

## **SUMMARY OF SAFETY AND EFFECTIVENESS DATA**

### **1. GENERAL INFORMATION**

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Device Generic Name:	Electrosurgical Device
Device Trade Name:	AtriCure Synergy Ablation System
Applicant's Name and Address:	AtriCure, Inc. 6217 Centre Park Drive West Chester, OH 45069 USA
Date(s) of Panel Recommendation:	
Premarket Approval Application (PMA) Number:	P100046
Date of FDA Notice of Approval:	
Expedited:	Yes

### **2. INDICATIONS FOR USE**

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The AtriCure Synergy Ablation System is intended to ablate cardiac tissue for the treatment of persistent or longstanding persistent atrial fibrillation in patients who are undergoing open concomitant coronary artery bypass grafting and/or valve replacement or repair.

### **3. CONTRAINDICATIONS**

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The AtriCure Synergy Ablation System is not indicated for contraceptive coagulation of fallopian tubes.

### **4. WARNINGS AND PRECAUTIONS**

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The warnings and precautions can be found in the AtriCure Synergy Ablation System Instructions for Use.

## **5. DEVICE DESCRIPTION**

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The AtriCure Synergy Ablation System devices included in this PMA are:

- AtriCure Synergy Ablation Clamps - Product Codes: OLL2, OSL2
- Ablation and Sensing Unit – ASU – RF Generator
- Isolator Switch Matrix– ASB – allows user to connect multiple AtriCure devices to ASU

### **5.1. System Description**

The Synergy Ablation clamps are available in two models, the OLL2 (open long left curved) and OSL2 (open short left curved), to aid in accessing varying patient body habitus. The OLL2 and OSL2 are the same with the exception of jaw geometry and shaft length. The OSL2 jaws are slightly shorter than the OLL2's to provide surgeons with different options for accessing patient anatomy.

#### *5.1.1. Synergy Ablation Clamp*

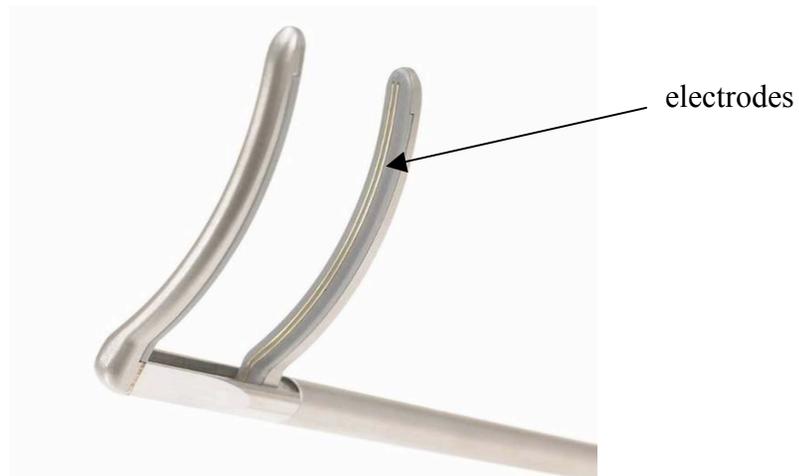
The Synergy Ablation Clamps resemble standard surgical clamps and are always under the direct control of the surgeon. The devices include a syringe type grip handle/actuator, cylindrical shaft of varying lengths; varying jaw curvatures, lengths, and apertures, rounded jaw tips, and a cable that plugs into the ASB switch matrix and ASU RF generator (Figure 1).

The Clamp device handle is connected by a cylindrical shaft to a pair of grasping jaws with electrodes on each jaw. Each jaw contains two (2) linear electrodes located medially and axially on the centerline of each insulated jaw of the clamp type end effector (Figure 2). These directly opposing linear electrodes, two on each jaw, make up two electrode pairs. Within an electrode pair, energy flows from the electrode on the proximal or top jaw to the electrode on the distal or bottom jaw. To activate RF energy, the AtriCure Synergy Ablation Clamp is connected via an integral cable to the AtriCure Ablation and Sensing Unit (ASU) and the Isolator Switch Matrix (ASB).

Figure 1: AtriCure Synergy Ablation Clamp (OLL2)



Figure 2: AtriCure Synergy Ablation Clamp End Effector



#### 5.1.2. Ablation and Sensing Unit

The Ablation and Sensing Unit (ASU) is a radiofrequency (RF) generator used to power AtriCure Handpieces (Figure 3). The ASU is a portable reusable device that produces and delivers RF bipolar energy through the AtriCure Synergy Ablation Clamp to ablate cardiac tissue. The ASU limits the amount of voltage, current, and time for which the RF

power is delivered to the Clamp. In addition, the ASU lights a visual indicator and sounds an audible tone signaling that the conditions for a complete ablation cycle have been satisfied. The footswitch is used to initiate (depress footswitch) and terminate (release footswitch) the RF energy delivery.

Figure 3: RF Generator- AtriCure Model ASU/ASB



### 5.1.3. Isolator Switch Matrix

The ASU is used in conjunction with the Isolator Switch Matrix (ASB). The Isolator Switch Matrix (ASB) is an accessory interface module allowing various AtriCure ablative devices to connect to the RF generator (ASU) (Figure 3). The ASB also provides the RF switching mechanism for the two electrode pairs in the AtriCure Synergy Ablation Clamps. The ASU and ASB are connected via a short cable. These units (ASU/ASB) are always outside of the sterile field and function to provide the RF energy (ASU) and to direct the energy delivery to the Handpieces.

The ASB utilizes a mechanical switching system to allow the user to select a pathway for a specific source to communicate to a specific output. The operator can select which device will be activated via a rotating selection knob on the front of the ASB. The operator is able to mechanically select and switch between ablation handpieces connected to the ASU RF generator.

## **6. ALTERNATIVE PRACTICES OR PROCEDURES**

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Alternative therapies for atrial fibrillation include surgical ablation, use of anti-arrhythmic and/or rate control medications, cardioversion (electrical and/or pharmacologic), and transvenous ablation with standard electrophysiology catheters.

## **7. MARKETING HISTORY**

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The AtriCure Synergy Ablation System was cleared on January 26, 2007 via premarket notification K063630 for the following indication: The AtriCure Ablation System is intended to ablate soft tissues during general surgery using radiofrequency energy. The indications for use for the AtriCure Synergy Ablation System was modified under K101174 to the following: The AtriCure Synergy Ablation System including Synergy Dual Electrode Clamps is intended for the ablation of cardiac tissue during surgery. This PMA is being filed in order to better align with the current clinical use of the device. The AtriCure Synergy Ablation System first received the CE Mark in December 2005 for ablation of soft tissue, and thereby began commercial distribution in the European Union. In March 2009, the CE Mark approval was updated for the treatment of cardiac arrhythmias including atrial fibrillation. The list of countries where the AtriCure Synergy Ablation System is approved for commercial distribution is provided below:

United States, European Union, Canada, Japan, Lebanon, Colombia, Panama, Ecuador, Peru, China, Hong Kong, Argentina, Chile, Brazil, Thailand, Australia, Mexico, Turkey, Georgia, Azerbaijan, Russia, Norway, Taiwan, Costa Rica, Korea, Lithuania, and Malaysia.

The AtriCure Synergy Ablation System has not been withdrawn from marketing in any country for any reason.

