SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:

Ablation Catheters

Device Trade Name:

Therapy™ Cool Flex™ Ablation Catheter System

Applicant's Name and Address:
Irvine Biomedical, Inc.
a St. Jude Medical Company
2375 Morse Avenue
Irvine, California 92614 USA

Date(s) of Panel Recommendation: None
Premarket Approval Application (PMA) Number: P110016/S008
Date of FDA Notice of Approval: December 18, 2013
Priority Review: Not Applicable

The original PMA (P110016) was approved on October 5, 2011 and its Indications For Use Statement is provided below:

> *The catheter is intended for use with the compatible Irrigation pump and 1500T9-CP Radiofrequency (RF) Generator at a maximum of 50 watts. The catheter is intended for creating endocardial lesions during cardiac ablation procedures (mapping, stimulation and ablation) for the treatment of typical atrial flutter.*

The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to introduce the Therapy™ Cool Flex™ Ablation Catheter System into interstate commerce.

II. INDICATIONS FOR USE

The Therapy™ Cool Flex™ Ablation Catheter is intended for use with the compatible Irrigation pump and 1500T9-CP Radiofrequency (RF) Generator at a maximum of 50 watts. The catheter is intended for creating endocardial lesions during cardiac ablation procedures (mapping, stimulation and ablation) for the treatment of typical atrial flutter.

III. CONTRAINDICATIONS

The Therapy™ Cool Flex™ Ablation Catheter is contraindicated for:

- Patients with active systemic infection
- Patients with intracardiac mural thrombus or those who have had a ventriculotomy or atriotomy within the preceding four weeks

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Therapy™ Cool Flex™ Ablation Catheter and 1500T9-CP v.1.7 Cardiac Ablation Generator labeling.

V. DEVICE DESCRIPTION

The Therapy™ Cool Flex™ Ablation Catheter and 1500T9-CP v.1.7 Cardiac Ablation Generator consist of:

The Therapy™ Cool Flex™ Ablation Catheter is a sterile, single use 7F catheter that is constructed of thermoplastic elastomer material and noble metal electrodes. This catheter has a novel flexible tip electrode. It has a lumen connected to open conduits at the tip electrode and interlocking groves on the flexible tip electrode for saline irrigation during the ablation procedure. The tip curvature may be manipulated by the thumb control mechanism located on the handle of the proximal end of the catheter. The catheter is available in four distal curve configurations (M, L, L1 and XL).

- The catheter connects to the 1500T9-CP (v.1.7) RF Generator using an IBI 1641 connecting cable and also connects to the Cool Point™ Irrigation Pump
- The Cool Point™ Irrigation Pump is a peristaltic pump that is intended for use in administration of irrigation solutions into the patient through an open irrigated ablation catheter. The Cool Point™ Irrigation Pump is intended for use only with the Cool Point™ Tubing Set.
- The Cool Point™ Tubing Set is a sterile and single use device which provides access for the administration of fluids from a container. This tubing set is intended for use with the Cool Point™ Irrigation Pump only. The Cool Point™ Tubing Set consists of a vented drip chamber with a spike, a pump head tubing section, and a pressure sensor with a jack connecting to the Cool Point™ Irrigation Pump and terminating in a rotating 3-way stopcock.
- The Cool Point™ Irrigation Pump and Cool Point™ Tubing Set were approved as an accessory to 1500T9-CP generator under PMA P060019/S005.
- The 1500T9-CP v.1.7 Cardiac Ablation Generator is a microprocessor-controlled RF generator that produces a continuous unmodulated radio frequency (RF) power output at 485 kHz. The front panel displays power output (W), measured tip electrode temperature (°C), impedance (Ω), and

ablation duration. The generator display incorporates a visual indication to show whether an irrigated catheter and compatible irrigation pump are connected and initialized. The physician may establish settings for the following parameters: target tip temperature, maximum impedance, maximum power output, and ablation time. The maximum power output can be set up to 50Watts when a Therapy Cool Flex catheter is connected. The power output is regulated by the measured tip temperature, and is limited to the user selected maximum power output. The generator has built-in safety features, which include automatic power shut-offs for RF power when RF power, impedance or temperature exceeds a target set value. When used with a Therapy Cool Flex catheter, the generator will also shut off if the connected compatible irrigation pump alarms.

Other required and optional accessories include:

- IBI 1779 series cable for connecting the generator to the Cool Point™ irrigation pump
- IBI 1804-S cable for electrogram output
- IBI 1641 cable for connecting the generators to the catheters
- IBI 1710 cable for grounding the generator chassis
- Commercially available indifferent grounding pad and cable
- IBI 1452 optional foot switch
- IBI 1726 connecting cable for connecting the generator to the EP recording system
- Optional 1500T extender module (20 foot extension connector)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of atrial flutter, including the following:

- Ablation with another commercially available PMA-approved ablation catheter
- Pharmacological therapy for rate and/or rhythm control
- Electrical or pharmacologic cardioversion
- Surgical intervention to create atrial lesions
- Implantable devices to control heart rate

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Therapy™ Cool Flex™ Ablation Catheter is currently marketed outside the United States in Europe, Canada and Australia.

There are no countries from which these catheters have been withdrawn from the market for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects (e.g., complications) that may be associated with cardiac ablation using the device include the following:

- Abnormal vision
- Anaphylaxis
- Anemia
- Angina
- Arrhythmia
- Arterial/venous thrombus
- Atypical flutter
- Arteriovenous (AV) fistula
- Cardiac tamponade
- Catheter insertion site hematoma
- Chest Pain (non-specific)
- Congestive heart failure (CHF) exacerbation
- Component damage to implantable cardioverter defibrillator (ICD) or implantable pacemaker
- Coronary artery dissection
- Death
- Dislodgement of implantable cardioverter defibrillator or permanent pacing lead
- Dizziness
- Endocarditis
- Exacerbation of chronic obstructive pulmonary disease (COPD)
- Exacerbation of pre-existing atrial fibrillation as evidence by hospitalization, cardioversion, or worsening of atrial fibrillation Symptoms
- Hemothorax
- Hypotension
- Hypoxia
- Inadvertent Atrioventricular (AV) block
- Infection
- Myocardial infarction (MI)
- Neck pain/back pain/groin pain related to the procedure
- Palpitations
- Perforation (cardiac)
- Pericardial effusion
- Pericarditis
- Peripheral venous thrombosis
- Phrenic nerve damage
- Pleural effusion

- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Radiation injury resulting in dermatitis (inflammation of the skin), erythmia (redness), etc
- Respiratory failure
- Seizure
- Sepsis
- Stroke/Cerebrovascular Accident
- Syncope
- Thromboembolic event
- Transient ischemic attack (TIA)
- Vasovagal reaction
- Ventricular arrhythmia requiring defibrillation
- Vessel wall/Valvular damage or insufficiency (i.e. new tricuspid regurgitation)

For the specific adverse events that occurred in the clinical study, please see **Section IX** below.

