Summary of Safety and Effectiveness

P000009

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BIOTRONIK, Inc.
Lake Oswego, OR 97035

Phylax AV ICD with
Programmer Software
(I-GAV.2.U)

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Division of Cardiovascular Respiratory & Neurological Devices

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Summary of Safety and Effectiveness

I. GENERAL INFORMATION

Device Generic Name:	Implantable Cardioverter Defibrillator System & Programmer Software
Device Trade Name:	Phylax AV ICD, Model 122 382 Software Cartridge SWM / I-GAV.2.U, Model 128 814
Applicant's Name:	Sponsor: BIOTRONIK, Inc. 6024 Jean Road Lake Oswego, OR 97035 Manufacturer: BIOTRONIK GmbH & Co. Woermannkehre 1, Berlin, Germany
Premarket Approval (PMA) Application Number:	P000009
Date of Panel Meeting:	Not Applicable
Date of Notice of Approval To Applicant:	September 29, 2000

II. INDICATIONS AND USAGE

The Phylax AV ICD System is indicated for use in patients who are at high risk of sudden death due to ventricular arrhythmias and have experienced one or more of the following situations: (1) survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyarrhythmia, (2) recurrent, poorly tolerated sustained ventricular tachycardia (VT). *NOTE: The clinical outcome for hemodynamically stable VT patients is not fully known. Safety and effectiveness studies for this indication have not been conducted.*

III. CONTRAINDICATIONS

The use of Phylax AV Implantable Cardioverter Defibrillator (ICD) is contraindicated in: (1) patients whose ventricular tachyarrhythmias may have transient or reversible causes such as acute myocardial infarction, digitalis intoxication, drowning, electrocution, electrolyte imbalance, hypoxia, and sepsis; (2) patients with incessant VT or VF (ventricular fibrillation); (3) patients who have a unipolar pacemaker; and (4) patients whose only disorder is bradyarrhythmias or atrial arrhythmias.

IV. DEVICE DESCRIPTION

The BIOTRONIK Phylax AV Implantable Cardioverter Defibrillator System consists of implantable components (pulse generator and lead), external programming system and various accessories used during implantation and follow-up electrophysiological procedures. Similar to several commercially available ICD systems, the Phylax AV ICD System is a dual-chamber pulse generator capable of delivering antitachycardia pacing (ATP), cardioversion and defibrillation shock therapy. The device shock output ranges from 0.5 to 30 joules in the form of biphasic waveform. In addition to ventricular defibrillation therapy, it also provides dual chamber bradycardia pacing support. The system may also be used to collect diagnostic data to aid the physician's assessment of a patient's condition and the response of the implanted device.

ICD Pulse Generators –Phylax AV ICD, model number 122 382.

The Phylax AV ICD has a hermetically sealed titanium can with an epoxy resin header. The Phylax AV has two DF-1 and two IS-1 header ports. In addition, the device uses the outer metallic housing of the ICD as an additional electrode to augment the implanted lead system. The ICD uses bipolar atrial and ventricular sensing/pacing leads to provide enhanced discrimination of atrial and ventricular tachyarrhythmias. The Phylax AV dimensions are 109 g, 69 cc, 76 x 63 x 17 mm.

The Phylax AV continuously monitors the patient's cardiac rhythm and classifies arrhythmias based on the cardiac rate and independently programmable detection criteria such as High Rate, Sudden Onset and/or Stability, in addition to an available SMART Detection algorithm. Depending on the rate of the arrhythmia, as well as the additional detection criteria, therapy is appropriately inhibited or delivered to the patient. The therapy available to respond to a detected ventricular tachyarrhythmia includes antitachycardia pacing (ATP), cardioversion (CV), and defibrillation shock therapy.

The SMART Detection algorithm is an integral portion of the Phylax AV ICD and is designed to discriminate life-threatening ventricular tachycardias from relatively harmless atrial tachyarrhythmias. This algorithm uses information about the signals from the atrial and ventricular lead systems and is designed to reduce the amount of inappropriate therapy that might be delivered as a result of a supraventricular tachycardia (SVT). Neither the SMART Detection algorithm nor the Phylax AV are designed to detect or deliver therapy to terminate atrial arrhythmias, and therefore this is not the purpose of the algorithm or the device.

Lead Compatibility

The Phylax AV was tested and is compatible with BIOTRONIK's previously approved ICD leads (P980023, dated 10-27-98) and any market released atrial IS-1 pacing and sensing lead. During the clinical study, a number of different atrial pacing and sensing lead models from different manufacturers were implanted and tested. Table I summarizes the different atrial leads that were used in the clinical study.