## **8. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

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The AtriCure Synergy Ablation System is indicated for use as a concomitant procedure with open cardiac surgery. Below is a list of potential adverse effects (e.g., complications) that are associated with this combined procedure:

- Death,
- Excessive bleeding related to the procedure which may require reintervention,
- Cardiac tamponade (if either open or catheter drainage is required),
- Pulmonary vein stenosis,
- Restrictive (constrictive) pericarditis,
- Infection which may include Sepsis or Endocarditis,
- Myocardial infarction (MI) per ACC guidelines,
- Stroke or Transient Ischemic Attack (TIA),
- Thromboembolism,
- Diaphragmatic paralysis,
- Esophageal-LA fistula or esophageal rupture,
- Atrial perforation or rupture,
- Ventricular perforation or rupture,
- Atelectasis,
- Pneumonia,
- Congestive Heart Failure,
- Cardiac Valve Injury,
- Persistent Pneumothorax (requiring intervention),
- Excessive Pain and Discomfort,
- Deep Sternal Wound Infection,
- Ventricular Arrhythmia (V. Tachycardia or V. Fibrillation),
- Drug Reaction,
- Perioperative heart rhythm/conduction disturbance (atrial and/or ventricular),
- Pericardial effusion or tamponade,
- Injury to the great vessels,
- Injury to unintended surrounding tissue structures, including tears and punctures,
- Extension of cardiopulmonary bypass.

## 9. SUMMARY OF PRECLINICAL STUDIES

*In vitro* and *in vivo* testing was performed to demonstrate the safety and effectiveness of the AtriCure Synergy Ablation System in bench and animal models. As demonstrated in the data below, the results support the safety and effectiveness of the AtriCure Synergy Ablation System.

### 9.1. *In Vitro* Bench Testing

*In vitro* bench testing to support the AtriCure Synergy Ablation System was developed based on design specification and applicable standards. The tests summarized in Table 1 were conducted to demonstrate the safety and effectiveness of the AtriCure Synergy Ablation System in an *in vitro* setting. All results support the safety and effectiveness of the AtriCure Synergy Ablation System.

Table 1: Summary of *In Vitro* Testing and Results

In Vitro Test	Overall Purpose and Description	Results & Conclusions
Drop Testing	To verify that the OLL2 and OSL2 devices do not present a safety hazard as a result of a free fall drop from a height of 1 meter onto a hard surface per EN60601-1:1990.	Pass. The OLL2 and OSL2 devices met the safety requirement were not considered a safety hazard as a result of a free fall drop from a height of 1 meter onto a hard surface per EN 60601-1:1990 Section 21.5.
Strain Relief	To demonstrate the OLL2 and OSL2 cable meets the Cable Strain Relief Requirements as described in ANSI/AAMI HF 18:2001.	Pass. The OLL2 and OSL2 cable meets the Cable Strain Relief Requirements as described in ANSI/AAMI HF 18:2001 section 4.2.5.5.
Reliability Testing	To verify the reliability of the OLL2 and OSL2 Handpiece design per the product life profile using rate reliability testing and Weibull Analysis.	Pass. The OLL2 and OSL2 demonstrated 99% reliability with 95% confidence. The OLL2 meets the reliability target and lesion performance criteria.
Bench Ablations Comparison	To investigate the ablation performance of the OLL2 and OSL2 on different types of tissue on bench testing.	Pass. The OLL2 and OSL2 successfully created lesions on bench tissue. All lesions were 100% transmural. No adverse tissue effects were observed with the OLL2 and OSL2.
Dielectric Withstand	To verify the OLL2 and OSL2 meet electrical safety requirements specified in the product specification and IEC 60601-2-2 and AAMI HF-18.	Pass. The OLL2 and OSL2 met electrical safety requirements specified in the product specification and IEC 60601-2-2 and AAMI HF-18.
Surface Temperature	To verify the OLL2 and OSL2 meets the External Surface Temperature Requirements per EN 60601-1 Section 42.	The OLL2 and OSL2 meet the External Surface Temperature Requirements per EN 60601-1 Section 42. Thirty (30) instruments demonstrated 90% reliability with 95% confidence.

In Vitro Test	Overall Purpose and Description	Results & Conclusions
Closing Force	To verify the OLL2 and OSL2 (post 2x EtO Sterilization) meets the Closing Force requirements has a maximum force of 10 lbf and maximum momentary force spike of 25 lbf through the device range of motion.	Pass. The OLL2 and OSL2 (2x EtO Sterilization) meets the Closing Force requirements.
Closure Latch	To verify the OLL2 and OSL2 meet the Closure Latch unlatching requirement after exposure to 2x EtO sterilization.	Pass. The OLL2 and OSL2 meet the Closure Latch unlatching after exposure to 2x EtO sterilization.
Tip Splay/ Lateral Alignment	To verify the OLL2 and OSL2 meet the lateral alignment requirement after 2x EtO sterilization.	Pass. The OLL2 and OSL2 meet the lateral alignment requirement set forth in the product specification after 2x EtO sterilization.
Shaft Stiffness	To verify that the OLL2 and OSL2 meet shaft stiffness as evidenced by retaining the ability to open and close under loading.	Pass. The OLL2 and OSL2 met shaft stiffness specifications.
Force Testing	To verify that the OLL2 and OSL2 meet jaw force specifications.	Pass. The OLL2 device met jaw force specifications.

## 9.2. In Vivo Animal Studies

The AtriCure Synergy Ablation System was tested in multiple acute and chronic animal studies. The *in vivo* studies were performed to verify ablation performance in live tissue. In all studies, device efficacy was assessed by gross examination of tissue after staining with 2,3,5,-triphenyl-tetrazolium chloride (TTC). The ablation performance was determined by assessing transmurality; the ablation was successful if the ablation was transmural (full thickness). All lesions were also examined for any signs of adverse tissue effects such as tissue charring, tissue perforation, and lateral thermal spread. When possible, the lesions were also assessed for effectiveness by pacing and/or histology.

In all cardiac tissue ablations, all lesions were 100% transmural. In addition to effectiveness, safety was evaluated by examining the lesions grossly for adverse tissue effects such as charring or perforation, and chronically by examining the health of the animal over the duration of the study. In both acute and chronic studies, the animals demonstrated no adverse effects specifically associated with ablation energy delivery. Although not formally assessed in the acute studies, there were no instances of thrombosis observed in any animal. In the chronic study, animals survived to the terminal surgery with no complications attributed to the ablation protocol. Results from these studies demonstrate that the AtriCure Synergy Ablation Clamps are able to

effectively ablate cardiac tissue with a reasonable safety profile. A summary of all animal studies is provided below in Table 2.