IX. SUMMARY OF PRECLINICAL STUDIES

Pre-clinical testing of the Therapy™ Cool Flex™ Ablation Catheters, included verification and validation testing (device level, system level and software), biocompatibility of patient-contacting materials, sterilization, packaging and shelf life testing, and animal studies. Performance testing was conducted to demonstrate design integrity. All tests performed which were identified in standards or guidance documents were based on the product specification requirements. In the tests described below, the catheters were manufactured by trained manufacturing operators. "Pass" as used below denotes that the devices and system met established product specifications and/or performance criteria, or were in conformance with the requirements of the standards identified. Testing results confirmed that the catheters meet product specifications.

A. In Vitro Bench Studies - Catheter

The bench testing for the Therapy™ Cool Flex™ Ablation Catheter is discussed below. This testing includes reliability, mechanical and electrical integrity, and performance test results. The bench testing is separated into the following 3 categories:

1. Bench testing performed with the Therapy™ Cool Flex™ Ablation Catheter

2. Bench testing leveraged from the Therapy Cool Path Ablation Catheter

3. Bench testing performed with the Therapy™ Cool Flex™ Ablation Catheter, but could have been leveraged from the Therapy Cool Path Ablation Catheter

Table 1 below summarizes the bench testing for the catheters including reliability, mechanical and electrical integrity, and performance test results.

Table 1 Summary of In Vitro Bench Testing for Cool Flex Ablation Catheters

Bench testing performed with the Therapy™ Cool Flex™ Ablation Catheter

Test	Acceptance Criteria	Results
Noise	The catheter passes the noise test if the signal is clean.	Pass
Temperature Response & Accuracy	• Tip temperature accuracy should be within ± 3ºC of the reference thermocouple temperature. • The response time should be equal to or less than 3 seconds.	Pass
Mechanical Integrity Bond Test	Bond strength must be greater than 3.37 lbs.	Pass
Sheath Insertion and Withdrawal	• The force for withdrawal of the catheter should be ≤ 3 lbs. • No visual damage sustained by the catheter after insertion and withdrawal through the introducer sheath.	Pass
Tip/Thermocouple Bond Characterization	The test is for characterization only, there are no acceptance criteria.	Pass
Inflow Pressure and Flow Test	The flow output must be: • within ±10% of flow input for flow rates 1ml/min to 30ml/min • within ±15% for flow rates 31ml/min to 40ml/min.	Pass

Test	Acceptance Criteria	Results
3 Year Accelerated Aging Study	• Pass the final inspection. • No electrical failure, shorting, or open circuits and have a resistance value ≤ 7Ω. No visual defect to tip bond to shaft, TC bond to tip and shaft bond to handle. • Tip temperature accuracy should be within ± 3ºC of the reference thermocouple temperature. The response time should be ≤ 3 seconds. • Torque: the bond and electrical integrity must withstand 2 full rotations or 1.6 ozf-in., before any bond failure occurs. • Bond Strength must be a greater than 3.37lbs.	Pass

Bench testing leveraged from the Therapy Cool Path Ablation Catheter

Test	Acceptance Criteria	Results
Pull & De-Curving Load Test	• Pull force must be less than 1 lb. • De-curving force must be less than 2 lbs.	Pass
High Frequency Current Leakage Test	The high frequency leakage current shall not exceed 4.02 mA/cm of catheter length	Pass

Bench testing performed with the Therapy™ Cool Flex™ Ablation Catheter, but could have been leveraged from the Therapy Cool Path Ablation Catheter

Test	Acceptance Criteria	Results
Buckling Load Test	The results must be less than 96g.	Pass
Dielectric Strength Breakdown (Hypot)	No electric breakdown at 500V in one minute.	Pass
Integrity after Repetitive Deflection and Flexion Test	• Pictures of the curves before and after 40 repetitive deflection and flexion cycles must show no significant changes in either catheter curve or shaft straightness. • Conductor (electrode to conductor wire to connector) must conduct electricity without shorting or open circuits and have a resistance value equal to or less than 7Ω. There should be no failures related to the design. • The catheter shall maintain a pressure of 25 psi for 30 seconds without leakage.	Pass

Torque	The bond and electrical integrity must withstand 2 full rotations or 1.6 ozf-in, before failure occurs.	Pass

The sponsor could have leveraged the majority of the bench testing from the previous versions of the catheter. However, they chose to conduct new testing on the Therapy™ Cool Flex™ Ablation Catheter to provide valuable confirmatory evidence on the product design, as illustrated above in **Table 1**.

In addition to the testing described in **Table 1** , flex tip fatigue testing was performed to demonstrate that the distal flexible tip of the device could withstand mechanical stress and maintain functionality (electrical continuity, ablation, curve and flow test) and structural integrity following mechanical stress (fatigue) testing. The devices were cycled (stress test) to a pre-defined minimum of cycles with 100g and 45g contact force. At specific inspection points, devices were evaluated for catheter functionality and mechanical integrity. The devices met the pre-determined requirements identified in the testing protocol.

B. Biocompatibility Testing

Therapy™ Cool Flex™ biocompatibility testing was conducted in accordance with ISO 10993 and FDA Blue Book Memorandum G95-1. In accordance with ISO 10993-1, the Therapy Cool Flex ablation catheter is classified as a circulating blood contact device with limited contact duration (less than 24 hours). The results of the biocompatibility testing demonstrate that the Therapy Cool Flex meet the requirements of ISO 10993. A summary of the biocompatibility results are summarized in **Table 2 .**

Table 2 Biocompatibility Testing Summary

Biological Test/Method	Result
Cytotoxicity –MEM Elution Assay (ISO 10993-5)	Pass
Sensitization – GP max (ISO 10993-10)	Pass
Intracutaneous Reactivity, Rabbit (ISO 10993-10)	Pass
Acute Systemic Toxicity – Mouse Systemic Injection (ISO 10993-11)	Pass
Pyrogenicity - Material Mediated Rabbit Pyrogen (ISO 10993-11)	Pass
ASTM Blood Compatibility Test for Hemolysis (ISO 10993-4)	Pass
Complement Activation (ISO 10993-4)	Pass
Hemocompatibility – Thrombogenicity, Canine ISO (10993-4)	Pass

Patient contacting materials of the Therapy Cool Flex Ablation Catheter are listed in **Table 3** below:

Table 3 List of Blood/Fluid Contact Material and Components

Description	Material	Patient Contact
Tip and Band Electrodes	Platinum-Iridium	Direct Tissue and Blood
Catheter Tubing	Pebax	Direct Tissue and Blood

Description	Material	Patient Contact
Adhesive	Urethane	Direct Tissue and Blood
Lumen	Polyimide	Indirect Fluid Contact
Luer	Polycarbonate	Indirect Fluid Contact
Adhesive	Loctite	Indirect Fluid Contact
Spring, Tip	Stainless Steel	Indirect Fluid Contact

C. Animal Studies

Acute and Chronic Good Laboratory Practice (GLP) *in vivo* animal testing was conducted using Therapy Cool Flex Ablation Catheters in conjunction with an SJM RF generator. Testing demonstrated that the catheters successfully delivered RF energy to target endocardial locations in canine and porcine tissue. Creation of myocardial lesions was visually verified in various cardiac locations; lesions were created using multiple ablation parameters including at maximum power and maximum temperature settings. Lesion sets included linear caval (CTI and SVC to IVC) lesions, linear mitral isthmus lesions, and focal RA or LA lesions in one acute and one chronic animal study. The overall device performance from a gross pathological perspective was characteristic of cardiac ablation. There were no procedural complications, such as stroke, embolism, myocardial infarction, myocardial perforation, pulmonary vein stenosis, or esophageal injury, with any of the test subjects. There was no incidence of coagulation or char formation during the course of the studies. However, due to the occurrence of steam pop at higher power settings, a "Precaution" statement in the IFU indicates a possibility of higher incidence of steam pop at power levels exceeding 40W and increased chance of collateral damage when maximum power settings (50W) are used. The IFU further indicates that power should only be increased to these levels if lower energies do not achieve the intended result. No unsafe device malfunctions occurred, with any of the test subjects in the *in vivo* GLP testing. A summary of the *in vivo* animal studies is presented in **Table 4** .

Table 4 *In Vivo* Animal Studies

Animal Model	Procedure	Number of Animals	Catheters
Porcine	Chronic GLP (CER095)	6	Therapy Cool Flex Ablation Catheter
Canine	Acute (CER054)	5	
Canine	Chronic GLP (CER060)	5	
Porcine	Acute GLP (CER061)	5	

D. Sterilization, Packaging, and Shelf Life

The Therapy Cool Flex Ablation Catheters are supplied sterile, single use, and are ready for use. The catheters are sterilized using ethylene oxide (EO) sterilant gas to a sterility assurance level (SAL) of 10^{-6}. The sterilization cycle uses the same process as for the current irrigated catheters and is validated according to *ISO*

11135-1:2007, Medical devices – Validation and routing control of ethylene oxide sterilization, Method C. Adoption of the catheters into the current SJM sterilization cycle is supported by resistance study data and formal product assessment. Catheters meet the ISO allowable limits for sterilant gas residuals as set forth in ISO 10993-7 *Biological Evaluation of Medical Devices – Part 7: Ethylene oxide sterilization residuals*. Catheters are routinely tested for pyrogens of non-material mediated origin and meet the USP criteria for devices in contact with blood.

The Therapy Cool Flex device is packaged into a polyethylene tray and sealed with a Tyvek® lid. Each sealed tray is subsequently sealed in a Tyvek®/LDPE pouch, which is a second sterility barrier. The packaging materials are commonly used throughout the medical device industry and used for currently approved Therapy Cool Path Duo (P110016). The package is comprised of materials known to withstand the sterilization environment and maintain sterility for the expected shelf life.

Expiration dating is 3 years for the Therapy Cool Flex Ablation Catheter.

E. Generator Testing

The 1500T9-CP was previously tested in accordance with the applicable electrical standards for medical electrical equipment for PMA P060019 and found to meet the performance criteria established by these standards and the SJM product specification. There is no change to the generator hardware, only the generator software/firmware.

The 1500T9-CP ablation generator with Cool Point pump and Cool Flex catheter met all the requirements of the applicable EMC/EMI related compliance testing per IEC/EN 60601-1-2: 2007 and IEC/EN 60601-2-2, 2009. The test was performed by a certified laboratory and the results are summarized in **Table 5** .

Table 5 Summary of EMC Testing

Test full name	Result
Emissions	
Radiated Emissions (CISPR 11)	Pass
AC Mains Conducted Emissions (CISPR 11)	Pass
Immunity	
Electrostatic Discharge Immunity Test (IEC 61000-4-2)	Pass
Radiated, radio-frequency, electromagnetic field immunity test (IEC 61000-4-3)	Pass
Electrical Fast Transient/Burst Immunity Test (IEC 61000-4-4)	Pass
Immunity to Surge (IEC 61000-4-5)	Pass

Test full name	Result
Conducted, radio-frequency, electromagnetic field immunity test (IEC/EN 61000-4-6)	Pass
Power Frequency Magnetic Field Immunity Test (IEC/EN 61000-4-8)	Pass
Voltage Dips/ Interruptions Immunity Tests (IEC 61000-4-11)	Pass

F. Software

The RF Generator utilizes non-volatile, pre-programmed firmware. During development, the firmware was tested independently and then integrated into the hardware and tested at the system level. The 1500T9-CP RF generator uses version 1.7 (v.1.7) software. Software validation and verification testing was conducted and demonstrates that the software controlled 1500T9-CP RF Generator adequately detects, controls and interfaces with the connected catheter and compatible irrigation pump and accessories.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The sponsor performed a clinical study to establish a reasonable assurance of safety and effectiveness of creating endocardial lesions during cardiac ablation procedures (mapping, stimulation and ablation) with the Therapy Cool Flex Ablation Catheter, 1500T9-CP Cardiac Ablation Generator, for the treatment of typical atrial flutter in the U.S. and Canada under IDE # G110064, the FLEXION AFL Study. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were enrolled between November 03, 2011 and June 07, 2012. Data reporting as October 4, 2013 on 200 enrolled / 179 treated subjects from the time of enrollment through the last follow up visit on October 24, 2012 is provided in this summary. There were 24 investigational sites that actively enrolled patients.

The Clinical Evaluation of Therapy ™ Cool Flex ™ Irrigated Ablation Catheter System For the Treatment of Typical Atrial Flutter (FLEXION-AFL) study was a prospective, multi-center, open-label, and non-randomized clinical trial. All patients who signed the consent form and who were verified to meet the inclusion/exclusion criteria received ablation therapy for typical atrial flutter using the Therapy Cool Flex. Clinical historical data from PMA # P060019 (Therapy Cool Path Cardiac Ablation System study) and PMA # P110016 (Therapy Cool Path Duo Cardiac Ablation System study) were used to determine performance goals for the primary study endpoints and derived the sample size.