Table I Atrial Lead Distribution

Atrial Lead Manufacturer	Atrial Lead Model	Number of Leads
BIOTRONIK	FH	2
BIOTRONIK	POLYROX	12
BIOTRONIK	RETROX	27
BIOTRONIK	SYNOX	14
Guidant	Fineline	3
Guidant	Sweet Tip	4
Intermedics	Thinline	1
Medtronic	CapSure	2
Medtronic	CapSureFix	4
Pacesetter	Tendril DX	51
Sulzer Oscor	Oscor	9

Programming and Monitoring System

External devices that interact with and test the implantable devices are also part of the ICD System. These external devices are U.S. market released and include the TMS 1000^{PLUS} Tachyarrhythmia Monitoring and the EPR 1000^{PLUS} Programming and Monitoring System. The programmers are used to interrogate and program the ICD.

Software System

The TMS 1000^{PLUS} and EPR 1000^{PLUS} programming systems use MS DOS 5.0 operating system, that is unchanged from the operating system used throughout the clinical study.

The software applications and the DOS operating systems used by the TMS 1000^{PLUS} and EPR 1000^{PLUS} are maintained on a single write-protected (read-only) PCMCIA Flash-EPROM cartridge.

The software included on the cartridge is divided into thee separate functional modules. The Manager software provides overall control and administration of the software applications. The manager permits the activation of only one application (TMS 1000 or Phylax AV) at a time.

V. WARNINGS AND PRECAUTIONS

See attached labeling.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative therapies for the treatment of life-threatening ventricular arrhythmias as deemed appropriate by the physician are based upon electrophysiology (EP) testing and other diagnostic evaluations. These include the use of antiarrhythmic medication, electrical ablation, cardiac surgery, pacemakers and other commercially available implantable cardioverter defibrillators or a combination thereof.

VII. MARKETING HISTORY

The Phylax AV ICD System began distribution outside the United States in the summer of 1998 and has been commercially distributed in the following countries: Germany,

France, England, Scotland, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Chile, China, Israel, Italy, Netherlands, Poland, Portugal, Russia, Slovakia, Spain, Czech Republic, Turkey, Hungary, and Switzerland. BIOTRONIK's Phylax AV ICD has not been withdrawn from these markets for any reason.

VIII. ADVERSE EVENTS

Reported Adverse Events

The clinical study involved 128 devices implanted in 126 patients with cumulative implant duration of 795.5 months (mean implant duration 6.3 months). There were a total of two deaths during the course of the trial; neither of which were judged by the clinical study investigator to be device related. The two deaths were related to heart failure and pneumonia. Both of the deaths occurred more than three months post implant.

Three devices were explanted during the trial. One device was explanted secondary to the patient reporting pain at the implant site; the patient was subsequently implanted with another device. One device was explanted due to a random component failure, and the other device was explanted after reaching ERI, which was anticipated based on the number of shocks delivered. These two patients were subsequently implanted with other Phylax AV ICDs.

Table II provides a summary of the adverse events that were reported during the clinical study regardless of whether or not the event was related to the ICD system. A complication was defined as a clinical event that resulted in additional invasive intervention, injury, or death. An observation was defined as a clinical event that did not result in additional invasive intervention, injury, or death.

Table II Reported Adverse Events

	# of patients with AEs	% of Patients with AEs	# of AEs	AE/pt-yrs
Complications Total	**14**	**11.1%**	**18**	**0.27**
Lead Repositioning	10	7.9%	12	0.18
Discomfort at Implant Site	1	0.8%	1	0.02
Infection	1	0.8%	1	0.02
Thrombus	1	0.8%	1	0.02
Pneumothorax	1	0.8%	1	0.02
ERI	1	0.8%	1	0.02
Random Component Failure	1	0.8%	1	0.02
Observations Total	**47**	**37.3%**	**74**	**1.12**
T-wave Oversensing	7	5.6%	7	0.11
Increased Pacing Threshold	7	5.6%	7	0.11
Required additional antiarrhythmic drug therapy	7	5.6%	7	0.11
SVT Therapy-Unrelated to SMART	6	4.8%	8	0.12
Software version I-GAV.1.U	6	4.8%	6	0.09
Detection	5	4.0%	5	0.08
Lead repositioning or revision at implant	5	4.0%	5	0.08
TMS 1000	4	3.2%	4	0.06
Lead difficulties at Implant	3	2.4%	3	0.05
Difficulties with Telemetry	3	2.4%	3	0.05
Atrial Lead Dislodgment	2	1.6%	2	0.03
SVT Therapy-Related to SMART	2	1.6%	4	0.06
Initial therapy did not convert arrhythmia	2	1.6%	2	0.03
Low P/R-Wave Amplitude	2	1.6%	2	0.03
Intermittent Undersensing/ Oversensing	2	1.6%	2	0.03
Lead Repositioning at implant	2	1.6%	2	0.03
Asynchronous Pacing	2	1.6%	2	0.03
Atrial Arrhythmias	2	1.6%	2	0.03
Atrial arrhythmia with ventricular tracking	1	0.8%	1	0.02
External cardioversion due to atrial tachyarrhythmias.	1	0.8%	1	0.02
P-wave Measurements Change with Position	1	0.8%	1	0.02
Patient Symptomatic at Upper Tracking Rate	1	0.8%	1	0.02
Diaphragmatic Pacing	1	0.8%	1	0.02
Myocardial Infarction	1	0.8%	1	0.02
Shock delivered as a result of electrocautery	1	0.8%	1	0.02
Phantom programming	1	0.8%	1	0.02

