# SUMMARY OF SAFETY AND EFFECTIVENESS DATA

## 1.0 GENERAL INFORMATION

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|---|---|
| **Device Generic Name:** | Cardiac Cryoablation Catheter and Console System |
| **Device Trade Name:** | 7F Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System |
| **Name & Address of Applicant:** | CryoCath Technologies Inc.<br>16771 Chemin Ste Marie<br>Kirkland, Quebec<br>Canada, H9H 5H3 |
| **U.S. Premarket Approval (PMA) Application Number:** | P020045 |
| **Representative:** | Fred Milder, Ph.D.<br>Applied Physics<br>204 Clinton Road<br>Brookline, MA 02445-5814 |
| **Date of Panel Recommendation:** | March 6, 2003 |
| **Date of Notice of Approval to Applicant:** | April 17, 2003 |

## 2.0 INDICATIONS FOR USE

The 7F Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System is indicated for the cryoablation of the conducting tissues of the heart in the treatment of patients with atrioventricular nodal reentrant tachycardia (AVNRT).

## 3.0 CONTRAINDICATIONS

Do not use this device:

- in patients with active systemic infection;
- in conditions where manipulation of the catheter would be unsafe (e.g., intracardiac mural thrombus); and
- in patients with cryoglobulinemia.

## 4.0 WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the instructions for use.

## 5.0 DEVICE DESCRIPTION

The 7F Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System (Freezor® Catheter and CryoConsole System) consists of the 7F Freezor® Cardiac Cryoablation Catheter (Freezor® Catheter), umbilicals and accessories, and the CCT.2 CryoConsole (CryoConsole). The device produces controlled cryogenic (extremely cold) temperatures at the distal tip of a long, flexible catheter by the injection of nitrous oxide refrigerant. The distal tip is placed on the inner walls of a beating heart, reached through the body's vasculature from a puncture in the skin.

The system has two modes of operation: diagnostic or mapping (termed cryomapping) and therapeutic or ablating (termed cryoablation). When operated in a therapeutic mode, the device is activated to correct electrophysiological abnormalities leading to irregular or errant heartbeats. This is achieved by selectively destroying (cryoablating) groups of heart cells (arrhythmogenic sites) that cause or propagate the abnormality.

The cryomapping mode will allow the physician to select the target temperature at the distal tip of the catheter. If the desired effect is seen during the cryomapping procedure, the physician may choose to proceed to cryoablation. The physician may also directly select the cryoablation option.

### 5.1 7F FREEZOR® CARDIAC CRYOABLATION CATHETER

The Freezor® Catheter is a 7 French (F) device consisting of a 4mm long, gold-plated metal tip, a flexible shaft, and a handle. The distal section of the catheter shaft is deflectable in one direction by pulling a lever on the handle. This feature facilitates the tracking and positioning of the tip to the required location inside the heart.

The catheter consists of an injection tube inside the hollow flexible shaft. The injection tube, which extends from the connector to the tip, delivers liquid refrigerant inside the tip. The refrigerant vapors produced in the tip are returned through the main lumen of the catheter by a vacuum line (umbilical) connected to the catheter.

There are two connectors at the proximal end of the handle. The coaxial connector contains the high-pressure injection tube that connects to the refrigerant injection tube and the larger vacuum tube that extracts the refrigerant vapors from the catheter after it has evaporated at the tip. The second connector is the electrical connector that transports tip temperature data and other data to the console. The connector also transports electrocardiogram (ECG) signals from the catheter to the Auto Connection Box.

### 5.2 UMBILICALS AND ACCESSORIES

There are several connections that need to be made within the system. The coaxial umbilical connects the catheter directly to the console and it is responsible for the delivery and retrieval of the refrigerant to and from the catheter. The electrical accessories consist of Electrical Umbilical, Electrical Extension cable, manual or Auto Connection Box, and ECG Cable. These components are used to transmit electrical signals to the console and transmit ECG signals to the hospital ECG system.

### 5.3 CCT.2 CRYOCONSOLE

The CCT.2 CryoConsole is responsible for transferring and controlling the refrigerant from the supply tank in the console to the coaxial umbilical. The console contains a vacuum pump. The vacuum pump is connected to the coaxial umbilical, extracts the refrigerant from the catheter and umbilical. The console also has a touch screen display, which allows the user to input patient information and select operating modes. The screen displays tip temperature, elapsed time, and other data that is useful for the user.

## 6.0 ALTERNATIVE PRACTICES AND PROCEDURES

For patients with AVNRT, alternative practices include antiarrhythmic drug therapy, ablation of the arrhythmogenic cardiac tissue using radiofrequency ablation catheters, surgery, pacing therapies or implantable pacemaker or cardioverter-defibrillators (ICD).

## 7.0 MARKETING HISTORY

The Freezor® Catheter and CryoConsole System have been marketed for generic indication of ablation of cardiac arrhythmia since 2001 in the European Union under CE Mark, Canada, Australia and other countries in the world.

The Freezor® Catheter and CryoConsole System have not been withdrawn from marketing in any country for any reason related to safety or effectiveness.