Clinical Endpoints

Primary Safety
Primary safety was defined as the incidence of composite, serious adverse events (SAEs) within 7 days post-procedure, regardless of whether a determination can be made regarding device relatedness.

Primary Effectiveness
Primary effectiveness or acute success was defined as the achievement of bi-directional block in the cavo-tricuspid isthmus and non-inducibility of typical atrial flutter at least 30 minutes following the last RF application with the investigational system.

Secondary Effectiveness
Secondary effectiveness or chronic success was defined as freedom from recurrence of typical atrial flutter three months post ablation. Repeat ablations, new anti-arrhythmia medication (Class Ia, Ic, or III) or increase in the dosage of existing anti-arrhythmic medication (Class Ia, Ic, or III) during the three months post ablation were considered chronic failures.

Statistical Analysis

Sample Size
Based on the statistical analysis presented in the study protocol, the number of treated subjects required to achieve adequate power for statistical hypothesis tests is 169 for the primary endpoints. These patients are included in the safety and effectiveness cohort. To account for patients who sign consent but are not treated with the investigational device (withdrew consent, did not meet criteria), enrollment was planned for 200 patients.

The sample size of 200 patients was calculated based on the assumption that this many subjects would provide adequate power for both the statistical tests of the primary safety and primary effectiveness endpoints. The statistical tests are based on comparisons against performance goals.

Primary effectiveness (Acute Success)
A performance goal of 12% for failure rate was deemed clinically acceptable. This was mathematically equivalent to a performance goal of 88% for the success rate. Based on this performance goal, with a one-sided 0.05 alpha level, a total of 169 patients (without attrition) would provide at least 80% power for this or any larger sample size. Those calculations were based on a one sample exact test of binomial proportions.

Primary safety (Procedural safety)
A performance goal of 14% was deemed clinically acceptable. Based on this performance goal, with a one-sided 0.05 alpha level, a total of 144 patients would provide at least 80% power for this or any larger sample size. Those calculations were based on a one sample exact test of binomial proportions.

The 169 patients required for evaluation of the primary efficacy endpoint would provide additional power for this safety endpoint.

Secondary Effectiveness (Chronic Success)
A performance goal of 72% was deemed clinically acceptable. Based on this performance goal, with a one-sided 0.05 alpha level a total of 124 subjects would provide at least 80% power for this or any larger sample size. These calculations are based on a one sample exact test of binomial proportions.

The 169 subjects required for evaluation of the primary efficacy endpoint would provide additional power for this secondary efficacy endpoint.

Hypothesis Testing

The hypothesis tests for the primary endpoints were formulated as follows:

Primary Safety (Procedural Safety)
For the primary safety hypothesis:
H_0: $\pi \geq \delta$
H_A: $\pi < \delta$

where π is the proportion of patients with procedural safety events. The performance goal, δ, is set at 14% (δ=0.14). An exact test of binomial proportions was performed at a one-sided 5% level of significance. The null hypothesis was rejected if the one-sided 95% exact confidence limit for the proportion was less than the performance goal of 0.14.

Primary effectiveness (Acute success)
For the primary effectiveness hypothesis:
H_0: $\pi \leq \delta$
H_A: $\pi > \delta$

where π is the proportion of patients with acute success. The performance goal was set at 88%. (δ=0.88). An exact test of binomial proportions was performed at a one-sided 5% level of significance. The null hypothesis was rejected if the one-sided 95% exact confidence limit for the proportion was greater than the performance goal of 0.88.

Secondary effectiveness (Chronic success)
For this endpoint, subjects who were acute failures or were discontinued prior to the 3-month follow-up visit (and were not a chronic failure at the time of discontinuation) were excluded from this analysis.

Success/Failure Criteria
Overall study success is defined as the rejection of the null hypothesis for both the primary safety and the primary effectiveness endpoint.

External Evaluation Group

Clinical Event Committee
The Clinical Event Committee (CEC) consisted of two medical monitors who were practicing electro-physiologists. The CEC adjudicated reported adverse events for the study. The CEC was appointed prior to study enrollment and was independent from the sponsor and participating investigators. The CEC members completed financial disclosures and were cleared of significant conflicts of interests with the sponsor. In addition, both members were not involved in the conduct of the trial in any other role than that of CEC.

Data Safety Monitoring Board
An independent Data Safety and Monitoring Board (DSMB) which consisted of two practicing electro-physiologists, one practicing cardiologist and one biostatistician, was established. All members were independent from the sponsor and the participating investigators. DSMB members completed financial disclosures and were cleared of significant conflicts of interests with the sponsor. In addition members could not be involved in the conduct of the trial in any other role than that of DSMB. The DSMB reviewed the progress of the clinical study, including CEC adjudicated adverse events. The members of CEC and DSMB did not overlap. The DSMB was established to make recommendations regarding the continuation, suspension or termination of this clinical study.

The following key areas evaluated by the DSMB to determine if the study is suspended or terminated were:

- Occurrence of unanticipated adverse device effects
- Occurrence of serious adverse events as defined in the protocol
- Safety and effectiveness trends
- Benefits versus risks of the study

Clinical Inclusion and Exclusion Criteria
Enrollment in the FLEXION AFL study was limited to subjects who met the following inclusion criteria:

- A signed written Informed Consent
- Presence of typical atrial flutter (cavo-tricuspid isthmus dependent)

- If subjects are receiving antiarrhythmic drug therapy (Class I or Class III AAD) for an arrhythmia other than typical atrial flutter, then the subject needs to be controlled on their medication for at least 3 months. If the subject had typical atrial flutter before starting the AAD(s) (Class I or Class III) and then subsequently had another arrhythmia (i.e. atrial fibrillation), then the 3 month AAD criteria did not apply.
- One documented occurrence of the study arrhythmia documented by ECG, Holter, telemetry strip, or trans-telephonic monitor within the past 6 months
- In good physical health
- 18 years of age or older
- Agree to comply with follow-up visits and evaluation

Subjects were <u>not</u> permitted to be enrolled in the FLEXION AFL study if they met any of the following exclusion criteria:

- Prior typical atrial flutter ablation treatment
- Pregnancy
- Atypical flutter or scar flutter (non-isthmus dependent)
- Significant coronary heart disease or heart failure; that is unstable angina pectoris and/or uncontrolled congestive heart failure (NYHA Class III or IV) at the time of enrollment
- Recent myocardial infarction within 3 months of the intended procedure date
- Permanent coronary sinus pacing lead
- Clinically significant Tricuspid valvular disease requiring surgery and/or a prosthetic tricuspid heart valve
- Evidence of intracardiac thrombus or a history of clotting disorders
- Participation in another investigational study
- Cardiac surgery within 1 month of the intended procedure date
- Allergy or contraindication to Heparin

<u>Treatment Procedure and Follow-up Schedule</u>

Subjects were required to sign the IRB / EC approved informed consent prior to participation in the clinical study. The subject was considered enrolled if he/she signed the consent form. An enrolled subject was considered a screen failure if he/she did not meet the study criteria. An enrolled subject was considered treatable once the investigational catheter had been used. Treatable subjects in whom the investigational catheter was introduced but no RF energy was delivered were only included in the safety cohort. Treatable subjects in whom the investigational catheter was introduced and RF energy was delivered were included in both the safety and efficacy cohort.

