

# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## **Irvine Biomedical Therapy™ Cardiac Ablation System**

### **Summary of Safety and Effectiveness Data**

#### **1.0 General Information**

<b>Device Generic Name</b>	Cardiac Radio Frequency (RF) Ablation System
<b>Device Trade Name</b>	IBI Therapy™ Cardiac Ablation System
<b>Applicant's Name and Address</b>	Irvine Biomedical, Inc. ("IBI") 2375 Morse Ave. Irvine, CA 92614
<b>Date of Panel Recommendation</b>	None
<b>Premarket Approval Application (PMA) #</b>	P040014
<b>Date Notice of Approval of Application</b>	January 14, 2005

#### **2.0 Indication for Use**

The IBI Therapy™ Cardiac Ablation System is indicated for mapping and for use with a compatible RF generator for: interruption of accessory atrioventricular (AV) conduction pathways associated with tachycardia; the treatment of AV nodal re-entrant tachycardia (AVNRT); or creation of complete AV nodal block in patients with a difficult to control ventricular response to an atrial arrhythmia.

#### **3.0 Contraindications**

Do not use the IBI Therapy™ Ablation Catheter:

- In patients with active systemic infection
- Via the retrograde transaortic approach in patients with aortic valve replacement
- Via the transeptal approach in patients with left atrial thrombus or myxoma, or interatrial baffle or patch

#### 4.0 Warning and Precautions

See WARNINGS AND PRECAUTIONS in the final draft labeling.

#### 5.0 Device Description

The IBI Therapy™ Cardiac Ablation System consists of the IBI Therapy™ Ablation Catheter, the IBI 1500T RF Ablation Generator, and accessories.

The IBI Therapy™ Ablation Catheter is a sterile, single use catheter with one 4mm ablation electrode at the tip and three diagnostic electrodes. The catheter includes a temperature sensor at the tip electrode for temperature monitoring and the handle is equipped with a push-pull type thumb control for steering to deflect the distal tip of the catheter. The Therapy™ Ablation Catheter is offered in six curve variations.

##### *Therapy™ Ablation Catheter Specifications*

Feature	Specification	
Catheter Diameter	7 French (.090 to .092")	
Catheter Usable Length	110 cm (approximate)	
Number of Electrodes	Four (1 Ablation and 3 Diagnostic)	
Tip Electrode	4 mm	
Band Electrodes	Three, 2 mm width	
Interelectrode Spacing	2mm-5mm-2mm	
Temperature Sensor	Thermocouple, Type T	
Curve Type	Steerable, Uni-directional	
Curve Configurations	1304-7-25-S	0.66" (1.7cm) Curve Diameter
	1304-7-25-M	0.875" (2.2 cm) Curve Diameter
	1304-7-25-L	1.125" (2.85 cm) Curve Diameter
	1304-7-25-XL	1.375" (3.5 cm) Curve Diameter
	1304-7-25-E	1.5" (4.0 cm) Curve Diameter
	1304-7-25-F	1.5" (4.0 cm) Curve Diameter
Connector Configuration	Redel type	

The IBI 1500T RF generator produces a continuous unmodulated radiofrequency (RF) output near 485 kHz and a maximum power output of 50 Watts. RF power from the generator is delivered in a monopolar mode between the distal electrode of the Therapy™ Ablation Catheter and a commercially available indifferent electrode (dispersive pad).

The generator is a temperature controlled system, where temperature measured by the temperature sensor in the Therapy™ Ablation Catheter is monitored and the power delivered by the generator is adjusted within the selected limit until the desired temperature is achieved. The generator provides safety power shutoffs based on pre-determined time, temperature, power and impedance settings. The generator includes a front panel for display and user interface. The physician may establish settings for the following parameters: temperature, maximum impedance, power and time.



## **8.0 Potential Adverse Effects of Device on Health**

### **Observed Adverse Events**

Among the 158 study subjects who underwent RF ablation 8 major complications in 6 subjects were observed within 7 days of the procedure. These included two instances of inadvertent heart block, one instance each of bradycardia, cardiac tamponade, perforation, sepsis, pneumothorax requiring hospitalization and one instance of prolonged hospitalization due to worsening congestive heart failure. One death was observed 22 days following successful ablation in a patient with congestive heart failure. The event was noted to be unrelated to the device or the procedure. There were no unanticipated, serious device-related adverse events.