Number of Patients = 126, Number of Patient-Years = 66.3

1. This category includes various anomalies that were related to the original programmer software used in the clinical study, I.GAV.1.U. Each of these events was resolved through revisions to the programmer software resulting in version I.GAV.2.U.
2. This category includes any difficulties encountered while using the TMS 1000 Tachyarrhythmia Monitoring System, which is a commercially available device that was used during the clinical investigation.

Potential Adverse Events

Adverse events (in alphabetical order) associated with ICD systems include the following:

- Acceleration of arrhythmias (caused by device)
- Air embolism

- Bleeding
- Chronic nerve damage
- Erosion
- Excessive fibrotic tissue growth
- Extrusion
- Fluid accumulation
- Formation of hematomas or cysts
- Inappropriate shocks
- Infection
- Keloid formation
- Lead abrasion and discontinuity
- Lead migration/dislodgment
- Myocardial damage
- Pneumothorax
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Potential mortality due to inability to defibrillate or pace
- Thromboemboli
- Venous occlusion
- Venous or cardiac perforation

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

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of shocking while conscious
- Fear that shocking capability may be lost
- Imagined shocking (phantom shock)

IX. SUMMARY OF PRE-CLINICAL STUDIES

The following tables summarize the validation testing (safety and performance) conducted on components and subassemblies of the BIOTRONIK Phylax AV ICD System, including testing of finished devices, packaging and shipping tests. Validation testing was performed to appropriate European, International and National standards, in addition to internal BIOTRONIK specifications. In addition, biocompatibility testing was conducted. In the table below, "Pass" denotes that the test results satisfied the company's device specifications.

Component Testing

Bench testing of all components of BIOTRONIK's Phylax AV ICD was successfully completed. These tests included testing of the battery, high energy capacitors, and feedthroughs used to assemble the Phylax AV. The testing also included the ICD header and sealing plugs used to isolate the setscrews from body fluids. The component testing is summarized in Table III.

Table III Summary of Component Tests

TEST PERFORMED	SAMPLE SIZE EACH TEST	TEST RESULTS (PASS/FAIL)
BATTERY INTEGRITY		
Pulse Discharge until Charge Time Limit:	10	Pass
Destructive Test Inspection and Validation of the Graphite Wire Mesh, Impedance Response, Rapid Discharge 5.1 kΩ, High and Low Temperature Storage, Temperature Shock Test, Short Circuit Test, Charge Test, Accelerated Pulse Test	1 to 5	Pass
PHYLAX AV CAPACITORS		
Electrical Ratings at 37°C, Determination of Mechanical Ratings, Visual Tests Before and After the Vacuum Stress Test, Electrical Rating Before and After Vacuum Stress Test, Initial Leakage Current	20 to 40	Pass
Formation Behavior, Cyclical Charging and Discharging Test, Electrical Ratings After Isolated Storage, Vibration Test, Determination of Breakdown Voltage, Solderability of the Terminals after Aging, Hot Solder Stability, Out-gassing Behavior in a Vacuum, Determination of the Voltage Polarity Changes, Temperature Cycle, Continuous Operation at Rated Voltage, Storage Temperature 50°C, Stored At Rated Voltage and 50°C	1 to 12	Pass
FEEDTHROUGHS (UNIPOLAR, BIPOLAR, GROUNDED)		
Temperature Shock, Helium Leak Test, Insulation Test, Dimensional Inspection, Pin Tensile Strength Test, Temperature Shock, Insulation Test, Dimensional Inspection, Pin Extraction and Tightness tests, Pin Flex Strength Test	10 to 1060	Pass
SUMMARY OF HEADER VALIDATION TESTING		
Mechanical Shock Test, Vibration Test (Maximum acceleration 10g), Vibration Test (Max. acceleration 20g), Temperature Cycle, Ultrasound, In Vitro Test 2000 Hour, Lead Insertion/ Extraction Force Testing of the ICD header, IS-1 Dimension Tests Verification of the Header to IS-1 and DF-1 Standards, Retention Forces of Header with Tightened Setscrew, Temperature shock, Header Shearing Test, Connecting with Leads from another Manufacturer, Current Load on Connector Port, High voltage isolation of Leak-proof Sealing Plug, Visual Control	1 to 11	Pass
SELF SEALING PLUG TESTING		
Adhesion Strength of the Connector Port, in-vitro Test, Passive - 2000 Hours, High-Voltage Insulation Resistance after in-vitro Test, Dimensional And Visual Inspection of the Sealing Plugs, Reconnection during in vitro Test, 8000 Hours – in vitro Test, Connection Force of the Connector Port Over Time, Determining the Maximum Screw Depth of the Setscrew in the Fixation Block, Test for the Possibility of the Torque Wrench Jamming in the Sealing Plug Port, Maximum Torque Moment Carryover from the Setscrew Hexagonal Socket, Test for Possible Damage to the Sealing Cap with the Screwdriver, Testing for Damage During Contacting, Test for Damage to the Sealing Plugs by Reversing the Torque Wrench	5 to 60	Pass
Dimensional And Visual Inspection of the Sealing Plugs,	160	Pass
Dimensional and Visual Inspection of the Connector Port,	211	Pass

Hybrid Testing

Bench testing of the hybrid electronic circuitry of BIOTRONIK's Phylax AV ICD was successfully completed. This testing was separated into testing of the control hybrid, high voltage flex circuit and the assembled module consisting of these two circuits. The

control hybrid is a standard chip and wire hybrid circuit containing the low power digital electronics used to control functions of the Phylax AV. The high voltage flex circuit is a surface mounted flexible construction containing the components to generate the high energy defibrillation shocks. The electronic module is the assembly of these two circuits. The testing is summarized in Table IV.

Table IV Summary of Hybrid Testing

Test Performed	Sample Size Each Test	Test Results (Pass/Fail)
Control Hybrid Tests		
Visual Inspection, Constant Acceleration, Die Shear, Wirebond Pull Strength Pre-Stabilization Bake, Wirebond Pull Strength Post-Stabilization Bake, Pin Bending Stress, Vibration / Variable Frequency, Mechanical Shock Test, Transportation Test in the Circuit Packaging	5 to 15	Pass
High-Voltage Flex Tests		
Visual Inspection after Temperature Cycle, Bond Pull after Temperature Cycle, Flex Testing, Die Shear, Physical Dimensions, Physical Dimensions, Charge Dump, Wirebond Pull Strength Post-Stabilization Bake	3 to 10	Pass
Module Tests		
Die Shear Strength, 1000 Shock Cycles, Physical Dimensions, Mechanical Stress (Temperature cycle), 1000 Hour Life Test	2 to 22	Pass
Wirebond Pull Strength	217	Pass

Embedded Software Testing

Bench testing of the embedded software contained within BIOTRONIK's Phylax AV ICD was successfully completed. The embedded software is contained within the components of the control hybrid and contains the necessary instructions to implement the Smart Detection algorithm and other device features and functions. The embedded software testing is summarized in Table V.

Table V Summary of Embedded Software Testing

TEST PERFORMED	SAMPLE SIZE EACH TEST	TEST RESULTS (PASS/FAIL)
SUMMARY OF EMBEDDED SOFTWARE VALIDATION TESTS PHYLAX AV ICD		
Defibrillation Shock Waveform Morphology, Committed and Non Committed DF and CV Shocks, Gain Switching and Detector Initialization, Noise Detection, Auto Sensitivity, Automatic Mode Conversion, Magnet Behavior, Emergency Shock and Emergency Pacing, Parameter Error Detection, ERI detection, VF Classification, Memory Self-Test, Detection Override and Safety Timer, Bipolar Sensing, Pacing Voltage and High Rate Pacing, Long Step Duration, Communication Error Checking, Bradycardia Support, Inhibition of Tachycardia Treatment, Redetection, Acceleration and Termination, ATP Treatment, Capacitor Reform, Arrhythmia Induction and Manual Shock, Pacing Threshold and Lead Impedance, IEGM, Event Counters, and Episode History, VT Classification, Power Saver and Watchdog, Refractory Test	Current Version of Embedded Software	Pass

EMC Testing

Testing of the susceptibility of BIOTRONIK's Phylax AV ICD electromagnetic interference was successfully completed and is summarized in Table VI.

Table VI Summary of EMC Testing

TEST PERFORMED	SAMPLE SIZE EACH TEST	TEST RESULTS (PASS/FAIL)
SUMMARY OF ELECTROMAGNETIC TESTING		
Programming Behavior During Electromagnetic Interference, Defibrillation Resistance, Protection Against Changes Caused By High Powered Electrical Fields Applied To Patient, Prevention of Erroneous Function Due To Unmodulated EMI, Safety Test of Monitoring Modulated EMI, Testing to ensure a significant demodulation signal is not generated during exposure to HF-Surgery equipment, High Frequency (HF) Surgical Equipment	1 to 5	Pass
SUMMARY OF BIOTRONIK CELLULAR TELEPHONE TESTING WITH THE PHYLAX AV		
esistance to Interference from Cellular Telephones (79 Mhz to 1100 Mhz)	1	Pass
esistance to Interference from Cellular Telephones (850 Mhz to 2500 Mhz)	1	Pass
esistance to Interference from Cellular Telephones. U.S. Cellular elephones. (NADC= TDMA-50) (MIRS = TDMA-11)	1	Pass

Finished Device Testing

Testing of the fully assembled Phylax AV ICD was successfully completed. Testing of the completed device was performed with the devices after various stages of post-assembly product processing. Tests were performed with sterilized product, product prior to sterilization and to devices that were packaged and ready for shipment. The testing is summarized in Table VII.

Table VII Finished Device Testing

Test Performed	Sample Size Each Test	Test Results (Pass/Fail)
Finished Device Validation Measurements – End Product		
Identification of the Shipping Packaging, Completeness of sales unit, Transportation Test, Test of the Accompanying Documents – Technical Manual, General Labeling Requirements, Wipe Test of the Outer Box Label, Wipe Test of the Blister Cover Label	1 to 3	Pass
Finished Device Validation Measurement – Sterile Unit		
Identification of the Sterile Packaging, Device Protection within the Shipping Container with regard to Temperature, Humidity and Air Pressure, Confirmation of Sterility and EtO residual analysis, Information About Microbial Impermeability, Visual Inspection of the Single Use Packaging	1 to 10	Pass
Finished Device Validation Measurement – Assembled Unit		
Mechanical Shock Test, Vibration Test, Temperature Cycle, Exposure to Diagnostic Ultrasound, Dimensional and Visual Inspection of the Header, Labeling and Recognition, Defibrillator Casting, Surface Inspection Test	1 to 10	Pass
Finished Device Validation Measurement – Assembly Groups		
Helium Leakage Test, Insertion/ Extraction Test, Lead Retention Force, Electrode deformation	5 to 10	Pass
Finished Device Long Term Tests		
In vitro Test 2000 Hour	3	Pass
Finished Device BIOTRONIK Test – End Product		
Adhesive Bond of the Label for Blister Cover and Carton	10	Pass
Finished Device BIOTRONIK Internal Test – Assembly Groups and Sterile Unit		
Temperature Shock Test, Header Shear Test, Visual Inspection: Inner Assembly, Visual Inspection, Holding Strength of the Connector Port, Backpressure from Pin Insertion (only for IS-1 and DF-1), Determination of Insertion/ Extraction forces of Non-BIOTRONIK Leads	2 to 10	Pass
Finished Device BIOTRONIK Internal Test – Individual Packaging Parts		
Wipe Test of QSI-Seal, Laser, and Lot Number Labels, Temperature Storage of QSI Seal, Laser and Lot Number Labels, Temperature Cycling for QSI-Seal, Laser and Lot Number Labels, Wipe Test of the Carton, Effect of Water on the Carton Surface	1 to 5	Pass

Test Performed	Sample Size Each Test	Test Results (Pass/Fail)
Finished Device Validation Tests – Fundamental Safety Test		
Defibrillation Resistance, Protection Against Changes Caused by High Powered Electrical Fields Applied to Patient, Safety Tests Related to Injected Currents. Tested in Common and Differential Modes with Sense/Pace Lead and in Common Mode with Shock Lead, Effects of Exposure to Static Magnetic Fields, Test of Noise Mode Switching, Prevention Of Erroneous Function Due to Unmodulated EMI, Safety Test of Monitoring Modulated EMI, Testing of ICD to Ensure that a significant demodulation signal is not generated during Exposure to HF-Surgery Equipment, Protection Against Electrostatic Discharge, Exposure of devices to Electrostatic Discharge Equivalent Signals, Electrical Neutrality of the ICD, High Frequency (HF) Surgical Equipment, High-Rate Protection, Test of Input Protection against ICD Output	1 to 5	Pass
Finished Device Validation Tests – Functionality		
Measurement of Input Impedance, Haversine Response, Pulse Behavior as a Function of Pulse Parameters, Pulse Behavior as a function of Pulse Parameters, Pulse Behavior as a Function of Load, Pulse Parameters, and Battery Voltage, Shock Behavior as a Function of Battery Supply Voltage, Stimulation Outputs – Pulse Behavior as a Function of Temperature, Shock Output as a Function of Load and Shock Parameters, Shock Outputs: Response as a Function of Temperature, Refractory Period Response after Pace and Sense, Synchronization Response, Functional Test of Components as a Function of Operating Voltage and Temperature, Functional Test of Magnet Effect, Programmability as a Function of Load Resistance, Programmability during Electromagnetic Coupling, Programming Behavior During Electromagnetic Interference, Influence of a Non-BIOTRONIK Programming Device on Function, Programming Response as a Function of Programming Time, Test of the Committed Shock, Test of the Non-committed Shock, Test of the ATP Mode, Test of the ATP Therapy Forms, Test of the Stimulation Response under the Effects of External Noise,	1	Pass
Finished Device Validation Tests – Hazard Analysis, Design Analysis		
Test of Leakage Distance and Air Gap within the High Voltage (HV) section. Risk Control: High Voltage Switches, Capacitor, and High Voltage Generator; Risk Control: MCU System	1	Pass
Finished Device Additional Tests		
Test of Latch-up Resistance, Hybrid Turn-ON Behavior, Effect of Light on Hybrid Circuit, Influence of Alternating Magnet Fields, Application of Electrocautery to an ICD within a Physiological NaCl Solution, Sensitivity as a Function of Time after Pace, Duty Cycle as a Function of Crystal Oscillator Resistance, Detailed Crosstalk Analysis, IGEM Tests	1 to 5	Pass
Finished Device Long-Term Validation Tests		
Shock Generation Before and After ERI Response, Modified Test of the ERI Response with Graphite-Coated Battery	3	Pass

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Test Performed	Sample Size Each Test	Test Results (Pass/Fail)
Current Consumption	55	Pass
Current Consumption	920	Pass
Service Time Calculation	N/A	Pass
Finished Device Validation Tests – Hazard Analysis, Design Analysis		
Determination of Programming and Interrogation Distances	10	Pass
Warming during Shock Release	1	Pass

Programmer Software Testing

Testing of the programmer software used to program and interrogate BIOTRONIK's Phylax AV ICD was successfully completed. The programmer software is contained in EEPROM write protected cartridges and is referenced as SWM 1000 / I-GAV.2.U. This software cartridge contains the operating system, application for the Phylax AV and the software application for the TMS 1000^{PLUS} Tachyarrhythmia Monitoring System. The software testing included a complete analysis of the available features and parameters and their programmability. The programmer software testing is summarized in Table VIII.

Table VIII Summary of Programmer Software Testing

Test Performed	Sample Size Each Test	Test Results (Pass/Fail)
Programmer Software Validation Testing		
Standard Parameter Check, Safe Parameter Check, Conflict Identification on Entry, Fuel Gauge-Display BOL, MOL1, and MOL2, Fuel Gauge – Display ERI and EOS, Fuel Gauge Error Detection, Safety Lockouts of Manual Shock, Safety Lockouts of Induction, Safety Lockouts of Capacitor Reform, Safety Lockouts of Emergency Shock, Emergency Pacing Error Recovery, Lockouts on EP – Test Entry, Lockouts On Program Transmit, Emergency Program Not Blocked by Serial Number, Emergency Program Key Availability, Safe Key can Interrupt Other Operations, Magnet Mode Behavior in EP Test, Operation of System Reset, Exclusion of Non-Release Features, Programming Head Safe Key Availability, Emergency Shock and Application Switching, Command Response Communication Errors, Serial Number Communication Error, Interrogation of High-/Low-Risk Errors, Lockouts on Pacemaker Version Number, Emergency Pacing Parameter Transposition, Display of Battery Voltage, Automatic Capacitor Reform Timing, Programmer User Test: TMS 1000^{PLUS} Assessment, Programmer Threshold Test, Arrhythmia Induction and Manual Shock, Pacing Threshold and Lead Impedance	Current Programmer Software	Pass

Test Performed	Sample Size Each Test	Test Results (Pass/Fail)
VALIDATION FOR APPLICATION "PHYLAX AV" AND "TMS 1000"		
Release Comparison of Validation samples (Difference Analysis), Verification of Implant list configuration and recognition, Service Time and Stress Test: TMS 1000 & SWM1000 I-GAV.2.U/1, Phylax AV: Interrogation Test, Phylax AV: Test of Base functions, Review of Validation Documents, Compatibility: Test Programmer/ Implant Versions, Test of the Basic Functions (TMS 1000)	Current Programmer Software	Pass

Bench Testing

Bench testing of BIOTRONIK's Phylax AV ICD, and Programmer Software, as detailed above, was successfully completed.

Biocompatibility (ICD)

All tissue-contacting materials of BIOTRONIK's ICD are currently utilized in BIOTRONIK market-released products in the U.S.. Biocompatibility testing of all tissue-contacting materials utilized in BIOTRONIK's ICDs was successfully completed for other market released BIOTRONIK products and therefore no additional biocompatibility testing was performed.

Animal Studies

BIOTRONIK, Inc. performed no animal testing with the Phylax AV in support the Premarket Approval application (PMA P000009).

The justification for no animal studies sent with the PMA was the inclusion of human clinical data gathered during the Phylax AV IDE clinical study. In regards to the animal testing for the IDE application, BIOTRONIK discussed the complete validation testing that was performed using actual patient-based intracardiac electrograms with FDA, these data were obtained with standard sensing and pacing leads, and 27 electrogram files from the Ann Arbor database that were specifically chosen for their ability to challenge the SMART Detection™ algorithm.

X. CLINICAL STUDIES

This multicenter study was a non-randomized clinical trial. The justification for the sample size was based on the UADE-free Survival Rate.

Study Objectives. The objective of the clinical study was to assess the safety and effectiveness of the Phylax AV in patients with standard ICD indications.

The endpoints had the following predefined goals:

- ≥ 90% unanticipated adverse device effects (UADE) free survival rate
- ≤ 11.6% morbidity (complication) rate
- ≥ 96% appropriate bradycardia sensing and pacing
- ≥ 98.7% ventricular tachyarrhythmia (VT) and ventricular fibrillation (VF) conversion rate

Patients Studied. The clinical investigation involved 126 patients (111 male (88.1%) and 15 female (11.9%) with a mean age of 66 years (range: 22 to 87 years) and a mean left ventricular ejection fraction of 31% (range: 10% to 60%). Most patients (80.2%) presented with coronary artery disease/ischemic cardiomyopathy; 65.1% presented with monomorphic ventricular tachycardia (MVT) as their primary tachyarrhythmia.

Methods. The multicenter non-randomized clinical investigation was designed to validate the safety and effectiveness of the Phylax AV through an analysis of the unanticipated adverse device effect (UADE) rate. The specific predefined endpoints included UADE-free survival rate, morbidity rate, sudden cardiac death (SCD) survival rate, the appropriate sensing and pacing rate, detection and conversion of ventricular tachyarrhythmias, and the appropriate rejection of atrial tachyarrhythmias. Patients underwent standard ICD implantation and were evaluated at pre-discharge, three months and every three months thereafter.

Results. The mean implant duration was 6.3 ± 0.4 months with cumulative implant duration of 795.5 months. There were 20 patients followed for over twelve months and 62 patients followed for over six months during the study period from February 5, 1999 to April 15, 2000. The patient follow-up compliance rate was 98.4% out of 319 follow-up procedures. Table IX provides a summary of the results of the study.

Table IX. Clinical Study Results

Endpoint	Endpoint Goal	Control Group [95% CI]	Study Group [95% CI]
UADE-free Survival Rate (for patients with at least 3 months follow-up)	90.0%	100% (117/117) [95.5%, 100.0%]	100% (85/85) [96.5%, 100%]
Complication Rate	11.6%	11.6% (14/126) [5.1%, 21.8%]	11.1% (14/126) [0%, 16.8%]
Sudden Cardiac Death Survival Rate	100.0%*	N/A	100% (124/124)*** [97.6%, 100%]
Appropriate Bradycardia Sensing and Pacing Rate	96.0%****	98.0% (703/717) [96.8%, 98.9%]	96.2% (1141/1186) [95.2%, 100%]
Detection and Conversion of Ventricular Tachyarrhythmias	98.7%	98.7% (650/662) [98.2%, 99.2%]	98.2% [97.0%, 100%]
Appropriate Rejection of Atrial Tachyarrhythmias	> 0%**	0%** (0/119)	93.9% (138/147) [89.6%, 100%]

* Implicit goal, not prospectively stated in protocol
** Rejection level for control group
*** Does not include two patients with unrelated deaths
**** Adjusted for dual chamber ICD, control data was obtained from a single chamber ICD

Bradycardia Pacing and Sensing

There was a total of 1141 appropriate bradycardia sensing and pacing evaluations out of 1186 evaluations completed. Therefore, the overall rate of appropriate bradycardia sensing and pacing is 96.2%. Table X and Table XI summarize the bradycardia sensing and pacing evaluations.

Table X: Atrial Bradycardia Sensing and Pacing

Procedure	Number of Tests	Number and Percentage of Appropriate Tests
Implant	133	132 (99%)
Predischarge Follow-up	132	127 (96%)
Three-Month Follow-up	73	70 (96%)
Other Follow-ups	251	235 (94%)
All Procedures	589	564 (96%)

Table XI: Ventricular Bradycardia Sensing and Pacing

Procedure	Number of Tests	Number and Percentage of Appropriate Tests
Implant	133	132 (99%)
Predischarge Follow-up	132	129 (98%)
Three-Month Follow-up	73	69 (95%)
Other Follow-ups	259	247 (95%)
All Procedures	597	577 (97%)

There were a total of 662 ventricular tachyarrhythmia episodes (204 spontaneous and 458 induced) with an overall conversion rate of 98.2%. Table XII provides a summary of all ventricular tachyarrhythmia conversion rates.

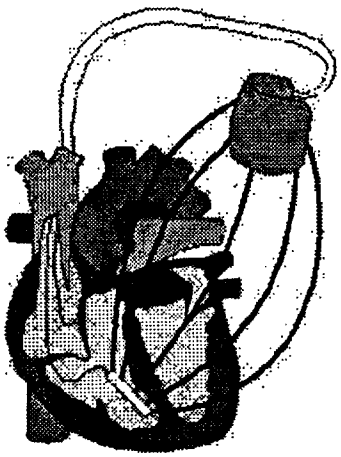
Table XII: Ventricular Tachyarrhythmia Conversion Rates

Type	Number of Patients	Rhythm	Number of episodes	Successful Device Conversions
Induced at Implant	123	VF/PVT	286	279 (98%)
	10	MVT	15	14 (93%)
Induced at Pre-Discharge Follow-up	27	VF/PVT	46	46 (100%)
	8	MVT	18	18 (100%)
Induced at Three-Month Follow-up	8	VF/PVT	12	11 (92%)
	3	MVT	7	7 (100%)
Induced at Other Follow-ups	19	VF/PVT	51	51 (100%)
	6	MVT	23	23 (100%)
Spontaneous Episodes	16	VF/PVT	53	53 (100%)
	25	MVT	151	148 (98%)
Total	124	VF/PVT	448	440 (98%)
	36	MVT	214	210 (98%)
Combined Total	125	VF/PVT/MVT	662	650 (98%)

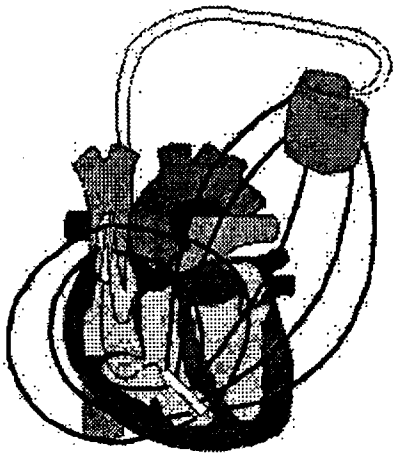
SMART Detection Algorithm. During the clinical study, specific data were collected to demonstrate the ability of the SMART Detection algorithm to discriminate between supraventricular tachycardias (SVT) and ventricular tachycardias VT. The Phylax AV demonstrated the ability to withhold inappropriate therapy in approximately 94% of the SVT episodes that were reported during the study. In addition, the SMART Detection algorithm appropriately delivered therapy in 100% of the ventricular episodes in which the feature was activated. At routine follow-ups, the algorithm was activated in 80% of patients enrolled into the study, which further supports the overall ability of the algorithm to appropriately discriminate between SVT and VT. In addition, during the clinical

study, the investigators indicated that the primary reason for selecting a dual-chamber ICD was SVT discrimination for 70% of the patients enrolled.

Lead Configurations. The following figures depict the two lead configurations used in the clinical study and identify the percentage of 126 patients implanted with each lead system.



Phylax AV with single shock coil ICD leads.
10.3% (13/126 patients)



Phylax AV with dual shock coil ICD leads.
89.7% (113/126 patients)

Gender Analysis

BIOTRONIK has investigated the appropriateness of the percentage of female patients implanted with the Phylax AV during the clinical study. There were 15 females out of 126 patients (or 11.9%). The relatively low percentage of females enrolled into the study is related to the incidence of heart disease. If females were just as likely to have heart disease as males, then you would expect the percentage to be much closer to 50%. Adverse events observed during the study and the effectiveness of the system were similar between males and females.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The multicenter clinical investigation evaluated the safety and effectiveness of the Phylax AV ICD System through an analysis of the unanticipated adverse device effect (UADE) rate. The specific predefined endpoints included UADE-free survival rate, morbidity rate, sudden cardiac death (SCD) survival rate, the appropriate sensing and pacing rate, detection and conversion of ventricular tachyarrhythmias, and the appropriate rejection of atrial tachyarrhythmias. The data collected during the clinical study provide reasonable assurance that the Phylax AV ICD system is safe and effective, when used as indicated in the labeling.

XII. PANEL RECOMMENDATION

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

XIII. FDA DECISION

Based on the reviews of the original PMA application and its amendments, FDA determined that the device provides reasonable assurance of safety and effectiveness when used as indicated in the labeling. FDA found BIOTRONIK, Inc.'s manufacturing facility to be in compliance with the Device Quality System Regulation (21 CFR Part 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

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

Post-approval Requirements and Restrictions: See approval order.

The Approval Order, Summary of Safety and Effectiveness Data, and labeling can be found on the Internet at http://www.fda.gov/cdrh/pmapage.html.