After completing the procedure, the investigator verified that bi-directional block and non-inducibility of typical atrial flutter was achieved at least 30 minutes following the last RF application with the investigational system for assessment of acute efficacy. Any adverse events that occurred during the procedure were collected on the appropriate case report form.

Post procedure, subjects were discharged after completing the pre-discharge evaluation. All treated subjects were required to return at the 10 day (+/- 3 day) follow- up visit for assessment of primary safety. Subjects who were acute failures were discontinued from the study after the 10 day follow up visit. Subjects in whom the catheter was introduced, but no RF therapy was delivered were followed for 10 days for safety and were discontinued from the study. In addition, those who had recurrence of typical atrial flutter, repeat ablation, as well as those who had new or increase in anti-arrhythmia medication (Class Ia, Ic, or III) were discontinued from further follow up. The remaining subjects were required to return at the 3 month (+/- 14 day) follow-up visit for assessment of chronic efficacy. **Table 6** below describes the study schedule of visits.

Table 6 Schedule of Visits

Study Period	Pre-Ablation	During Procedure	Pre-Discharge	10 Days ±3 Days	3 Months ±14 Days[d]	Un-Scheduled[d]
Consent	X					
Medical History	X					
TTE	X[a]					
TEE	X[b]					
12-Lead ECG	X		X	X	X	X[e]
Confirmation of BDB in CTI and non-inducibility of AFL		X[c]				
AAD medication Assessment	X		X	X	X	X[e]
Anti-coagulation med Assessment	X[b]		X[f]	X[f]	X[f]	
Adverse Event Assessment		X	X	X	X	X

a= A baseline TTE (Trans-thoracic echocardiogram) within 6 months prior to the ablation procedure is permissible. A TEE can be performed in lieu of a TTE.
b= TEE (Trans-esophageal echocardiogram), only if required. TEE will be required within 48 hours prior to the ablation procedure for those subjects who have chronic/persistent typical atrial flutter unless the subject has received therapeutic anti-coagulation for at least three weeks prior to the procedure. A TEE within 48 hours is also required for subjects who present in atrial flutter at the pre-procedure admission have not been anti-coagulated for at least three weeks prior to the procedure. This can be documented on an ECG (or similar such as telemetry, rhythm strips, etc.) taken prior to the start of the procedure (e.g. at admission).
c= At least 30 minutes after the last RF application with the investigational system.
d= To accommodate patient referrals from distant hospitals, the referring physician may conduct the indicated follow-up visits. In such cases, the investigator may contact the referring physician's office and/or obtain the appropriate source documents to complete Case Report Forms (CRFs).
e= These assessments during unscheduled visits may be done if required based on physician's judgment of the patient's medical condition.
f= Anticoagulants are required only for subjects who present in atrial flutter at the time of the procedure.

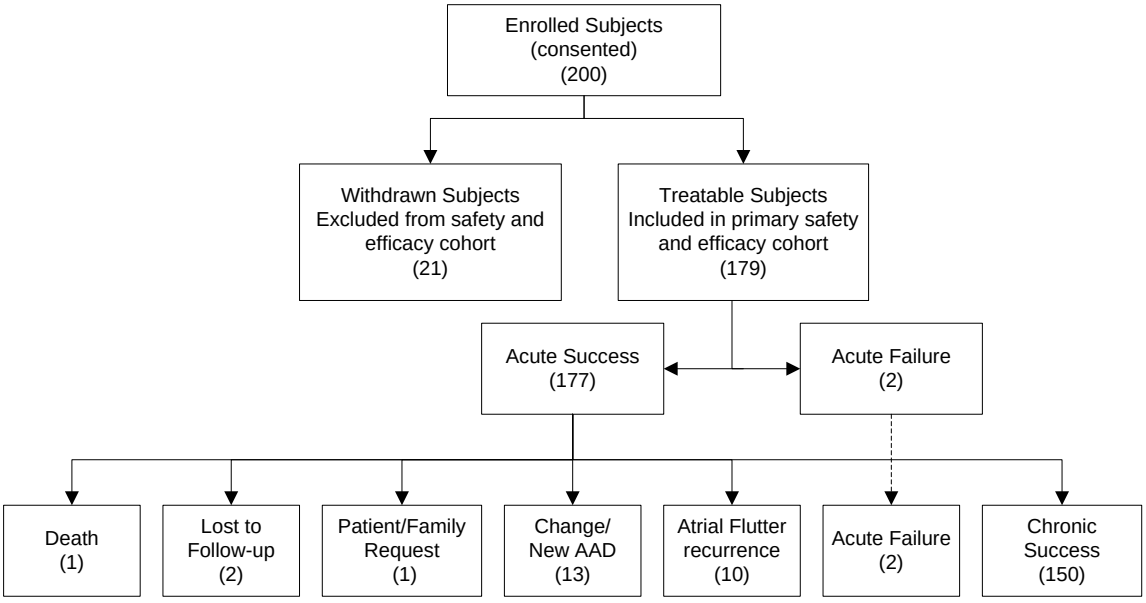
Adverse events and complications were recorded at all visits post-ablation.

B. Accountability of PMA Cohort

Of the 200 enrolled subjects, there were 21 subjects who did not meet entry criteria and were withdrawn prior to use of the investigational system (not treated). The remaining 179 subjects were treated with the investigational system and had data that was evaluable for analysis. Of the 179 subjects treated with the investigational device (primary efficacy and safety endpoints), 178 subjects completed the 10 day follow-up (primary safety endpoint) and 161 subjects completed the 3-month follow-up.

Figure 1 below provides a schematic of the 200 enrolled subjects' accountability in the study:

Figure 1 Subject Accountability Tree



C. Study Population Demographics and Baseline Parameters

A total of 200 subjects who met inclusion/exclusion criteria were enrolled (consented) at 24 investigational sites (22 in the US and 2 in Canada). Twenty-four (24) subjects were withdrawn from the study prior to the use of the investigational device.

Of the 179 subjects treated 143 subjects (79.89%) were male and 36 subjects (20.11%) were female. A pre-dominance of atrial flutter was noted in males when compared to females during this study. A meta-analysis performed by Pérez et. al which summarized 158 studies on clinical outcomes of atrial flutter ablation over a period of 20 years further indicated the predominance of atrial flutter in males [1].