### **Potential Adverse Events**

Adverse events that may be associated with catheterization and/or cardiac ablation are as follows, listed in order of clinical significance:

- Death
- Stroke
- Myocardial infarction
- Cardiac tamponade
- Pericardial effusion
- Air embolism
- Transient ischemic attack
- Pulmonary Embolism
- Cardiac perforation
- Arterial/venous thrombosis
- Thrombotic events
- Arterial spasm
- Blood loss requiring transfusion
- AV Fistula
- Hemothorax
- Pneumothorax
- Valvular damage (mitral or tricuspid)
- Unintended complete heart block requiring pacemaker insertion
- Unintended sinus node dysfunction requiring pacemaker insertion
- Infection
- Arrhythmia
- Pseudoaneurysm
- Chest pain
- Vasovagal reaction
- Radiation injury
- Skin burns caused by electrical current
- Groin hematoma
- Hypotension
- Vascular trauma
- Groin pain
- Back pain

**9.0 Summary of Nonclinical Laboratory Studies**

**In vitro testing**

A series of in vitro bench tests were conducted based upon the FDA guidance document, "Cardiac Ablation Preliminary Guidance", March 1995 to verify device conformance to the functional requirements defined in the product specifications. The integrity of assembled components and the proper function of the ablation catheter for its intended use were confirmed through specific tests designed to test physical and performance characteristics of the device. A summary of the tests performed on the ablation catheter is presented in the table that follows.

	Test	Requirement	Tested	Result
Reliability	Thermal Cycling	Catheter must demonstrate electrical continuity after 10 cycles of RF energy delivery	10	Pass
	Torsional Testing (Torque)	Rotate shaft one full rotation with tip fixed without failure	6	Pass
	Torque/Twist Angle	Measure torque with tip fixed at 45° twist angle	5	Pass
	Tensile Testing (Bond Strength / Joint Seal)	Tensile pull test of tip/tubing and tubing/tubing joints	10	Pass
	Leak Pressure Test	Pressurize catheter shaft to test for leaks or tubing bond failure	10	Pass
	Leakage Current (Dielectric Strength)	Apply 500-1000 VAC for 60 sec. between conductors	10	Pass
	Deflection Fatigue and Flexion Fatigue (Catheter Integrity after repetitive Deflection and Flexion cycles)	Test continuity and tensile strength after 60 repetitive deflection and 60 flexion cycles	10	Pass
	Performance Reliability	No evidence of material degradation, breakdown or damage after multiple applications of RF energy	10	Pass
Mechanical	Steering (Simulated pull/De-curving load)	Force for simulated pull through arch Force for de-curving load test	10	Pass
	Buckling Load (Buckling Force)	Test tip buckling load under simulated use conditions	10	Pass
	Radiopacity	Fluoroscopic visualization of catheters under simulated clinical conditions	10	Pass
	Bending	Measure shaft deflection at 30 grams midpoint	10	Pass

	Test	Requirement	Tested	Result
<b>Electrical</b>	Impedance	Measure impedance at operating frequency	10	Pass
	Noise	Check EKG signal for noise & clarity during simulated use	5	Pass
	Stimulation (Pacing)	Using PSA and EKG monitor, stimulate the heart and measure output levels at 120 bpm	10	Pass
	Mapping	Check EKG signal for identifiable patterns under simulated use	10	Pass
	Electrical Performance	After 10 applications of RF energy the catheter will pass the dielectric strength test and impedance specification	10	Pass
	Thermal Response and Accuracy	Verify accuracy between the thermometer reading and the catheter's temperature sensor. Verify thermal response time under simulated conditions.	15	Pass Pass
<b>Cable</b>	Connector Engagement and Separation Force	Tensile force to engaging and disengage the connector is 3.0 lbs or less.	10	Pass
	Accessory Cable Flex Fatigue	Maintain electrical continuity and physical integrity after 50 flexion cycles	10	Pass
	Dielectric Strength Breakdown	Apply 500 VAC for 60 sec. between conductors with no dielectric breakdown	10	Pass
	Cable Tensile Pull Test	No breaks up to 10.0 lbs	10	Pass

In summary, all tested catheters met the established acceptance criteria for all tests.

**Biocompatibility testing**

The patient contacting materials of the IBI Therapy™ Ablation Catheter were tested in accordance with ISO 10993 for external communicating devices in contact with circulating blood for limited/transient duration. Biocompatibility testing was performed to GLP standards and in accordance with applicable parts of ISO 10993 and establishes biocompatibility and material safety as used in the device.