Table 2: Summary of *In Vivo* Animal Testing and Results

Document Title	Chronic or Acute, # of Animals	Purpose and Description	Key Assessment Criteria	Key Outcomes
Evaluation of the AtriCure Synergy Ablation Technology in the Porcine	Chronic – n= 9 pigs	To evaluate the safety and performance of the AtriCure Synergy Ablation System in a porcine model 30 days post procedure, in compliance with Good Laboratory Practices (21CFR, Part 58).	<ul style="list-style-type: none"> <li>Endpoints used to evaluate the safety of the devices were gross pathology of heart, brain, liver, lung, kidneys, bowel, and spleen; histopathology of the tissue of the ablation site to assure no signs of thromboembolic events attributed to the devices.</li> <li>The device performance was evaluated by verification of conduction block across the right atrial appendage, left atrial appendage, and left pulmonary vein ablations via pacing, and the assessment of clinical observations.</li> </ul>	<ul style="list-style-type: none"> <li>Conduction block was achieved in all ablation lesions performed at time of surgery, and maintained at 1-month follow-up.</li> <li>The OLL2 ablations did not cause pulmonary vein stenosis, regurgitation at mitral/ tricuspid valves, no decrease in LV ejection fraction, nor thrombus.</li> <li>Histopathology of the ablation lesions showed 100% transmuralty at 1-month follow-up.</li> <li>No clinical observations or events attributed to ablation energy delivery.</li> </ul>
Performance Evaluation of the Dual Electrode System for Cardiac Ablation in a Chronic Porcine Model	Chronic – n=6 pigs	To verify the performance of the AtriCure Synergy Ablation Clamp (model OLL2) for ablation of cardiac tissue in the chronic porcine model (n=6 pigs). The study also compared the AtriCure Synergy Ablation Clamp (OLL2) to previous generation Handpieces for the following variables: RF time, energy delivered, lesion width.	<ul style="list-style-type: none"> <li>Ablation line gross exam and assessment: visual examination of lesions for transmuralty, width (lateral thermal spread), presence or absence of thrombus, charring, and pulmonary vein stenosis.</li> <li>Histological exams to confirm visual assessment of transmuralty.</li> <li>Engineering analysis of energy delivery: total energy delivery, duration of application.</li> </ul>	<ul style="list-style-type: none"> <li>The OLL2 device isolates cardiac tissue in one application.</li> <li>The OLL2 device creates ablations that are discreet and visible to the naked eye without damaging adjacent structures.</li> <li>The OLL2 ablations do not cause charring, thrombus, or pulmonary vein stenosis.</li> <li>Gross Exam and Histology of the lesions, showed 100% transmuralty at 28 days survival.</li> </ul>

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 Summary of Safety and Effectiveness Data

Document Title	Chronic or Acute, # of Animals	Purpose and Description	Key Assessment Criteria	Key Outcomes
OLL2 Acute Animal Lab	Acute – n=2 pigs	To verify that the AtriCure Synergy Ablation Clamp (OLL2) functions as required in live tissue. The following were assessed: device must be atraumatic to tissue (i.e. free of pinch surfaces, sharp edges, snags) in order to prevent unintended damage during tissue interface, device must be able to be operated with one hand, the device must be able to access and create transmural lesions on the porcine LAA, RAA, IVC, SVC. A comparison of the OLL2 device to previous AtriCure Handpieces was also performed to verify performance.	<ul style="list-style-type: none"> <li>• Ablation line gross exam and assessment: visual examination of lesions for transmurality, width (lateral thermal spread), presence or absence of thrombus, or charring.</li> <li>• Intraoperative device use was observed to determine whether the device was atraumatic to tissues.</li> </ul>	<ul style="list-style-type: none"> <li>• The OLL2 devices created 100% transmural lesions as evidenced by gross examination and measurement. Lesions did not exhibit thrombus or charring.</li> <li>• The OLL2 devices were atraumatic to tissue and did not cause any damage during tissue interface. The surgeon was able to operate the device with one hand.</li> <li>• The OLL2 device functioned as well as previous generation AtriCure Handpieces.</li> </ul>

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Document Title	Chronic or Acute, # of Animals	Purpose and Description	Key Assessment Criteria	Key Outcomes
OLL2 Animal Lab	Acute – n=2 pigs	To verify the ablation performance of the AtriCure Synergy Ablation Clamp (OLL2) device on various anatomical locations (IVC, small bowel, thigh muscle, diaphragm) in an in vivo porcine model. Ablation performance of the OLL2 was assessed on various tissues and compared to previous generation AtriCure Handpieces.	<ul style="list-style-type: none"> <li>• Ablation line gross exam and assessment: visual examination of lesions for transmural, width (lateral thermal spread), presence or absence of thrombus, or charring.</li> <li>• Tissue temperatures were captured to obtain data on the maximum tissue temperature.</li> <li>• Energy delivered per unit volume of tissue being ablated and time to transmural was also evaluated.</li> </ul>	<ul style="list-style-type: none"> <li>• Ablation times and energy delivered per unit volume to the tissue were comparable between the OLL2 and previous generation AtriCure Handpieces.</li> <li>• The OLL2 devices created 100% transmural lesions as evidenced by gross examination and measurement. Lesions did not exhibit thrombus or charring. No tissue damage beyond that intended by the ablation process occurred.</li> <li>• The average maximum temperature outside of the jaw was less than 50°C on all tissue types.</li> </ul>
OSL2 Animal Lab	Acute – n=2 pigs	To verify the ablation performance of the OSL2 Handpiece on cardiac tissue in an in vivo porcine model. The following were assessed: device must be atraumatic to tissue (i.e. free of pinch surfaces, sharp edges, snags) in order to prevent unintended damage during tissue interface. The study also compared the Handpiece to previous generation Handpieces for the following variables: RF time, energy delivered, lesion width.	<ul style="list-style-type: none"> <li>• Ablation line gross exam and assessment: visual examination of lesions for transmural, width (lateral thermal spread), presence or absence of thrombus, or charring.</li> <li>• Energy delivered per unit volume of tissue being ablated and time to transmural was also evaluated.</li> <li>• Intraoperative device use was observed to determine whether the device was atraumatic to tissues.</li> </ul>	<ul style="list-style-type: none"> <li>• The OSL2 device creates ablations that are discreet and visible to the naked eye without damaging adjacent structures.</li> <li>• The OSL2 ablations do not cause charring or thrombus.</li> <li>• Gross Exam of the lesions showed 100% transmural.</li> <li>• The OSL2 devices were atraumatic to tissue and did not cause any damage during tissue interface.</li> </ul>

### 9.3. Biocompatibility

The biocompatibility of the patient contacting materials of the AtriCure Synergy Ablation Clamp have been assessed and tested according to ISO 10993-1:2003, *Biological evaluation of medical devices*, and the applicable subparts of Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices May 1, 1995 (FDA Bluebook Memorandum G95-1) with 100% passing results. The device is typically used epicardially on the perfused heart or epi/endocardially in an evacuated heart (on cardiopulmonary bypass). As such, the AtriCure Synergy Ablation Clamps (OLL2, OSL2) are categorized as externally communicating devices that are intended for bone/tissue contact for limited contact duration (less than 24 hours).

Required testing was determined from ISO 10993 and with the independent contract biocompatibility test labs that AtriCure works with for biocompatibility testing. All test methods, sample sizes, and sample preparation are determined and performed by the contract laboratories that operate according to GLPs, ISO 10993, and other applicable standards. A summary of biocompatibility testing performed is included in Table 3.

Table 3: Summary of Biocompatibility Testing and Results

<b>Biological effect category</b>	<b>Test Methods</b>	<b>Results</b>
Sensitization	Maximization Sensitization Test ISO 10993-10	Pass
Systemic Toxicity	<b>Systemic Injection USP/ISO</b>	Pass
Cytotoxicity	ISO 10993-5 Elution Test (MEM Extract)	Pass
Intracutaneous Reactivity	(Intradermal) Reactivity Test ISO 10993-10	Pass
Hemocompatibility	Hemolysis ISO 10993-4 ASTM Method Complement Activation C3a and Sc5b-9	Pass
Material Mediated Pyrogenicity	ISO 10993-11:2006	Pass
Genotoxicity	AMES reverse bacterial mutation	Pass

### 9.4. Sterilization

The OLL2 and OSL2 are packaged at AtriCure Inc. and are ethylene oxide sterilized by a contract sterilizer in compliance with ISO 11135, EN550, and AAMI TIR 16. The AtriCure Synergy Ablation Clamps (models OLL2, OSL2) are the only devices in the AtriCure Synergy Ablation System that are provided sterile. The ASU Generator and ASB Switch Matrix are used outside of the sterile field at all times. All validations

follow ISO 11135, EN550 and AAMI TIR 16 regulations to ensure  $10^{-6}$  SAL and include: bioburden analysis, a minimum of 3 half-cycles (including consideration for a half-cycle using a refrigerated truck to simulate cold shipping conditions and a minimum load half-cycle study), and a full cycle study to examine EtO residuals.

#### **9.5. Packaging Design and Shelf Life**

The OLL2 and OSL2 are packaged in a thermoformed tray and sealed with a Tyvek® lid. Qualification testing was performed for packaging design performance, packaging shelf-life, and device shelf-life for the OLL2 and OSL2. A three year shelf-life has been established for the OLL2 and OSL2.

The results of the *in vitro* and *in vivo* testing demonstrate the safety and effectiveness of the AtriCure Synergy Ablation System.

## **10. SUMMARY OF CLINICAL STUDIES, PROPOSED INDICATION**

The ABLATE study met both of the pre-specified primary safety and primary efficacy study performance goals. The adaptive Bayesian study design allowed for the study to be precisely sized to reach the study goals with the minimum number of subjects. AtriCure established a continued registry study that enrolled subjects under the same protocol utilized for the ABLATE trial (continued registry entitled ABLATE AF trial) with the clarification of the inclusion criteria to include non-paroxysmal AF rather than permanent AF. Therefore, an updated presentation of the data has been compiled with the population for ABLATE enriched using subjects enrolled in the ABLATE AF trial that are through the 6-month follow-up assessment point. This analysis is intended to confirm that the conclusions of ABLATE are robust with the addition of subjects enrolled more recently under a consistent protocol.

The analyses presented herein include only the subset of ABLATE and ABLATE AF trial subjects that have been classified as non-paroxysmal. For completeness, the safety and efficacy presentation is provided for each cohort separately as well as for the combined ABLATE and ABLATE AF non-paroxysmal populations. The proposed labeling includes the combined population for non-paroxysmal subjects from ABLATE and ABLATE AF as this is the most comprehensive data available at this time.

### **10.1. Summary of ABLATE Clinical Study**

#### *10.1.1. Objective*

The objective of the ABLATE study was to demonstrate the safety and efficacy of the AtriCure Synergy Ablation System in the treatment of subjects with permanent atrial fibrillation that are undergoing a cardiac surgery procedure primarily for significant structural and/or coronary heart disease indications.

#### *10.1.2. Study Design*

ABLATE was a multi-center, prospective, non-randomized study based on a Bayesian adaptive design that provides high probability of demonstrating non-inferiority of the AtriCure Synergy Ablation System for the treatment of permanent atrial fibrillation. The safety and efficacy of the device was compared to current standards (historical controls).

All subjects were evaluated through the primary safety (30 days post-procedure) and efficacy (six months post-procedure) time points. In addition, long term follow up to investigate the durability of treatment has been completed in the cohort through a minimum of twelve months post procedure.

*10.1.2.1. Study Endpoints*

**PRIMARY SAFETY:**

The primary safety endpoint for the study was defined as the rate of Major Adverse Events occurring within the initial 30 days post procedure or discharge (whichever was later). Major Adverse Events consist of: Death, Excessive Bleeding (defined as > 2 units of RBCs with reoperation), Stroke, TIA or MI). A clinic visit was performed at 30 days to fully assess the patient for adverse events. It should be noted that this composite of events includes events regardless of attribution, and is not specific to events attributed to the investigational device or even the Maze IV component of the operation. In all cases, a determination of the causality of each endpoint event was made based on adjudication by an independent cardiac surgeon.

**PRIMARY EFFICACY:**

The primary efficacy endpoint was defined as the rate of subjects that achieved successful obliteration of atrial fibrillation while off of any antiarrhythmic medication (Class I or III) evaluated at six months post procedure via 24-hour Holter monitor assessment (or permanent pacemaker interrogation in the case of those subjects that have a pacemaker implanted).

***Secondary Endpoints:***

Several secondary endpoints are included in the study as well. It should be noted that additional rhythm assessments were added through discussions with FDA. The aim was to obtain a 48 Hour Holter/PPM interrogation on as many subjects as possible at one year or beyond. The final version of secondary endpoints are presented below:

**Secondary Safety**

- Composite six month post procedure major adverse event rate
- Overall adverse event rate at six months

**Secondary Efficacy**

- The proportion of patients in the treatment group who are free of atrial fibrillation (episodes < 5 min. duration and no more than 1 hr total AF duration in 24 hrs monitoring) independent of the need for anti-arrhythmic drugs (Class I and Class III) as determined by a 24-hour Holter recording at 6 months
- Effectiveness of pulmonary vein isolation to produce acute electrical conduction block
- Reduction of overall AF burden as measured on 24 hour Holter at 6 months

*10.1.2.2. Objective Performance Criteria (OPC)*

*10.1.2.3. Interim Analysis for Adaptive Sample Size Determination*

*10.1.2.4. Study Oversight*

The ABLATE trial utilized an independent core laboratory to read all of the Holter, PPM, and ECG results. This ensured that all efficacy evaluations are based on an unbiased assessment of the subject's results. In addition, all adverse events through one year were reviewed by an independent cardiac surgeon not involved with the clinical study. This ensured that the safety determination is based on an unbiased assessment of the patient outcomes. These independent assessments support the data integrity and conclusions drawn from the analysis of the data to support the expanded label claim for the product. Finally, a Data and Safety Monitoring Board (DSMB) was established for the trial and reviewed data periodically to ensure safety of subjects. The DSMB is still being utilized for the active clinical registry study that is ongoing (ABLATE AF) to maintain their role of ensuring safety of subjects.

*10.1.2.5. Inclusion/Exclusion Criteria*

Enrollment in the ABLATE study was limited to patients who met the following selection criteria.

Table 4: ABLATE Inclusion/Exclusion Criteria

<b>INCLUSION CRITERIA</b>
1. Subject is greater than or equal to 18 years of age.
2. ABLATE: Subject has history of permanent atrial fibrillation (AF in which cardioversion (electrical and/or pharmacologic) has failed or has not been attempted) as defined by the ACC/AHA/ESC Guidelines. ABLATE AF: Subject has history of a non-paroxysmal form of atrial fibrillation including: longstanding persistent atrial fibrillation (continuous AF of greater than one-year duration), or persistent AF (sustained beyond seven days, or lasting less than seven days but necessitating pharmacologic or electrical cardioversion) as defined by the HRS/EHRA/ECAS Guidelines.
3. Subject is scheduled to undergo elective cardiac surgical procedure(s) to be performed on cardiopulmonary bypass including open-heart surgery for one or more of the following: Mitral valve repair or replacement, Aortic valve repair or replacement, Tricuspid valve repair or replacement, and Coronary artery bypass procedures.
4. Left Ventricular Ejection Fraction $\geq 30\%$ * (determined by echocardiography or cardiac catheterization performed within 60 days of enrollment as documented in patient medical history).
5. Subject is willing and able to provide written informed consent.
6. Subject has a life expectancy of at least 1 year.
7. Subject is willing and able to return for scheduled follow-up visits.