The mean age of the treated subjects was 66.28 years. One of the inclusion criteria in the study was that the subject had to be 18 years or older in age. Hence, no pediatric population was included in the study.

The mean weight of treated subjects was 211.64 pounds and the mean body mass index (BMI) was 30.92.

Thus, the demographics of the study population was typical for a study of patients with atrial flutter performed in the US. Subject demographics are summarized in Table 7 .

Table 7 Subject Demographics

Demographic	Therapy Cool Flex Irrigated Ablation Catheter System (n=179)
Mean Age (years)	66.28 ± 10.18
Percent Male	79.89% (n=143)
Percent Female	20.11% (n=36)
Weight (lbs)	211.64 ± 54.43
Height (in)	69.41± 4.08
BMI	30.92± 7.84

The most commonly reported cardiac history for subjects treated with the investigational system were Hypertension (60.89%), Atrial Fibrillation (45.81%) and Coronary Artery Disease (28.49%). Cardiac history of treated subjects is summarized in **Table 8** .

Table 8 Cardiac History of Treated Subjects

Cardiac Condition	Therapy Cool Flex Irrigated Ablation Catheter System (n=179)
Hypertension	60.89% (n=109)
Atrial Fibrillation	45.81% (n=82)
Coronary Artery Disease	28.49% (n=51)
Coronary Artery Intervention	15.08% (n=27)
Valve Disease	14.53% (n=26)
Myocardial Infarction	11.73% (n=21)
Pacemaker/ICD Implant	11.17% (n=20)
Congestive Heart Failure	10.61% (n=19)
Stroke/TIA	8.38% (n=15)
Valve Surgery	7.82% (n=14)
Ventricular Tachycardia	6.15% (n=11)
Pericarditis	1.68% (n=3)
Atypical Atrial Flutter	0.00% (n=0)

D. Procedural Data

Procedural Parameters

Table 9 summarizes ablation parameters during the procedure for subjects treated with the Therapy Cool Flex Cardiac Ablation System.

Table 9 Procedural Parameters

Parameter	N	Mean ± SD
# of Applications per Procedure	179	12.40 ± 12.35
RF Time (Sec) per Application	2,212*	85.98 ± 99.78
RF Time (Min) per Procedure	179	17.71 ± 12.64
Procedure Time (Min) per Patient	179	98.73 ± 42.99
Temperature (°C) per Application	2,211*	28.35 ± 3.13
Mean Power (Watts) per Application	2,211*	31.78 ± 6.02
Impedance (Ohms) per Application	2,211*	93.64 ± 15.60
Total Fluid Administered (mL) per Patient	178¥	931.08± 497.53
Total Pump Saline (mL) per Patient	179	414.41 ± 314.42

* A total of 2,220 RF applications were delivered, however, the procedural data could not be collected on some RF applications. The percentage of such instances is less than 0.5%.
¥ A total of 179 subjects were treated with the investigational system; however the total fluid administered could not be collected for some subjects.

E. Safety and Effectiveness Results

Safety Results

The analysis of safety was based on the safety cohort of 179 subjects and availability data on composite serious adverse events within 7 days post procedure. Of the 179 subjects treated with the investigational catheter, 5 subjects had composite serious adverse events within 7 days of the procedure. The major complication rate (of composite serious adverse events) was 2.79% (5/179). This was compared against the pre-defined performance goal of 14% according to the protocol (Hypothesis Tests).

Thus, based on the quantitative assessment, the FLEXION AFL pivotal study demonstrated that the Therapy Cool Flex Cardiac Ablation System met the pre-defined performance goal of 14% major complication rate.

No unanticipated adverse device effects (UADE) were reported. The key safety outcomes for this study are presented in **Table 10** and **Table 11** .

Table 10 Primary Safety Comparison

Measure	Therapy Cool Flex Irrigated Ablation Catheter System	Hypothesis	95% CL[1]	Decision	Conclusion
Composite SAE within 7 days post procedure (Primary Safety)	5/179 (2.79%)	H_0: $\pi \geq 14\%$ H_A: $\pi < 14\%$	5.78%	Reject H_0	Equivalent Safety
[1] Based on exact binomial confidence limits.					

Adverse effects that occurred in the PMA clinical study:

Table 11 Composite serious adverse effects that occurred within 7 days post-procedure:

Event Description	Number of Subjects	Percent
Congestive Heart Failure (CHF) Exacerbation	2 / 179	1.12%
Arrhythmia	1 /179	0.56%
Death*	1 /179	0.56%
Stroke/Cerebrovascular Accident	1 /179	0.56%
*Primary Cause: Ventricular Fibrillation Cardiac Arrest. Secondary Cause: Acute Pulmonary Edema Congenital Heart Disease Atrial Flutter		

There was one subject death reported during the course of the clinical study. The CEC adjudicated this event to be serious, not device related, but related to concomitant procedure. The leading cause of death was considered by the Investigator and CEC as ventricular fibrillation cardiac arrest. Below is the description of this event:

The subject was a 62 year old male who had two (2) previous corrective surgeries for a congenital disease - Tetralogy of Fallot – a palliative procedure in childhood and a complete repair in 1987. Additional history includes ventricular dilatation, atrial fibrillation, aortic insufficiency, valve disease, hypertension, and dyslipidemia. At the time of enrollment in the study, the subject presented with problems of fatigue, significant bradycardia and very slow ventricular rates noted on Holter monitoring. The subject was noted to have intermittent atrial flutter, consistent with isthmus-dependent flutter and was enrolled in the study on April 16, 2012. Due to the long-standing history of significant conduction problems, it was anticipated that the subject would receive a dual chamber pacemaker implant following the flutter procedure.

Following the successful flutter ablation, and post-pacemaker implant procedure, the subject became progressively hypoxic and de-saturated and was in acute distress. Code blue measures were taken and CPR commenced. Despite these measures, the patient expired **(death).** Final autopsy including tissue microscopy showed no gross or microscopic evidence of cardiac perforation, acute myocardial infarction or pulmonary embolism.

Effectiveness Results

The Primary and Secondary Effectiveness analysis are described below.

Primary Effectiveness

The analysis of primary effectiveness was based on the procedural success of 179 subjects treated with the investigational system. Of the 179 subjects treated, 177 subjects had acute procedural success and 2 subjects were acute failures. The acute procedural success rate in this study was 98.88% (177/179). This was compared against the pre-specified performance goal of 88% according to protocol section 10.3.2 (Hypothesis Tests).