**Comparison of Test Article to Therapy™ Ablation Catheter (Patient Contact Materials)**

Component	Test Catheter 1	Test Catheter 2	Therapy™ Material	Patient Contact
Extruded Shaft	Pebax™ polyether block amide thermoplastic	Pebax™ polyether block amide thermoplastic and Urethane	Pebax™ polyether block amide thermoplastic	Direct Tissue and Blood
Tip	Platinum/Iridium (90/10%)	Identical	Identical	Direct Tissue and Blood
Band Electrodes	Platinum/Iridium (90/10%)	Identical	Identical	Direct Tissue and Blood
Adhesives	Urethane Adhesive	Identical	Identical	Indirect
Adhesives	Cyanoacrylate 4981	Identical	Identical	Indirect
Connector	Polysulfone (PSU)	Identical	Identical	Indirect

**Biocompatibility Testing Performed**

Biological Effect	Test	Method	Result
Cytotoxicity	Cytotoxicity	ISO 10993-5, 1X MEM Extract	Pass
Sensitization	Sensitization	ISO 10993-10, maximization in guinea pigs	Pass
Irritation or Intracutaneous Reactivity	Intracutaneous Reactivity	ISO 10993-10	Pass
Systemic Toxicity	Systemic Toxicity	ISO 10993-11, intravenous and intraperitoneal routes in mice	Pass
Hemocompatibility	Hemolysis	ISO 10993 – <i>In Vitro</i> Procedure (Extraction Method)	Pass
	In-Vivo Thromboresistance	ISO 10993 (In Dog, Venous Implant)	Pass
	Plasma Recalcification	International Organization for Standardization	Pass
Pyrogenicity	Rabbit Pyrogen Test	ISO 10993-11, Material-Mediated Rabbit Pyrogen	Pass

### **Packaging/shelf life/sterilization testing**

The packaging materials, comprised of a polyethylene tray with a Tyvek® lid and sealed within a Tyvek®/LDPE pouch, are commonly used throughout the medical device industry and are the same as those used for existing legally marketed IBI catheters. Package sealing was validated and packaging integrity was tested based on International Safe Transit Association procedure ISTA 2A Transportation Protocol. Real-time and accelerated aging were performed to support the three-year shelf-life of the catheter.

The catheter is sterilized with ethylene oxide (EtO) gas. The sterilization cycle was validated based on the recognized standard ISO 11135: 1994, Medical devices -- Validation and routine control of ethylene oxide sterilization. The process validation demonstrated that the sterilization process provides a sterility assurance level (SAL) of  $10^{-6}$ . Residual levels for EtO and ECH met the requirements for limited exposure devices in accordance with recognized standard ISO 10993-7 Biological evaluation of medical devices -- Part 7: Ethylene oxide sterilization residuals.

### **In vivo animal studies**

The safety and performance of the IBI Therapy™ Ablation Catheter along with the 1500T Radiofrequency (RF) Generator was demonstrated in both an acute (n=5) and chronic (n=1) canine model. In anesthetized animals, lesions were created in the atrioventricular (AV) junction with the goal of creating complete AV block. RF energy was delivered through the 4mm tip electrode. Cardiac function was monitored during the ablation procedure and post-ablation to evaluate the stability of the electrophysiological effects and to monitor the occurrence of adverse events. Animals were subsequently sacrificed and each heart was examined grossly and microscopically.

All catheters were able to acquire intracardiac signals. During catheterization, two acute animals suffered ventricular fibrillation, but both dogs were brought back to sinus rhythm immediately. In the acute cases, complete AV block was achieved in three animals, while a transient heart block was achieved in the fourth and a blockage of the Right Bundle Branch in the fifth. Complete AV block was attained in one chronic animal and this block was confirmed again 1 month later. At necropsy, lesion sizes were consistent with the expected lesion sizes based on the tip electrode dimensions. The animals had normal coronary anatomy after ablation. Microscopic examination of the lesion sites showed necrosis compatible with thermal injury, while the surrounding tissues appeared normal.

The catheter handled adequately and was able to acquire intracardiac electrograms. The data showed the feasibility of the ablation system to create AV block, without damaging adjacent tissues or other structures. This AV block was maintained for 1 month and the lesion area healed as anticipated to scar tissue.

### **Electrical Safety and EMC Testing**

Electrical Safety testing was performed on the RF ablation generator in accordance with the requirements of ISO 60601-1 and Electromagnetic Compatibility (EMC) testing was performed in accordance with the requirements of ISO 60601-1-2. The device utilizes non-volatile, preprogrammed firmware. During development, the firmware was tested independently and then integrated into the hardware and tested at a system level. Test results as documented and confirmed by independent review were satisfactory.

## **10.0 Summary of Clinical Studies**

### **10.1 Objectives**

A prospective, multicenter study of RF ablation was conducted of the following supraventricular tachycardias (SVT): atrioventricular (AV) accessory pathways (AP) associated with tachycardia; AV nodal re-entrant tachycardia (AVNRT), or creation of complete AV nodal block in patients with difficult to control ventricular response to an atrial arrhythmia.

### **10.2 Background**

Supraventricular tachycardia (SVT) is a rhythm disturbance of the heart originating above the ventricles. Specific types of SVT include AV nodal re-entrant tachycardia (AVNRT), accessory pathway-mediated disturbances and atrial fibrillation with a fast ventricular response.

Symptoms of SVT are caused by abnormal heartbeats which can suddenly increase to 100 or even 200 beats per minute. A sudden, rapid, regular fluttering sensation and tightness in the chest may occur. Patients may also experience weakness, faintness, palpitations, frequent urination (polyuria), and shortness of breath. Attacks of chest pain (angina) may occur in older patients.

At present, radiofrequency ablation is considered to be the procedure of choice for many patients with drug refractory SVT. Ablation sites for AVNRT are typically located in the posterior septal or anterior region of the right atrium. Ablation sites for accessory pathways are located around the mitral or tricuspid valves. Ablation sites to treat atrial fibrillation with a fast ventricular response are located in the region of the heart known as the His Bundle, specifically the AV Node. Ablation at this location creates complete heart block and a permanent artificial pacemaker must be inserted to provide an adequate heart rate.

IBI's Therapy™ Cardiac Ablation System ("the Device") consists of a diagnostic (mapping) and therapeutic (ablation) catheter used in conjunction with a compatible radiofrequency (RF) generator used to deliver RF energy to the appropriate endocardial structures and to map cardiac electrophysiology, as necessary.

### **10.3 Study Design**

The Device was evaluated in a prospective, non-randomized, multi-center clinical study for the treatment of supraventricular tachycardias (SVT). The study involved 165 subjects at eleven investigational sites.

The objective of the clinical study was to demonstrate the safety and effectiveness of the Therapy™ Cardiac Ablation System for the treatment of SVT based primarily on three objective performance criteria (OPC). The OPCs that specified acceptable limits for acute success, chronic success and major complications were as follows: acute success  $\geq 85\%$ ; chronic success  $\geq 80\%$ ; and, rate of adverse events  $< 7\%$ . These limits were consistent with FDA guidance documents regarding the evaluation of cardiac ablation catheters.

For AV Nodal Re-entrant Tachycardia (AVNRT) and Accessory Pathway (AP) treatments, "Acute success" was defined as the inability to induce the targeted arrhythmia within 60 minutes of ablation. For complete heart block patients, acute success was defined as the presence of complete AV block, as shown on a 12-lead electrocardiogram.

For all patients, "chronic success" was defined as the absence of recurrence of the target arrhythmia over a 3-month period following an acute success. In addition, the complete block had to be demonstrated on a 12-lead electrocardiogram for complete AV block patients and no evidence of recurrent pre-excitation had to be demonstrated for manifest AP patients.

For all patients, "Major Complication" was defined as any occurrence of death, cardiac tamponade, myocardial infarction, stroke, perforation, valvular damage (new mitral or tricuspid damage), inadvertent AV block, coronary artery injury, arterial thrombosis, pulmonary embolism, thromboembolic event (stroke or TIA), peripheral venous thrombosis, endocarditis, hemothorax, pneumothorax, sepsis, catheter insertion site hematoma or AV fistula requiring a blood transfusion and/or surgical repair or any other "serious" cardiovascular adverse event within one week of the study ablation.