*\*EF can be assessed intraoperatively*

<b>EXCLUSION CRITERIA</b>
1. Stand alone AF without indication(s) for concomitant CABG and/or valve surgery
2. Previous cardiac ablation including catheter ablation, AV-nodal ablation, or surgical Maze procedure
3. Wolff-Parkinson-White syndrome
4. Prior cardiac surgery (Redo)
5. Patients requiring surgery other than CABG and/or cardiac valve surgery and/or patent foramen ovale repair, and/or atrial septal defect repair.
6. Class IV NYHA heart failure symptoms
7. Prior history of cerebrovascular accident within 6 months or at any time if there is residual neurological deficit
8. Documented MI within the 6 weeks prior to study enrollment
9. Need for emergent cardiac surgery (i.e. cardiogenic shock)
10. Known carotid artery stenosis greater than 80%
11. LA size greater than or equal to 8 cm
12. Current diagnosis of active systemic infection
13. Severe peripheral arterial occlusive disease defined as claudication with minimal exertion
14. Renal failure requiring dialysis or hepatic failure
15. A known drug and/or alcohol addiction
16. Mental impairment or other conditions which may not allow the subject to understand the nature, significance and scope of the study
17. Pregnancy or desire to get pregnant within 12-months of the study treatment
18. Preoperative need for an intra-aortic balloon pump or intravenous inotropes
19. Requires anti-arrhythmic drug therapy for the treatment of a ventricular arrhythmia
20. Patients who have been treated with thoracic radiation
21. Patients in current chemotherapy
22. Patients on long term treatment with oral or injected steroids (not including intermittent use of inhaled steroids for respiratory diseases).
23. Patients with known connective tissue disorders

### *10.1.3. Study Methods*

Investigators were required to perform the Maze IV procedure using the investigational system. This procedure has been well described and is performed routinely by surgeons worldwide. It includes both right and left pulmonary vein isolation as well as a series of ablation lines to create “the box lesion”. On the right side of the heart lesions include a right anterior freewall appendage lesion as well as a lesion from the right atrial appendage to the tricuspid annulus. On the left side of the heart, a lesion to the mitral annulus is performed as well as a lesion completed on the posterior mitral valve annulus. Confirmation of exit block was highlighted to be performed to ensure that the pulmonary vein isolation was effective.

Subjects were followed through discharge, at 30 days, 3 months, 6 months, 12 months, 18 months, 2 years and annually for five years thereafter (Table 5). The clinical assessments included a targeted history and physical exam as well as an assessment of medication and ECG. At two months an optional clinical assessment was encouraged as a means of evaluating the subject’s AF status while on antiarrhythmic agents. All subjects were required to have a clinic visit at three and six months. The three month visit was intended to be the time to have subjects discontinue their antiarrhythmic medications in an effort to allow for washout and evaluate the treatment efficacy while off any Class I or III antiarrhythmic medication at six months (the primary efficacy time point). At each clinic visit, subjects were evaluated for safety as well.

Upon completion of the primary efficacy endpoint evaluation at six months post procedure, subjects are entered into a long term surveillance phase to assess long term results. The study originally outlined a surveillance plan that consisted of a phone call assessment with the subjects at twelve months and then annually thereafter for a total of five years. A supplemental rhythm status at 12 months or greater was added to provide more insights on the durability of the procedure in these non-paroxysmal AF patients receiving concomitant procedures.

A protocol was established for weaning the subjects off the antiarrhythmic medication. It provided recommendations for cardioversion and discontinuation of antiarrhythmic drugs (AADs) through the six month assessment.

Table 5: Overall Schedule of Events



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#### *10.1.4. Subject Accountability*

A total of 57 subjects were screened and consented for enrollment in the ABLATE study. There was one subject that was consented but expired before the date of procedure. This subject does not appear in any data tables as the subject did not have a baseline case report form entered into the EDC system. A total of 56 subjects presented for surgery and 55 subjects were treated (Figure 4). One subject who presented for surgery was noted by intraoperative TEE to have a left atrial size that did not meet the eligibility criteria (observed LA size > 8 cm diameter) and therefore was not treated with the investigational system. All other subjects that were consented received treatment with the AtriCure Synergy Ablation System.

A total of 53 of the 55 subjects treated were discharged and followed through 30 days post operatively. Two subjects expired in the early post operative phase

. At three months post procedure, a total of 48 subjects out of the 53 potential evaluable subjects had an assessment performed. One subject had withdrawn from the trial after their 30 day assessment was performed indicating that he no longer wanted to participate in the follow-up assessments. It was not appreciated at the time of consent that this subject would not comply with the follow-up regimen. There was one additional subject that had expired due to co-morbid conditions prior to the three-month assessment. The remaining three subjects that do not have a three-month assessment ) had missed their visit and are documented as protocol deviations.

At six months, 50 of the subjects were available for assessment. One additional subject expired after the 3-month visit and prior to the 6 month assessment due to co-morbid conditions. All 50 of the remaining subjects had the 6-month visit performed with either a Holter assessment or Pacemaker interrogation conducted resulting in an excellent compliance rate for the critical Primary Efficacy Endpoint assessment.

The 12-month phone call assessment (original protocol) was obtained in 46 subjects out of the 48 subjects that were available at this point in time. The two subjects that did not have this follow up assessment performed had multiple unsuccessful attempts at a phone contact; one had a certified letter sent as well. Despite the fact that they were not available for the 12 month phone assessment, these subjects were assessed at 18 months via phone call as well rhythm status assessment.

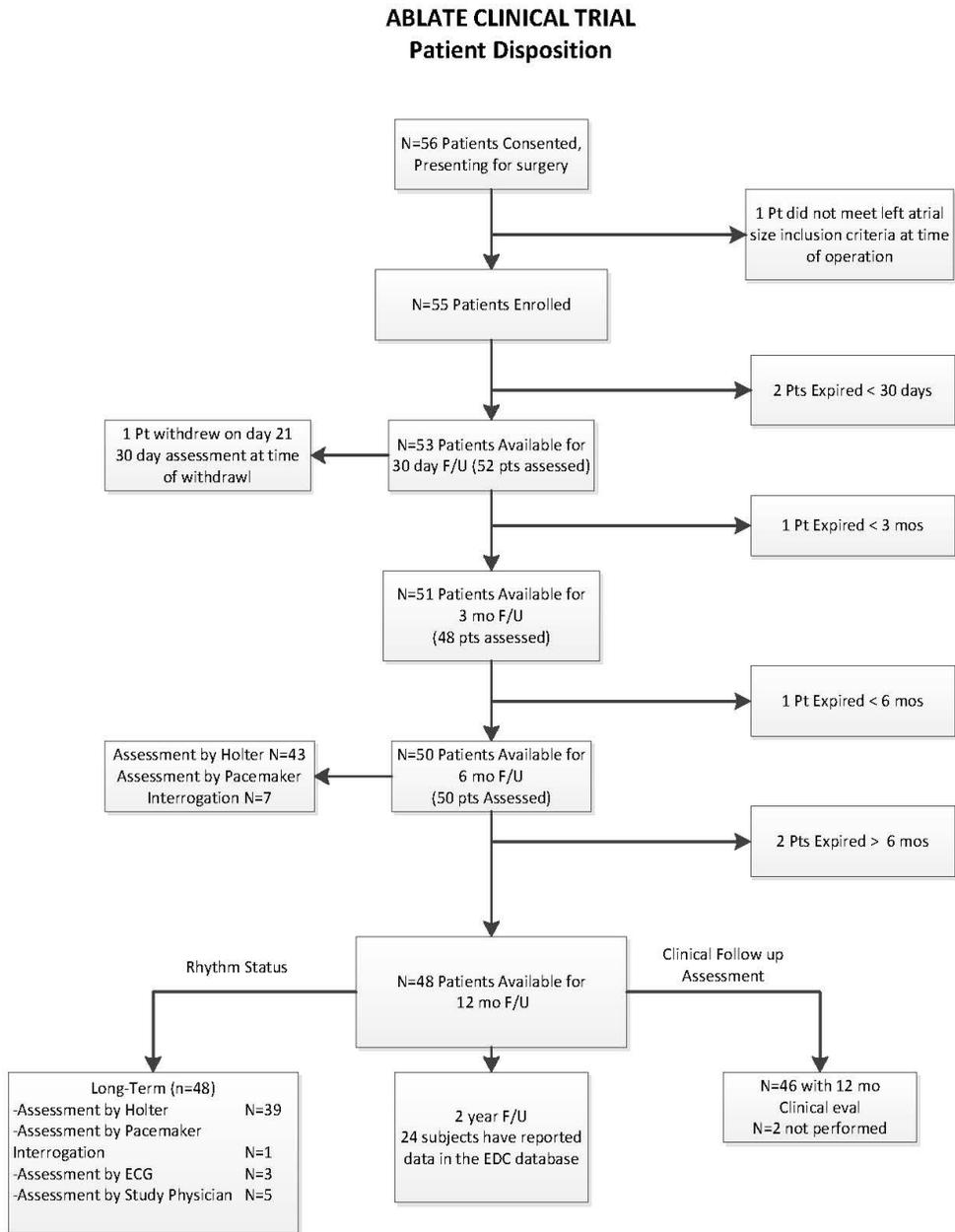
Additional rhythm assessments were requested by FDA to assess long term AF status. A rhythm and AAD status assessment at one year or greater was obtained in all available subjects (n = 48). The aim was to have this assessment performed via 48 hour Holter/PPM interrogation. This was achieved in nearly all subjects (n = 40). The balance of subjects had their rhythm reported to the sponsor through ECGs or referring physician notes that referenced an ECG, or documented interim recurrence of arrhythmia, or

symptoms. The compliance on this added protocol assessment was very high with over 80% of the potential subjects having obtained a 48 hour Holter/PPM assessment and 100% of potential subjects providing supportive information on rhythm status and AAD usage.

At the time of the database closure, a total of 29 subjects were eligible and potentially assessable for an evaluation at two years. Of this group, 28 had an assessment performed at this interval. Four of these patients have had the two year visit performed but entry of data into the database was pending at the time of report writing. One subject of the 29 who were eligible had not had the assessment yet, but was still within the visit window. The assessment may be performed by phone contact with a clinic visit, with or without Holter evaluation as optional. All subjects evaluated at two years' post procedure were assessed via a telephone assessment, an office visit including the 48 hour Holter or pacemaker interrogation (PMI) required at 12 months or after, or a telephone assessment and a 48 hour Holter assessment or PMI with no office visit. Longer term follow-up beyond two years is not yet available since no subjects have reached this time point.

The follow-up compliance for the trial is 90% for every follow-up interval through 6 months, with 100% of available subjects having assessments at the primary endpoint follow-up points (30 days and 6 months). The a priori safety and efficacy performance goals of the ABLATE study have been met. The conclusions are robust across the multiple sensitivity analyses performed. These results support the efficacy and safety of the treatment of atrial fibrillation subjects using the AtriCure Synergy Ablation System in subjects with intractable forms of AF that are already undergoing a primary open surgical procedure to correct their underlying structural heart disease.

Figure 4: ABLATE Clinical Trial Patient Disposition



*10.1.5. Subject Demographics*

Table 6 below summarizes the demographic information of all subjects who received ablation therapy.

Table 6: Subject Demographics

Parameter	ABLATE N=51	ABLATE AF N=13	ABLATE+ABLATE AF Combined N=64
Age [years]			
Mean +/- SD (N)	70.8 +/- 9.6 (51)	70.7 +/- 7.8 (13)	70.8 +/- 9.2 (64)
Median	73.0	72.0	72.5
Min, Max	45.0, 88.0	52.0, 81.0	45.0, 88.0
Gender [% (n/N)]			
Male	60.8% (31/51)	76.9% (10/13)	64.1% (41/64)
Female	39.2% (20/51)	23.1% (3/13)	35.9% (23/64)
Ethnic Group [% (n/N)]			
Caucasian	90.2% (46/51)	100.0% (13/13)	92.2% (59/64)
Black	3.9% (2/51)	0.0% (0/13)	3.1% (2/64)
Asian	2.0% (1/51)	0.0% (0/13)	1.6% (1/64)
Hispanic	3.9% (2/51)	0.0% (0/13)	3.1% (2/64)
Height [in]			
Mean +/- SD (N)	68.0 +/- 5.1 (51)	69.5 +/- 4.0 (13)	68.3 +/- 4.9 (64)
Median	68.0	71.7	69.0
Min, Max	54.9, 79.0	59.0, 72.5	54.9, 79.0
Weight [lbs]			
Mean +/- SD (N)	200.0 +/- 55.2 (51)	209.7 +/- 51.6 (13)	201.9 +/- 54.2 (64)
Median	185.0	213.4	187.5
Min, Max	113.0, 349.8	128.0, 320.0	113.0, 349.8
BMI			
Mean +/- SD (N)	30.1 +/- 6.6 (51)	30.4 +/- 6.5 (13)	30.2 +/- 6.6 (64)
Median	28.6	30.4	28.8
Min, Max	20.4, 47.4	19.5, 43.4	19.5, 47.4

The demographics for this study are consistent with the general population with cardiac disease.

Table 7 provides a summary of the significant baseline risks and comorbidities.

Table 7: Significant Baseline Risks and Comorbidities

	<b>ABLATE N=51</b>	<b>ABLATE AF N=13</b>	<b>ABLATE+ABLATE AF Combined N=64</b>
<b>Parameter</b>	<b>% (n/N)</b>	<b>% (n/N)</b>	<b>% (n/N)</b>
Cardiomyopathy	7.8% (4/51)	15.4% (2/13)	9.4% (6/64)
Congestive Heart Failure	37.3% (19/51)	38.5% (5/13)	37.5% (24/64)
Coronary Artery Disease	56.9% (29/51)	84.6% (11/13)	62.5% (40/64)
COPD	15.7% (8/51)	23.1% (3/13)	17.2% (11/64)
Diabetes	21.6% (11/51)	30.8% (4/13)	23.4% (15/64)
Hyperlipidemia	68.6% (35/51)	92.3% (12/13)	73.4% (47/64)
Hypertension	76.5% (39/51)	100.0% (13/13)	81.3% (52/64)
Myocardial Infarction	7.8% (4/51)	15.4% (2/13)	9.4% (6/64)
Obesity	23.5% (12/51)	38.5% (5/13)	26.6% (17/64)
Smoking	3.9% (2/51)	53.8% (7/13)	14.1% (9/64)
CVA/Stroke	3.9% (2/51)	7.7% (1/13)	4.7% (3/64)
TIA	7.8% (4/51)	23.1% (3/13)	10.9% (7/64)
Valvular Heart Disease	84.3% (43/51)	76.9% (10/13)	82.8% (53/64)
EF (%)			
Mean +/-SD (n)	49.6 +/- 10.6 (50)	52.5 +/- 8.7 (13)	50.2 +/- 10.2 (63)
Median (Min, Max)	50.0 (20.0, 70.0)	55.0 (30.0, 65.0)	50.0 (20.0, 70.0)
LA Size (cm)			
Mean +/-SD (n)	6.0 +/- 1.0 (46)	5.4 +/- 1.3 (13)	5.9 +/- 1.1 (59)
Median (Min, Max)	6.0 (3.9, 7.7)	5.3 (3.0, 7.3)	5.8 (3.0, 7.7)
NYHA Classification [% (n/N)]			
I	17.6% (9/51)	38.5% (5/13)	21.9% (14/64)
II	41.2% (21/51)	7.7% (1/13)	34.4% (22/64)
III	39.2% (20/51)	46.2% (6/13)	40.6% (26/64)
IV	2.0% (1/51)	0.0% (0/13)	1.6% (1/64)
Missing	0% (0/51)	7.7% (1/13)	1.6% (1/64)

10.1.6. Results

10.1.6.1. Safety Results

The safety results demonstrate that the Primary safety endpoint event rate through 30 days is acceptable as shown in Table 8.