## 8.0 POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events (listed in alphabetical order) that may be associated with cardiac ablation for the treatment of AVNRT include, but are not limited to, the following:

- access site complications including pain, hematoma, ecchymosis, infection, thrombosis or AV fistula;
- arrhythmias include new arrhythmias and/or worsening of existing arrhythmias;
- cardiac arrest and/or death;
- cardiac perforation with hemopericardium and/or tamponade;

- catheter entrapment in cardiac structures requiring surgical intervention;
- chest pain;
- coronary artery spasm/dissection/thrombosis;
- endocarditis;
- exposure to X ray energy with possible cancer risk or harm to fetus;
- gas embolism with possible tissue infarction;
- heart block, partial or complete, potentially requiring implantation of a permanent pacemaker;
- hemorrhage;
- hemothorax;
- myocardial infarction;
- pericardial effusion;
- pericarditis or pericardial effusion;
- pleural effusion;
- pneumothorax;
- pseudoaneurysm;
- pulmonary edema;
- pulmonary embolism;
- stroke;
- thrombus,
- intravascular or intracardiac;
- thromboembolism with potential tissue infarction;
- transient ischemic attack;
- valvular damage;
- vasovagal reaction.

For a summary of the adverse events observed in the clinical study please refer to sections 10.5 and 10.7

## 9.0 SUMMARY OF PRECLINICAL STUDIES

Non-clinical bench testing and animal testing have been conducted to demonstrate the safety, reliability and performance of the Freezor® Catheter and Cryoconsole System. The following sections summarize the results of this testing.

### 9.1 BENCH TESTING

Bench testing of the Freezor® Catheter and CryoConsole System consisted of reliability (Table 2), mechanical and electrical (Table 3), and CryoConsole testing (Table 4). Reliability, mechanical, and electrical testing were performed on the catheters and cables sterilized by ethylene oxide.

**Table 1: Reliability Testing of Freezor® Catheter**

| Test | Sample Size | Acceptance criteria | Results |
|---|---|---|---|
| Thermal cycling & soak in saline (0.99) for 8 hours @ 37°C | 32 | N/A | All samples passed |
| Tensile Test | 16 | Bond set at 1.5 kg | All samples passed |
| Torque Test: Shaft transition | 16 | No failure after one (1) full rotation at 360° | All samples passed |
| Torque Test: Tip to handle | 16 | No failure after 1 full rotation at 360° | All samples passed |
| Burst Test (Joint Seal) | 16 | No bubbles escape at 15 psig | All samples passed |
| Deflection Fatigue | 16 | No loss of catheter integrity & electrical continuity after 100 deflections | All samples passed |
| Flexion Fatigue | 16 | No lost of integrity after 100 cycles of flexion apply on the handle | All samples passed |
| Connector | 8 | No loss of catheter electrical integrity maximum load of 2kg | All samples passed |
| Accessory Cable Fatigue | 8 | No loss of cable integrity after 250 deflections | All samples passed |

**Table 2: Mechanical and Electrical Testing of Freezor® Catheter**

| Test | Sample Size | Acceptance criteria | Results |
|---|---|---|---|
| Torsion | 16 | No failure after one (1) full rotation 360° | All samples passed |
| Deflection | 16 | No deflection failure after 100 deflections | All samples passed |
| Steering | 18 | Safety & effectively steered in vascular model | All samples passed |
| Bending (stiffness) | 9 | Stiffness between 30 – 55 x $10^3$ psi | All samples passed |
| Buckling force (Compression test) | 16 | Compression force between 30 – 128 g | All samples passed |
| Radiopacity | 3 | Complies to ASTM F640-79 | All samples passed |
| Noise | 11 | Level of noise same as reference signal of 27 mV & frequency 1 Hz | All samples passed |
| Stimulation | 2 | Ability to pace in animal | All samples passed |

| Test | Sample Size | Acceptance criteria | Results |
|---|---|---|---|
| Mapping | 27 | Ability to capture ECG signals | All samples passed |
| Performance test | 16 | -68°C after 10 freeze thaw cycles | All samples passed |

**Table 3: Summary of CryoConsole Testing (with Console 10000-002AS)**

| Test | Acceptance criteria | Results |
|---|---|---|
| Sound Pressure Level Testing | Sound pressure < 85dBA, measured at Operators normal position | passed |
| Safety Assessment of Automatic Switch implementation | Equivalent level of Risk to the patient and user associated w/ implementation of automatic switch | passed |
| CDM Software version (3.0) Hazard Analysis | Equivalent level of risk as compared to Console 10000-002 | passed |
| Software & System (3.0) Verification & Validation | Equivalent level of functionality evaluated, as compared to Console 10000-002 | passed |
| Radiated Emissions Limits 30 MHz and 1000 MHz | CISPR 11:1997<br>EN55011:1998 Class A | passed |
| Immunity- Electrical Interference 0 Hz to 400 GHz | EN60601-1-2:1993<br>EN61000-4-2, 3, 4/IEC1000-4-2, 3, 4 ENV50204<br>EN61000-3-2/IEC1000-3-2<br>EN60111-4-5/IEC801-5:1984<br>EN61000-3-3 | passed |
| Emissions from low-voltage Electrical & Electronic Equipment 9KHz and 40 GHz | FCC Part 15 Subpart 13, Sec. 15.107(B) and 15.109(B) | passed |
| General Requirements for Safety | Per the standards stipulated:<br>IEC 601-1:1998 | passed |
| Thermister (in-risk current limiter) | In rush current < 180A and duration of 6-10 minutes | passed |

## 9.2 BIOCOMPATIBILITY

The following table lists the patient and user contacting materials of the components included in the 9F Freezor® catheter:

**Table 4: Patient Contacting Materials of the Freezor® Catheter**

| Component | Material Description |
|---|---|
| **Tip Electrode** | Gold plated copper/tellurium |
| **ECG Ring Electrodes** | