SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Cardiac Ablation Radiofrequency Generator and Interface Cable

Device Trade Name: Stockert 70 RF Generator for Cardiac Ablation

Device Model Numbers: S7001 (generator and accessories)
C6-MR10/MSTK-S and C10-MR10/MSTK-S (cables)

Applicant's Name and Address: Biosense Webster, Inc
3333 Diamond Canyon Road
Diamond Bar, CA 91765

Date of Panel Recommendation: None

PMA Application Number: P990071

Date of Notice of Approval to Applicant: May 31, 2000

II. INDICATIONS FOR USE

The Stockert 70 radiofrequency generator and accessory cable are indicated for use in conjunction with a Biosense Webster Diagnostic/Ablation Deflectable Tip catheter for cardiac ablation procedures.

III. CONTRAINDICATIONS

Do not use this device:

- in patients with active systemic infection;
- via the transseptal approach in patients with left atrial thrombus or myxoma, or interatrial baffle or patch; and
- via the retrograde transaortic approach in patients with aortic valve replacement.

IV. WARNINGS AND PRECAUTIONS

See Warnings and Precautions in the final approved labeling (User's Manual).

V. DEVICE DESCRIPTION

The Stockert 70 RF Generator system consists of a radiofrequency (RF) generator and accessories, and two reusable interface cables. The device is intended to generate RF energy that is delivered to the heart by a percutaneously-placed catheter for the treatment of cardiac arrhythmias. The thermal energy at the site of application produces a lesion that interrupts a defective electrical conduction pathway in the cardiac wall. The Stockert 70 RF Generator is used in unipolar mode only, and includes functions for controlling temperature at the catheter tip and for monitoring impedance and ECG signals. Ablation parameters, such as power, impedance, voltage, current, and temperature, can be recorded and displayed using the optional Stockert 70 Global Port and an optional Personal Computer (PC) system.

A. Generator and Accessories

The complete list of generators, accessories, and model numbers (where applicable) are listed below:

- Stockert 70 RF Generator, with software version 1.032
- power cord
- remote control foot pedal
- global port computer interface
- indifferent patch - electrode, 3M, package of 5
- indifferent patch - electrode connection cable, 3M
- grounding cable
- software - EPWIN, version 3.010
- ValleyLab patch cable
- serial computer interface cable D-Type
- global port digital - ECG connection cable
- ECG connection cable (Redel 10-2 mm tip pin)

Below is a more detailed description of the device components and features.

(1) Global Port Computer Interface and EPWIN software

The Global Port Computer Interface provides the interface between the generator and the external components. Five port channels (ECG distal, ECG proximal, Temperature, RF power, and Impedance) allow for recording of all measurement data for the system. All communication is by electrically isolated optical fibers. An RS232 connection to a personal computer running the EPWIN software can be used to document and display data collected by the Global Port Interface.

(2) Temperature Control

Two modes of ablation control are provided: manual (power control) and automatic (temperature control). In manual mode, the user controls the power using the rotary knob on the front panel. Power can be controlled to between 0 and 50 watts. If temperature exceeds a user-selected cutoff value (ranging from 47°C to 95°C), the power is deactivated immediately. In automatic mode, the power is adjusted automatically to achieve a temperature at the catheter tip that is selected by the user. The Stockert Generator provides temperature control for thermistor- and thermocouple-based catheters, and is able to detect which is being used. The set temperature ranges from 43-90°C. In automatic mode, the user can select the rate of temperature change from 0.02 - 50°C/sec.

(3) Impedance Monitoring

The impedance monitoring feature allows the user to select lower (20 to 200 ohms) and upper (30 to 300 ohms) impedance cut-offs. If the impedance falls above or below these values, power is deactivated. The user can select a delta impedance cut-off value to monitor for rapid changes in impedance. If the change in impedance (measured over a 3 second traveling window) exceeds this delta value, power is deactivated

(4) ECG Monitoring

The device system allows for the connection of external systems for monitoring and recording of electrograms signals obtained by the ablation catheter. Both digital and analog interface options are available, and a low-pass filter is activated to minimize interface due to the RF ablation signal during the ablation procedure. The system also allows for electrical stimulation (pacing) to aid in the diagnosis of arrhythmias.

B. Catheter Interface Cables

The device system may use Biosense Webster interface cables for use with the Stockert 70 RF Generator and Biosense Webster Diagnostic/Ablation Deflectable Tip Catheter. Cables are available in lengths of 6 feet (model C6-MR10/MSTK-S) or 10 feet (C10-MR10/MSTK-S). The cables are reusable and may be resterilized up to ten times using ethylene oxide.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Alternative therapy for cardiac arrhythmia includes direct surgical ablation, use of drugs for tachycardia control, antitachycardia pacing, and RF ablation with various market-approved catheters and generators.

VII. MARKETING HISTORY

The Stockert 70 RF Generator has not been marketed in the United States or any foreign country.

VIII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

This section summarizes the observed and potential adverse events associated with the use of the device.

A. Observed Adverse Events

The Stockert 70 Generator, used with the Biosense Webster Celsius™ Diagnostic/Ablation thermocouple or thermistor catheters, was evaluated in 210 patients, most of whom were treated for Wolff-Parkinson White (WPW) syndrome or atrioventricular nodal re-entrant tachycardia (AVNRT).

Five patients (2.4%) were reported as having major adverse events, all of which were reported as procedure-related. Major and minor adverse events were classified according to the FDA's recommended definitions for evaluating ablation safety. The major adverse events, occurring within seven days post ablation, included pulmonary embolus/urinary tract infection, unintentional heart block, small ecchymosis/hematoma, deep vein thrombosis, and femoral artery pseudoaneurysm.

Thirteen minor adverse events (6.2%) were reported, including small ecchymosis, superficial thrombophlebitis, pneumothorax, hematoma, pulmonary embolus, pain at catheter insertion site, chest pain, groin pain, transient 2:1 heart block, esophagitis, congestive heart failure, right occipital stroke, and malignant lung/bronchial cancer.

Three deaths were reported for the study, all of which occurred more than seven days post-procedure. None of these deaths were related to the investigational device or procedure.

A summary of observed adverse events for all ablated patients is provided in the following table:

Table 1 - Observed Adverse Events/Deaths (N=210)

Adverse Event Classification*	% patients	Number of patients	95% Confidence Interval**	
Minor	6.2	13/210	3.3	10.5
Major	2.4	5/210	0.8	5.7
Death	1.4	3/210	0.3	4.5

* Categories are mutually exclusive

** Confidence intervals by exact (binomial) method

B. Potential Adverse Events

Potential adverse events may be categorized as those which were observed in the clinical study of the device, and those which were not observed but which may occur. Adverse events (in alphabetical order) which may be associated with catheterization and ablation include:

- Air embolism
- Arrhythmias
- AV fistula
- Cardiac perforation/tamponade
- Cardiac thromboembolism
- Cerebrovascular accident (CVA)
- Chest pain/discomfort
- Complete heart block
- Coronary artery dissection
- Coronary artery spasm
- Coronary artery thrombosis
- Hemothorax
- Increased phosphokinase level.
- Laceration
- Local hematomas/ecchymosis
- Myocardial Infarction
- Pericardial effusion
- Pericarditis
- Pleural effusion
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism/tamponade
- Thrombi
- Thromboembolism
- Thrombosis
- Transient ischemic attack (TIA)
- Valvular damage
- Vascular bleeding/local hematomas
- Vasovagal reactions
- Ventricular tachyarrhythmia

IX. SUMMARY OF PRECLINICAL STUDIES

Pre-clinical evaluation of the device system consisted of verification testing of the generator, system functional testing, verification testing of the device accessories, software validation, and electromagnetic compatibility testing.

A. Verification of generator features, functions, and display

The table below summarizes the generator-related verification testing.

Table 2 - Verification testing of generator functions

Parameter Test	Methods	Acceptance Criteria	Results
Display Accuracy Tests			
impedance	calibrate resistors at 50, 100 and 150 ohms	accuracy ± 10%	maximum error: 6.5%
time	compare to stopwatch at 30, 60 and 120s	accuracy ± 0.5 sec	times within 0.28 sec
temperature (static)	measure temperature in a saline bath at 37, 45, 55, 65, 80, and 85 °C	accuracy ± 5°C	maximum error: < 2.4°C
temperature (during RF)	record last reading while 50 W is generated in a saline bath	accuracy ± 5°C	maximum error: < 3.2°C
power	measure using known resistances over a range of power settings	± 10%	maximum error: < 5.7 W
Generator Cutoff Tests			
temperature	37±1°C temperature bath and system cutoff set at 47° C	accuracy ± 5°C for thermistor and thermocouple	Maximum error 3.2°C (thermistor) 2.4°C(thermocouple)
impedance	verify that generator shuts off when impedance exceeds max value (250 ohms) and min value (50 ohms)	see methods	pass
voltage	set limit to 50 V, then 100V; operate RF into known load	verify that voltage does not exceed set limits	pass
current	set limit to 500mA; operate RF into known load	verify that current does not exceed set limits	pass

B. System Functional Testing

System functional testing consisted of simulation ablation testing, temperature accuracy testing, and temperature ramping testing.

(1) Simulated Ablation Testing

Simulated ablation testing was conducted using the Stockert 60 RF generator and two commercially-available RF generators (i.e., EPT-1000 and Medtronic Atakr), along with Biosense Webster Celsius catheters (5 thermocouple and 5 thermistor catheters). Lesions were created in beef heart tissue samples submerged in a saline bath. The length and depth of the lesions created with the Stockert generator were consistent with those created with the EPT-1000 and Medtronic Atakr generators for all test conditions.

(2) Temperature Accuracy Testing

The Stockert and Biosense Webster Celsius catheters were tested to determine temperature accuracy. Temperature accuracy was determined at six temperatures ranging from 37-85°C and was shown to be within ±5°C.

(3) Temperature Ramp Testing

Temperature ramp testing in a simulated environment using a saline bath with a temperature of 37°C was conducted on the Medtronic Atakr and EPT 1000 generators to confirm that the recommended lower and upper temperature ramp rates of 12-50°C per second used in the Stockert clinical study are comparable to those of these generators. Test data demonstrated that the recommended ramping rates of 12-50°C per second for the Stockert 70 RF generator was within the ramping range of the above currently marketed generators.

C. Verification of Accessories

The table below summarizes the accessory-related verification testing.

Table 3 - Verification Testing of Accessories

Test and Methods (where applicable)	Acceptance Criteria	Results
Foot Switch		
electrical, per IEC 60601-2-2, section 44.6 addition: aa	Footswitch will function and pass dielectric strength test after being actuated 50 times while completely submerged in 150 mm of water.	pass: Footswitch withstood 1500 VAC with leakage occuring at 220 VAC. No flashover or breakdown recorded up to 3000 VAC.
mechanical, per IEC 60601-2-2, section 56.101	Footswitch will not operate with a force less than 10.0 Newton (2.25 lbs).	pass: Footswitch operated with a minimum force of 7 lbs
Global Port Interface		
electrical (leakage current), per EN 60601-1, section 19.3	normal connection < 100 μA single-fault connection < 500 μA	pass: leakage current = 1 μA pass: leakage current = 4 μA
mechanical, per ANSI/AAMI HF-18, section 4.2.5.5	Cable retention is a pull force of 40 Newton minimum. Impulse withstand energy requirement is 0.64 joules minimum.	pass
Interface Cable		
electrical, per ANSI/AAMI HF-18, section 4.2.5.4: - HF catheter cable leakage current - HF patch cable leakage current - Dielectric withstand	 <549 mA <713mA No flashover or breakdown	 pass: leakage current = 30mA pass: leakage current=57mA pass: no leakage < 3000 VAC

Test and Methods (where applicable)	Acceptance Criteria	Results
mechanical, per ANSI/AAMI HF-18, section 4.2.5.5	Cable retention is a pull force of 40 Newton minimum. Impulse withstand energy requirement is 0.64 joules minimum.	pass

D. Software Validation

Validation test activities of system performance and functionality were conducted to determine whether the operational behavior of the Stockert 70 generator correctly implemented the software and safety requirement specifications. All software testing passed the acceptance criteria.

E. Electromagnetic Compatibility

The Stockert 70 RF Generator was tested in accordance with the European Standard EN 60601-1-2: 1993 and other applicable International Standards. The tests performed and the results of the testing are detailed in the table below:

Table 4 - Electromagnetic Compatibility Tests

Test	Results
conducted emissions	meets EN 60601-1-2: 1993
electric field radiated emissions	meets EN 60101-1-2: 1993
electrostatic discharge	meets EN 60601-1-2: 1993
electric field radiated susceptibility	meets EN 60601-1-2: 1993
electrical fast transient	meets EN 60601-1-2: 1993
surges	meets EN 60601-1-2: 1993
voltage dips and interruptions	meets EN 50082-1: 1997

X. SUMMARY OF CLINICAL STUDIES

The Biosense Webster Stockert 70 Generator was studied to determine the safety and effectiveness of the generator, global port and interface cable in conjunction with the Biosense Webster Celsius(TM) Diagnostic/Ablation catheter.

A. Background and Endpoints

The study was a prospective, multi-center study of 230 patients at 10 institutions.

Acute success was defined as complete elimination of Wolfe-Parkinson-White syndrome (WPW) or atrioventricular (AV) condicton pathways, inability to re-induce Atrioventricular Node Reentry Tachycardia (AVNRT), or complete AV nodal block. Chronic success was defined as the absence of recurrence of the arrhythmia over a 3 month monitoring period.

B. Results

Of the 230 enrolled patients, a total of 210 patients were ablated and provide the data set for which safety was evaluated.

Regarding effectiveness endpoints, the patient count included all patients treated with the investigational device for an arrhythmia indicated in the study. Patients who began treatment with the investigational device but were switched to a non-investigational device were considered failures. A total of 203 patients were treated with the investigational device for an arrhythmia indicated in the study and were assessed for acute effectiveness. A total of 200 patients were assessed for chronic effectiveness (3 patients who were evaluated for acute effectiveness died due to reasons not related to the device). Seven patients underwent ablation to treat an arrhythmia which was not indicated in the study. The other 20 patients were discontinued prior to ablation for the reasons and occurrence indicated in the table below:

Table 5 - Study Discontinuation

Reason	Number of Patients
physician chose not to ablate due to difficult pathway, close proximity to AV node, unusual location, or other	2
unable to induce protocol arrhythmia	8
non-protocol arrhythmia	5
appropriate cable equipment unavailable	5
Total	20

Of the patients enrolled in the study, 56% were female and 44% of the patients were male. The percentages of male and female patients is consistent with disease prevalence. The table below describes the patient population by indication and age.

Table 6 - Enrollment and patient age by indication (n=203)

Indication	Number of Patients		Age of patients (years)	
	%	#	Mean	Range
WPW	25.6	52	34.0	10-71
AVNRT	56.7	115	50.6	7-82
AV Node Ablation	13.8	28	66.3	22-90
WPW and other[a]	0.5	1	40.0	40
AVNRT and other[b]	3.4	7	50.1	20-66
Total	**100**	**203**	**48.2**	**7-90**

[a] Sinus node reentrant tachycardia

[b] Atrial tachycardia (n=6) and intra-atrial reentrant tachycardia (n=1)

A total of 1,716 RF energy applications were delivered with a mean number of applications of 10.3 (range 1-60 per patient). The tables below summarize success by indication.

Table 7 - Acute Success, by indication (n=203)

Indication	% patients	# patients	95% Confidence Interval
WPW	94.2	49/52	(84.1, 98.8)
AVNRT	94.8	109/115	(89.0, 98.1)
AV Node Ablation	96.4	27/28	(81.7, 99.9)
WPW & Other[a]	100	1/1	(2.5, 100)
AVNRT & Other[b]	100	7/7	(59.0, 100)
Total	**95.1**	**193/203**	**(91.1, 97.6)**

[a] Sinus node reentrant tachycardia
[b] Atrial tachycardia (n=6) and intra-atrial reentrant tachycardia (n=1)

Table 8 - Chronic Success (freedom from Recurrence at 3 months), by indication (n=200[c])

Indication	% patients	# patients	95% Confidence Interval
WPW	92.2	47/51	(81.1, 97.8)
AVNRT	92.1	105/114	(85.5, 96.3)
AV Node Ablation	92.6	25/27	(75.7, 99.1)
WPW & Other[a]	100	1/1	(2.5, 100)
AVNRT & Other[b]	100	7/7	(59.0, 100)
Total	**92.5**	**185/200**	**(87.9, 95.7)**

[a] Sinus node reentrant tachycardia
[b] Atrial tachycardia (n=6) and intra-atrial reentrant tachycardia (n=1)
[c] Three (3) patients who were acute successes were lost to follow-up due to death not related to the device.

In separate clinical studies, Biosense Webster collected the data shown in the table below, which represents an acceptable historical control population. The same catheters were used in the control studies as in the Stockert RF generator study, but ablation was performed using other RF generators.

Table 9. Results for Control Patient Population

Study Endpoint	Ablation System	# patients	% patients
acute success	Celsius catheter + Radionics/Atakr/EPT-100	676/734	92.1
chronic success (freedom from recurrence at 3 months	Celsius catheter + Radionics	280/306	91.5
major complications	Celsius catheter + Radionics/Atakr/EPT-100	26/741	3.51

The results from a comparison of the study data to the historical data are shown in the table below.

Table 10 - Device Performance Compared to Control Group

Endpoint	Success Proportion		Difference in Success Proportions*	One-sided 95% Upper Confidence Bound[1] on Difference in Success Proportions	Window of Equivalence
	Control	Stockert			
acute success	92.1%	95.1%	-3.0%	0.01%	5.0%
chronic success	91.5	92.5%	-1.0%	3.04%	4.0%
safety success	96.49%	97.62%	-1.13%	0.93%	4.0%

* Difference in success proportions (control minus treatment)

The safety and effectiveness results from the Stockert study were demonstrated to be statistically equivalent to the control data. The one-sided 95% upper confidence bound of the difference in proportions (control minus treatment) for all three endpoints are well within the window of equivalence with the historical control.

C. Temperature Ramping Experience

The table below summarizes the various temperature ramping rates that were using during ablation in a subset of 23 patients in the clinical study. The most common temperature ramp rate used was 20°C/sec (60.9%, 14/23 patients).

Table 11. Temperature Ramping Experience

Temperature Ramping Rate	# patients (n=23)
12°C/sec	4 (17.4%)
20°C/sec	14 (60.9%)
30°C/sec	3 (13%)
50°C/sec	1 (4.3%)
12°C/sec and 20°C/sec	1 (4.3%)

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Pre-clinical testing demonstrated that the system meets or exceeds safety, reliability and performance specifications.

Clinical testing and statistical analyses demonstrate that the Stockert 70 RF generator is reasonably safe and effective for the stated indications under the proposed conditions of use.

XII. PANEL RECOMMENDATION

Pursuant to the provision of Section 515 (c) (2) of the Food and 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, and FDA Advisory Panel Committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this Panel.

XIII. FDA DECISION

FDA determined that the device is reasonably safe and effective when used as indicated in the labeling. CDRH issued an approval order for the applicant's PMA, P990071, on May 31, 2000.

XIV. APPROVAL SPECIFICATION

Directions for Use: See final approved labeling (User's Manual).

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings and Precautions, and Adverse Events in the final approved labeling (User's Manual).