Table 8: Primary Safety Endpoint

<b>Bayesian Analysis</b>			
<b>Summary of Primary Safety Endpoint</b>			
<b>Primary Safety Endpoint</b>	<b>ABLATE % (n/N)</b>	<b>ABLATE AF % (n/N)</b>	<b>ABLATE + ABLATE AF % (n/N)</b>
Major Adverse Event through 30 days	9.8% (5/51)	0.0% (0/13)	7.8% (5/64)
<b>95% 1-sided Bayesian Credible Interval[1]:</b>			<b>(0.0, 0.155)</b>
<b>POSTERIOR PROBABILITY &lt; 18.95%:</b>			<b>0.990</b>
[1] Beta (0.005, 0.005) prior in accordance with the statistical plan.			

The Primary Safety Endpoint events which occurred in the ABLATE trials are detailed below in Table 9. The primary safety endpoint events which occurred during the trial were primary associated with the concomitant surgical procedure performed as opposed to the ablation procedure or AtriCure device.

Table 9: Summary of Primary Safety Endpoint Events

	<b>ABLATE N=51</b>	<b>ABLATE AF N=13</b>	<b>ABLATE + ABLATE AF N=64</b>
	<b>% (n/N)</b>	<b>% (n/N)</b>	<b>% (n/N)</b>
Primary Endpoint (Acute MAE within 30 days post procedure)	9.8% (5/51)	0% (0/13)	7.8% (5/64)
Death	3.9% (2/51)	0% (0/13)	3.1% (2/64)
<=30 days	3.9% (2/51)	0% (0/13)	3.1% (2/64)
>30 days, procedure related	0.0% (0/51)	0% (0/13)	0.0% (0/64)
Stroke/TIA	2.0% (1/51)	0% (0/13)	1.6% (1/64)
Stroke (with significant permanent disability)	2.0% (1/51)	0% (0/13)	1.6% (1/64)
TIA	0.0% (0/51)	0% (0/13)	0.0% (0/64)
MI	0.0% (0/51)	0% (0/13)	0.0% (0/64)
Excessive Bleeding (>2 units blood and surgical intervention)	3.9% (2/51)	0% (0/13)	3.1% (2/64)

A summary of the adjudicated clinical events based on attribution is provided in Table 10. It should be noted that there have been no observed device related events in the ABLATE and ABLATE AF trials and only a small number of procedure or ancillary device related events (9/64 or 14%), with only eight of these events being considered serious (8/64 or 12.5%). These events occurred within the first 30 post-operative days.

Table 10: Summary of Adjudicated Adverse Events

Parameter	ABLATE Cumulative to 30 Days N=51		ABLATE AF Cumulative to 30 Days N=13		ABLATE+ABLATE AF Cumulative to 30 Days N=64		ABLATE Cumulative to 6 mos. N=51	
	# of Evts	% (n/N) of Pts with Event	# of Evts	% (n/N) of Pts with Event	# of Evts	% (n/N) of Pts with Event	# of Evts	% (n/N) of Pts with Event
<b>Any Adverse Event</b>	160	92.2% (47/51)	47	84.6% (11/13)	207	90.6% (58/64)	188	94.1% (48/51)
Investigational Device	0	0.0% (0/51)	0	0.0% (0/13)	0	0.0% (0/64)	0	0.0% (0/51)
AF Procedure	8	15.7% (8/51)	0	0.0% (0/13)	8	12.5% (8/64)	8	15.7% (8/51)
Ancillary Device	1	2.0% (1/51)	0	0.0% (0/13)	1	1.6% (1/64)	1	2.0% (1/51)
General Surgical Procedure	134	90.2% (46/51)	35	84.6% (11/13)	169	89.1% (57/64)	138	90.2% (46/51)
Other Relationship	17	21.6% (11/51)	12	69.2% (9/13)	29	31.3% (20/64)	41	43.1% (22/51)
<b>Serious Adverse Event</b>	80	64.7% (33/51)	14	69.2% (9/13)	94	65.6% (42/64)	99	76.5% (39/51)
Investigational Device	0	0.0% (0/51)	0	0.0% (0/13)	0	0.0% (0/64)	0	0.0% (0/51)
AF Procedure	7	13.7% (7/51)	0	0.0% (0/13)	7	10.9% (7/64)	7	13.7% (7/51)
Ancillary Device	1	2.0% (1/51)	0	0.0% (0/13)	1	1.6% (1/64)	1	2.0% (1/51)
General Surgical Procedure	63	60.8% (31/51)	11	53.8% (7/13)	74	59.4% (38/64)	66	62.7% (32/51)
Other Relationship	9	15.7% (8/51)	3	23.1% (3/13)	12	17.2% (11/64)	25	33.3% (17/51)

A summary of the adjudicated clinical events specifically associated with the AF ablation procedure is provided in Table 11. Of the nine events associated with the AF ablation procedure, one event met the criteria of a primary safety event. These events are described further below.

Table 11: Adverse Events Adjudicated as Associated to the AF Ablation Procedure or Ancillary Device Use

<b>Subject</b>	<b>Event Name</b>	<b>Adjudication</b>	<b>Relationship</b>	<b>Treatment</b>	<b>Primary Safety Endpoint</b>
	Atrioventricular Block First Degree	Non-Serious AE	AF Ablation Procedure	Recovery	NO
	A-V Node Dysfunction	Serious AE	AF Ablation Procedure	PPM	NO
	A-V Node Dysfunction	Serious AE	AF Ablation Procedure	PPM	NO
	A-V Node Dysfunction	Serious AE	AF Ablation Procedure	PPM	NO
	A-V Node Dysfunction	Serious AE	AF Ablation Procedure	PPM	NO
	Cardiac Akinesis	Serious AE	Ancillary Device Related	CAB x2	NO
	Pulmonary Vein Tear (LPV)	Serious AE	AF Ablation Procedure	Suture	NO
	Torn IVC Cannulation Site	Serious AE	AF Ablation Procedure	Patch	NO
	Left Atrial Tear	Serious AE	AF Ablation Procedure	Suture	DEATH

Table 12 summarizes the secondary endpoints of MAE through six months, as well as any adverse event through six months. The combined ABLATE and ABLATE AF primary safety endpoint event rate appears consistent with results from ABLATE alone, and remains acceptable.

