycardia; atrial fibrillation; atrial arrhythmias.
Chronic myocardial irritability due to epicardial defibrillation patch	Constrictive pericarditis leading to reduced cardiac output; abrasion of coronary vessels; tissue damage.
Elevated defibrillation threshold	Failure to defibrillate.
Elevated pacing threshold	Loss of capture and/or sensing.
Transvenous introduction	Acute hemorrhage, thrombus formation, air embolism, pneumothorax, hemothorax, hematoma, nerve injury, etc.
<b>Patient response</b>	
Physiological reactions	Skin erosion; migration of defibrillator; formation of hematomas, cysts or keloids; fluid accumulation.
Infection	Skin erosion; sepsis.
Change in drug therapy or patient's underlying cardiovascular status	Increased defibrillation threshold; failure to defibrillate; induction of arrhythmia by device shock; detection of atrial flutter/fibrillation causing inappropriate shock discharge; changes in sinus rate which may be detected as tachycardia during exercise; changes in tachycardia cycle length or appearance of a new, and untested, morphology.
Psychological effects	Imagined pulsing; dependency; fear of inappropriate pulsing; fear that pulsing capability may be lost.

## 5.

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# CLINICAL STUDY

### Summary

The GUARDIAN ATP II was evaluated in a multicenter clinical study involving 85 patients.

### Primary Objective

The primary objective of the study was to determine the total cumulative survival of patients implanted with the GUARDIAN ATP II system compared to historical controls.

### Method

The GUARDIAN ATP II clinical study involved 88 devices implanted in 85 patients for a cumulative total of 1785.36 implant months (mean implant duration =  $21.0 \pm 7.9$  months, range 5 days to 35.1 months).

The patients had a mean age of 64 years (range 37 to 79 years) and a mean ejection fraction of  $33 \pm 12\%$ . Eleven patients (13%) were females. Inclusion and exclusion criteria were chosen to avoid gender bias. The preponderance of male patients reflects both the gender referral pattern for cardiac disease and the severity of disease in the centers involved. Separate analyses of safety and effectiveness data for both male and female groups indicated no difference between the genders. The data reported below is therefore representative for both men and women.<sup>1 2</sup>

### Results

A summary of the results is presented below.

### Patient Survival

Patient survival was calculated using the Kaplan-Meier product-limit method. A total of eleven patients died during the clinical study. Two

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1. Tobin JN, Wassertheil-Smollers, Wexler JP, et al: Sex bias in considering coronary bypass surgery. *Ann Intern Med* 1987; 107: 19-25.
  2. Mark DB, Shaw LK, DeLong ER, Califf RM, Pryor DB: Absence of sex bias in the referral of patients for cardiac catheterization. *N Eng J Med* 1994; 330: 1101-6.

Sudden Cardiac Deaths (SCD) were reported at 410 and 462 days post-implant. Four non-sudden cardiac deaths and five non-cardiac deaths also occurred; one of these was a perioperative death (within 30 days of implant). SCD and total survival results are shown in Table 3 with 95% confidence intervals (CI).

**Table 3: Patient Survival**

	<i>Result</i>	<i>95% CI</i>
SCD Survival at 12 months	100%	-
Total Survival at 12 months	94.0%	88.9%, 99.1%
Mean implant duration (days)	638	-

### **Efficacy of Therapy**

The clinical study demonstrated the efficacy of the GUARDIAN ATP II sensing and therapy. There were no reports of failure to sense or detect a spontaneous arrhythmia out of a total of 10,526 recorded episodes. Only two sensing errors were reported in response to induced arrhythmias; both of these occurred at the Prior to Discharge electrophysiology study.

Data obtained from the GUARDIAN ATP II episode log (see page 92 in Chapter 12) shows an overall reversion rate for all ventricular arrhythmias of 97.8% (97.4% for VT, 100% for VF). Arrhythmias were reverted using all three levels of therapy provided by the GUARDIAN ATP II: antitachycardia pacing (ATP), cardioversion shocks and defibrillation shocks. This data is summarized in Table 4

Safety: See Chapter 4 ADVERSE EFFECTS

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**Table 4:** *Efficacy of Tachyarrhythmia Therapy*

	<i>Result</i>	<i>95% CI</i>
Overall reversion (VT & VF)	97.8%	96.0%, 99.0%
Overall reversion (VT only)	97.4%	95.2%, 98.7%
Overall reversion (VF only)	100%	95.4%, –
ATP reversion of VT	83.6%	81.3%, 85.7%
ATP acceleration rate	2.6%	1.7%, 3.7%
Cardioversion reversion of VT	95.3%	86.9%, 99.0%
Cardioversion acceleration rate	4.7%	1.0%, 13.1%
Defibrillation reversion of VT	99.2%	95.6%, 100%
Defibrillation reversion of VF	100%	95.4%, –

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