Thus, based on a quantitative assessment, the FLEXION AFL pivotal study demonstrated that the Therapy™ Cool Flex™ Cardiac Ablation System met the pre-defined performance goal of 88% acute procedural success. Table 12 illustrates the primary effectiveness results.

Table 12 Primary Effectiveness Comparison

Measure	Therapy Cool Flex Irrigated Ablation Catheter System	Hypothesis	95% CL[1]	Decision	Conclusion
Acute Procedural Success (Primary Effectiveness)	177/179 (98.88%)	H_0: $\pi \leq 88\%$ H_A: $\pi > 88\%$	96.52%	Reject H_0	Equivalent Effectiveness
[1] Based on exact binomial confidence limits.					

Secondary Effectiveness

179 subjects treated with the investigational system, were evaluated for the chronic endpoint, 175 had evaluable chronic outcome data at 3 months. One hundred fifty (150) of these subjects met the chronic success endpoint criteria. Multiple imputation modeling was used to evaluate the chronic success endpoint. The model derived chronic success rate was 85.47%. The 95% confidence limit was 81.10% which was compared against the pre-specified performance goal of 72% according to the protocol.

Thus, based on a quantitative assessment, the FLEXION AFL pivotal study demonstrated the Therapy™ Cool Flex™ Cardiac Ablation System met the pre-defined performance goal of 72% chronic success. **Table 13** illustrates the secondary effectiveness results.

Table 13 Secondary Effectiveness Comparison

Measure	Therapy Cool Flex Irrigated Ablation Catheter System	Hypothesis	95% CL[1]	Decision	Conclusion
Freedom from recurrence of typical AFL or increase/new dosage of Class I/III AAD for any arrhythmia (Secondary Efficacy)[2]	85.47%	H_0: $\pi \leq 72\%$ H_A: $\pi > 72\%$	81.10%	Reject H_0	Equivalent Effectiveness

[1] Based on confidence limits obtained from PROC MIANALYZE.
[2] PROC MI used to obtain outcome for subject that died post-ablation procedure and subjects who discontinued prior to availability of 3 month data.

Missing Data

To supplement the primary analyses, sensitivity analyses were performed that examined the impact of missing data on study primary outcomes. There were no missing data for the primary efficacy or primary safety endpoints.

There were 4 subjects with no evaluable secondary effectiveness endpoint data. Multiple imputation methods were used in the evaluation of the secondary effectiveness endpoint. Additional sensitivity analyses to determine the effect of missing data on the secondary endpoint where performed and results show that even in the worst-case scenario where all 4 subjects were counted as failures, the study still met the pre-defined performance goal of 72%.

Assessment of Consistency by Center

Sites enrolling less than 5 subjects were combined based on the process outlined in section 10.3.5 of the protocol. For the primary safety endpoint, results were consistent across all investigational sites with no evidence of a statistically significant difference (p=0.6926 from Fisher's exact test). For the primary efficacy endpoint of acute procedural success, results were consistent across the investigational sites (p=0.2352 from Fisher's exact test).

Subgroup Analyses

Gender & Subgroup Analyses

The results of the primary endpoints were presented by pre-specified subgroups as proposed in the protocol: age, height, weight, gender, history of coronary artery disease, history of atrial fibrillation, history of congestive heart failure (CHF), Class I or Class III anti-arrhythmic therapy at the time of enrollment. Results were also presented by BMI subgroups. These analyses were considered descriptive in nature. For the purpose of these analysis, statistical significance was assumed as a nominal alpha level of <0.05.

For continuous variables such as age, height and weight, subjects were divided into two groups based on the median value. BMI was split based on obesity categories: BMI < 30 and BMI ≥ 30. Logistic Regression models were fit to obtain odds ratio estimates, 95% confidence interval, and p-values for comparing the levels of a subgroup. Due to the small number of primary safety events and acute procedural failures, Firth's method was used to calculate the two-sided 95% confidence interval of the odds ratio.

Results examining the consistency of primary safety and primary efficacy results by subgroup analyses are displayed below in **Table 14** and **Table 15** , respectively.

For the primary safety endpoint, there were no significant differences in the occurrence of composite SAEs within 7 days post procedure for the following subgroups: age, height, weight, obesity, gender, history of coronary artery disease, history of atrial fibrillation, and Class I and III AAD therapy. There was an observed statistical difference in primary safety rates between subjects with and without history of primary congestive heart failure (p=0.0345). Out of 179, 19 subjects had history of CHF. There was a higher primary safety rate observed among subjects with history of CHF (10.53%) as compared to those with no history of CHF (1.88%).

For the primary efficacy endpoint, there were no significant differences in acute procedural success rate for any subgroup.

Table 14 Composite Serious Adverse Events (Primary Safety) by Subgroup Analyses

Subgroup	N	Subjects With 1+ Events	Percent	OR [95% CI][1]	P-value[2]
Age					
< 67 (median)	83	2	2.41%	1.22 [0.23 to 6.41]	0.8141
≥ 67 (median)	96	3	3.13%		
Height					
< 70in (median)	83	4	4.82%	0.28 [0.04 to 1.82]	0.1818
≥ 70in (median)	96	1	1.04%		

Subgroup	N	Subjects With 1+ Events	Percent	OR [95% CI][1]	P-value[2]
Weight					
< 202lb (median)	89	4	4.49%	0.32 [0.05 to 2.09]	0.2333
≥ 202lb (median)	90	1	1.11%		
Obese (BMI ≥ 30)					
No	98	3	3.06%	0.86 [0.16 to 4.51]	0.8565
Yes	81	2	2.47%		
Gender					
Male	143	3	2.10%	2.91 [0.54 to 15.63]	0.2132
Female	36	2	5.56%		
Coronary Artery Disease					
No History of CAD	128	3	2.34%	1.81 [0.34 to 9.60]	0.4854
History of CAD	51	2	3.92%		
Atrial Fibrillation					
No History of AF	97	3	3.09%	0.84 [0.16 to 4.41]	0.8352
History of AF	82	2	2.44%		
Congestive Heart Failure					
No History of CHF	160	3	1.88%	6.43 [1.14 to 36.10]	0.0345
History of CHF	19	2	10.53%		
Class I AAD Use at Enrollment					
No Class I AAD Use	163	5	3.07%	0.87 [0.04 to 17.95]	0.9297
Class I AAD Use	16	0	0.00%		
Class III AAD Use at Enrollment					
No Class III AAD Use	145	5	3.45%	0.37 [0.02 to 7.14]	0.5103
Class III AAD Use	34	0	0.00%		

[1] Firth's method used to calculate 95% confidence interval of the odds ratio.
[2] P-value from logistic regression model.