Table 12: Summary of Secondary Safety Endpoints

<b>Secondary Safety Endpoints</b>	<b>ABLATE % (n/N) N=51</b>	<b>ABLATE AF % (n/N) n=13</b>	<b>ABLATE + ABLATE AF % (n/N) N=64</b>
Secondary Endpoints			
MAE through 6 months	11.8% (6/51)	7.7% (1/13)	10.9% (7/64)
Death	7.8% (4/51)	0.0% (0/13)	6.3% (4/64)
Stroke/TIA	2.0% (1/51)	7.7% (1/13)	3.1% (2/64)
Stroke (with significant permanent disability)	2.0% (1/51)	7.7% (1/13)	3.1% (2/64)
TIA	0.0% (0/51)	0.0% (0/13)	0.0% (0/64)
MI	0.0% (0/51)	0.0% (0/13)	0.0% (0/64)
Excessive Bleeding (>2 units blood and surgical intervention)	3.9% (2/51)	0.0% (0/13)	3.1% (2/64)
Any Adverse Event through 6 months	94.1% (48/51)	84.6% (11/13)	92.2% (59/64)
Any Serious Event	76.5% (39/51)	69.2% (9/13)	75.0% (48/64)
Any Device Related Event	0.0% (0/51)	0.0% (0/13)	0.0% (0/64)
Any Procedure Related Event	15.7% (8/51)	0.0% (0/13)	12.5% (8/64)
Any Serious Device Related Event	0.0% (0/51)	0.0% (0/13)	0.0% (0/64)
Any Serious Procedure Related Event	13.7% (7/51)	0.0% (0/13)	10.9% (7/64)

The summary of MAEs that occurred through six months post procedure includes the primary safety endpoint event MAEs which have been previously presented. For ABLATE, there were a total of six patients with an MAE through six months cumulative. This includes the 5 subjects with an MAE through 30 days. One additional patient died between 30 days and 6 months. In addition, the subject with a stroke within 30 days died in the interval between three months and six months. None of these events were attributed to the AtriCure device or the Maze procedure. They were adjudicated instead to be related to the subject's underlying medical condition or the primary cardiac surgical procedure to address the underlying structural heart disease.

were for Sinus Node Dysfunction. The rate is within the range that was outlined in the

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10.1.6.2. *Primary Effectiveness Results*

The analysis of effectiveness was based on the 57 evaluable subjects at the six month time point. The effectiveness results are presented in Table 15. The results demonstrate the successful outcome of the ABLATE trial with the statistical endpoint being achieved.

Table 15: Summary of Primary Efficacy Endpoint

<b>Bayesian Analysis</b>			
<b>Summary of Primary Efficacy Endpoint</b>			
<b>Primary Efficacy Endpoint</b>	<b>ABLATE % (n/N)</b>	<b>ABLATE AF % (n/N)</b>	<b>ABLATE + ABLATE AF % (n/N)</b>
AF Free and Off AADs at 6 months	73.9% (34/46)	81.8% (9/11)	75.4% (43/57)
<b>97.5% 1-sided Bayesian Credible Interval[1]:</b>			<b>(0.628, 1.00)</b>
<b>POSTERIOR PROBABILITY &gt;60%:</b>			<b>0.992</b>
[1] Beta (0.005, 0.005) prior in accordance with the statistical plan.			

A summary of the Secondary Efficacy Endpoints is provided in Table 16.

Pulmonary vein isolation was confirmed in all subjects that were amenable to having their pulmonary vein lesions assessed. For the 31 subjects in whom isolation was evaluated, there was 100% confirmation of pulmonary vein isolation. The primary endpoint for the ABLATE trials is to be AF Free and off all Class I and III antiarrhythmic drug (AAD). This was achieved in 75.4% (43/57) in the combined ABLATE and ABLATE AF population at 6 months. For patients with a long history of intractable AF however, being able to achieve sinus rhythm with the aid of an AAD is considered positive. The rate of AF Free despite the use of medication raised the overall efficacy to 84.2% (48/57) at 6 months in the combined ABLATE and ABLATE AF population.

The efficacy at follow up of twelve months or greater was assessed in 45 available ABLATE subjects (no ABLATE AF subject is eligible for 12 month follow-up at the time of this writing). At this long term assessment (median of 21 months), 62.2% (28/45) of subjects were AF free without the assistance of any AADs and 73.3% (33/45) were AF free regardless of the use of AADs. These results confirm the ability of the Maze add on procedure to provide a benefit to patients.

Table 16: Summary of Secondary Efficacy Endpoints

<b>Secondary Efficacy Endpoints</b>	<b>ABLATE % (n/N)</b>	<b>ABLATE AF % (n/N)</b>	<b>ABLATE + ABLATE AF % (n/N)</b>
Planned Secondary Efficacy Endpoints			
Both Right & Left Pulmonary Vein Isolation			
Evaluable [1]	43.1% (22/51)	69.2% (9/13)	48.4% (31/64)
Isolation Confirmed [2]	100.0% (22/22)	100.0% (9/9)	51.7% (31/31)
Efficacy Evaluable at 6 month Follow-up	N=46	N=11	N=57
Free of AF [2]	82.6% (38/46)	90.9% (10/11)	84.2% (48/57)
AF Burden [3] [4]			
= 0 min	82.6% (38/46)	90.9% (10/11)	84.2% (48/57)
<= 5 min	0.0% (0/46)	0.0% (0/11)	0.0% (0/57)
> 5 min - 1 hr	2.2% (1/46)	0.0% (0/11)	1.8% (1/57)
> 1 hr	15.2% (7/46)	9.1% (1/11)	14.0% (8/57)
Additional Unplanned Secondary Efficacy Endpoints			
Efficacy Evaluable at 12 month Follow-up or greater	N=45	N=0	N=45
Free of AF [2]	73.3% (33/45)	--	73.3% (33/45)
Free of AF and off AAD	62.2% (28/45)	--	62.2% (28/45)
AF Burden (initial 24 hrs or >24 - 48 hrs) [3][4]			
= 0 min	76.3% (29/38)	--	76.3% (29/38)
<= 5 min	0.0% (0/38)	--	0.0% (0/38)
> 5 min - 1 hr	0.0% (0/38)	--	0.0% (0/38)
> 1 hr	23.7% (9/38)	--	23.7% (9/38)
[1] Includes patients evaluable on both sides. [2] Proportion of patients who are free of AF by holter, independent of need for meds. [3] Patients with Pacemaker Interrogation (PMI) included as 0 min if no Atrial Fibrillation (AFib) on PMI, otherwise included based on equivalent proportion of AFib burden per total pacemaker interrogation period. [4] Evaluable only in patients with a Holter or Pacemaker Interrogation (PMI)			

## **11. CONCLUSIONS DRAWN FROM THE PRECLINICAL AND CLINICAL STUDIES**

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The results support the overall safety and efficacy of the product in the treatment of subjects that had intractable cases of AF that were unable to be effectively treated by a medical or electrical cardioversion or in whom such treatment is indicated. In many cases these subjects have been in AF for many years and the risk of mortality and stroke along with the morbidity associated with this risk warrants this concomitant procedure to be performed. The incremental risk of the additional Maze portion of the surgery is minimal, given the potential benefit for these patients. The results demonstrate that the overall benefit of performing the procedure in non-paroxysmal patients with AF that are undergoing an open concomitant coronary artery bypass grafting and/or valve replacement or repair procedures outweighs the risks, and supports the expansion of the label claim for the device to allow for treatment of persistent or longstanding persistent forms of atrial fibrillation.

## **12.PANEL RECOMMENDATION**

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## **13.CDRH DECISION**

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## **14.APPROVAL SPECIFICATIONS**

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**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.