"Serious" was defined as any event that was:

- Life threatening; or
- Resulted in permanent impairment of a body function or permanent damage to a body structure; or
- Necessitated significant intervention, such a major surgery, to prevent permanent impairment of a body function or permanent damage to a body structure; or
- Required hospitalization or an extended hospital stay; or
- Resulted in moderate transient damage to a body structure; or
- Required intervention such as medication or cardioversion to prevent permanent impairment of a body function or damage to a body structure.

"Minor Complication" was defined as any non-serious cardiovascular adverse event within one week of the study ablation. A non-serious event was any reported sign, symptom or diagnosis that did not satisfy any of the criteria for "serious" described above.

Data collection included basic demographics, presenting signs and symptoms, characteristics of the index arrhythmia, procedural parameters (ablation duration, impedance, power and temperature), cardiac medications, treatment outcome, adverse events and assessments for recurrence of the treated arrhythmia. Patients were evaluated one and three months after the initial ablation procedure.

**10.4 Subjects Studied**

Status	Number of Patients
Total Enrolled	165
Discontinued	6
Unable to induce an arrhythmia	3
Non-protocol arrhythmia	3
Enrolled	159
Diagnostic use only	1
Treated	158

**10.5 Demographics and Gender Bias**

Of the 159 patients enrolled, 114 (71.7%) were female and 45 (28.3%) were male. The average age ( $\pm$ SD) of all treated patients was 55.7 ( $\pm$ 15.5) (range 21-99). The majority (67.3% = 107/159) of patients were treated for AVNRT. All patients had symptomatic target arrhythmias at the time of ablation.

***Arrhythmias Types Treated***

Indication	Number of Patients	Percent
AV Nodal Re-entrant Tachycardia(AVNRT)	107	67.30%
AF with Rapid Ventricular Response	32	20.13%
Accessory Pathway (AP) (AVRT)	17	10.69%
Non Protocol Arrhythmias	3	1.89%

**10.6 Procedural Data**

Energy was applied a total of 947 times with an average of 6.2 ( $\pm$ 7.2) applications per patient (range 0-41). The mean duration of energy delivery per application was 40.9 ( $\pm$ 28.2) seconds (range 1.0-120) at an average temperature of 53.6 ( $\pm$ 6.0) degrees (range 32.0-77.0). Mean fluoroscopy time was 13.5 ( $\pm$ 13.7) minutes (range 1.1-86.4) and mean treatment time was 37.7 ( $\pm$ 35.3) minutes (range 1.0-300). Procedure time was defined as the number of minutes from the first ablation attempt until the time that the generator was turned off.

**10.7 Results**

The acute effectiveness, chronic effectiveness and safety results for the Therapy™ Cardiac Ablation System satisfied all three Objective Performance Criteria (OPCs) specified in the study protocol.

Criteria	Rate	95% CL	Meets OPC?
Acute Success > 85%	90.6%	86.1%	Yes
Chronic Success > 80%	86.8%	81.5%	Yes
Major Complications < 7%	3.8%	6.9%	Yes

Major adverse events included two instances of inadvertent heart block, one instance each of bradycardia, cardiac tamponade, perforation, sepsis, pneumothorax requiring hospitalization and one instance of prolonged hospitalization due to worsening congestive heart failure. One death was observed 22 days following successful ablation in a patient with congestive heart failure. The event was noted to be unrelated to the device or the procedure. There were no unanticipated, serious device-related adverse events and there were no device failures.

#### **11.0 Conclusions Drawn From Studies**

Preclinical testing demonstrates that the Therapy™ Cardiac Ablation System should maintain mechanical and electrical integrity and materials which contact patients should be biocompatible under the proposed conditions for use. Bench testing has established an acceptable degree of energy delivery accuracy and control.

Clinical data submitted under P040014 demonstrated that the Therapy™ Cardiac Ablation System performed effectively, with an acceptable rate of complications, for the stated indications under the proposed conditions for use. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

#### **12.0 Panel Meeting**

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Cardiovascular Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

#### **13.0 CDRH Decision**

FDA issued an approval order on January 14, 2005.

The applicant's manufacturing facility was inspected on February 2, 2003 (NAMSA), September 23, 2004 (Partner) and October 14, 2004 (Irvine) and was found to be in compliance with the Quality System Regulation (21 CFR 820).

#### **14.0 Approval Specifications**

- Directions for Use: See Final Draft Labeling
- Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings and Precautions, and Adverse Events in the final draft labeling.
- Post-approval Requirements and Restrictions: See Approval Order