Table 15 Acute Procedural Success (Primary Efficacy) Subgroup Analyses

Subgroup	N	Successes	Percent	OR [95% CI][A]	P-value[B]
Age					
< 67 (median)	83	82	98.80%	1.16 [0.12 to 11.49]	0.9006
≥ 67 (median)	96	95	98.96%		
Height					
< 70in (median)	83	81	97.59%	5.92 [0.28 to 127.15]	0.2557
≥ 70in (median)	96	96	100.00%		
Weight					
< 202lb (median)	89	87	97.75%	5.17 [0.24 to 111.13]	0.2938
≥ 202lb (median)	90	90	100.00%		
Obese (BMI ≥ 30)					
No	98	96	97.96%	4.22 [0.20 to 90.87]	0.3576
Yes	81	81	100.00%		
Gender					
Male	143	143	100.00%	0.05 [0.00 to 1.04]	0.0531

Subgroup	N	Successes	Percent	OR [95% CI][A]	P-value[B]
Female	36	34	94.44%		
Coronary Artery Disease					
No History of CAD	128	127	99.22%	0.40 [0.04 to 3.96]	0.4305
History of CAD	51	50	98.04%		
Atrial Fibrillation					
No History of AF	97	96	98.97%	0.84 [0.09 to 8.38]	0.8853
History of AF	82	81	98.78%		
Congestive Heart Failure					
No History of CHF	160	158	98.75%	0.62 [0.03 to 14.23]	0.7618
History of CHF	19	19	100.00%		
Class I AAD Use at Enrollment					
No Class I AAD Use	163	161	98.77%	0.51 [0.02 to 12.03]	0.6769
Class I AAD Use	16	16	100.00%		
Class III AAD Use at Enrollment					
No Class III AAD Use	145	143	98.62%	1.20 [0.05 to 26.64]	0.9072
Class III AAD Use	34	34	100.00%		

[A] Firth's method used to calculate 95% confidence interval of the odds ratio.
[B] P-value from logistic regression model.

F. Results by US / OUS Sites

Two (2) sites in the study were located outside the United States (OUS): Institut de Cardiologie de Quebec (Hopital Laval) enrolled 11 subjects (11 were treated) and Royal Jubilee Hospital enrolled 7 subjects (5 were treated). To assess the consistency of sites within and outside the US, the summary statistics for the endpoints were calculated separately for the US and OUS sites. Logistic Regression models were fit to obtain odds ratio estimates, 95% confidence interval, and p-values for comparing the geographic regions. Due to the small number of primary safety events and acute procedural failures, Firth's method was used to calculate the two-sided 95% confidence interval of the odds ratio.

For the primary safety endpoint, there was no statistically significant difference between the US and OUS sites (p=0.9297 from Logistic regression). The rate of composite serious adverse events within 7 days of the index procedure was 3.07% for the US sites and 0% for the OUS sites.

For the primary effectiveness endpoint, there was no statistically significant difference between the US and OUS sites (p=0.6769 from Logistic regression). Rates of acute procedural success were 98.77% for the US sites and 100% for the OUS sites.

G. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 57 investigators of which none were full-time or part-time employees of the sponsor and 1 investigator had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0 investigators
- Significant payment of other sorts: 1 investigator
- Proprietary interest in the product tested held by the investigator: 0 investigators
- Significant equity interest held by investigator in sponsor of covered study: 0 investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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 Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The adverse events of the device are based on data collected in the clinical study conducted to support PMA approval of the Therapy Cool Flex Ablation Catheter as described above. The FLEXION AFL pivotal study demonstrated that the Therapy Cool Flex Ablation Catheter met the safety goal of its intended use as defined in the clinical protocol.

B. Effectiveness Conclusions

The FLEXION AFL pivotal study demonstrated that the Therapy Cool Flex Ablation Catheter met the efficacy performance goal for its intended use as defined in the clinical protocol.

C. Benefit-Risk Conclusions

Patients diagnosed with atrial flutter can be managed with either catheter ablation, or antiarrhythmic medications and cardioversion to try to restore sinus rhythm, or with rate-controlling drugs that allow the flutter to continue but with a slower ventricular response to prevent persistent tachycardia and the adverse sequelae that persistently elevated heart rates can cause. Often the rate is difficult to control making the rate control strategy challenging. The antiarrhythmic strategy can be effective, especially for patients who have other indications for an antiarrhythmic medication such as atrial fibrillation, however, recurrences can occur and taking these medications indefinitely can cause side effects and toxicity. Recent guidelines have focused on atrial fibrillation since it is much more common and treatment for atrial fibrillation is more rapidly evolving, however, treatment Guidelines from 2003 state that long term treatment of atrial flutter with catheter ablation is a class I indication regardless of symptoms.* Therefore, for typical isthmus dependent atrial flutter, catheter ablation has become the standard of care because it rids the need for long term anti arrhythmic medications, it can rid the need for anticoagulation in some patients, and the risk profile of the procedure is less than other ablation procedures such as atrial fibrillation ablation.

Patients derive much clinical benefit from restoring sinus rhythm and not having ongoing atrial flutter. Many patients prefer the approach that has the best long term success and least chance of recurrence which is the ablation approach.

There are currently several market approved ablation catheters for atrial flutter including some catheters that use an open irrigation system. The open irrigation system provides a deeper, bigger lesion with radiofrequency applications to the endocardial tissue which increases the chance for procedural success as well as long term success without late recurrence.

The Cool Flex catheter has a different distal electrode tip than its predecessors allowing the tip to be flexible and provide a more uniform distribution of fluid for the open irrigation. The FLEXION AFL study did not show an increased risk to patients when using this device. There were no device-related complications. There were procedural complications that were similar in nature and in frequency to other atrial flutter ablation catheter trials.

In conclusion, the pre-clinical and clinical information presented support that the probable benefits outweigh the probable risks for using the Cool Flex for the treatment of isthmus dependent atrial flutter.

**ACC/AHA/ESC Guidelines for the Management of Patients with Supraventricular Arrhythmias-Executive Summary. Circulation 2003*

D. Overall Conclusions

The data in this application supports the reasonable assurance of safety and effectiveness of this device when used according to the product labeling.

XIII. CDRH DECISION

CDRH issued an approval order on December 18, 2013. The final conditions of approval cited in the approval order are described below.

XIV. APPROVAL SPECIFICATIONS

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

XV. REFERENCES

1. Francisco J. Pérez, Christine M. Schubert, Babar Parvez, Vishesh Pathak, Kenneth A, Ellenbogen and Mark A. Wood - Long-Term Outcomes After Catheter Ablation of Cavo-Tricuspid Isthmus Dependent Atrial Flutter: A Meta-Analysis : Circ Arrhythm Electrophysiol 2009;2;393-401; originally published online Jun 23, 2009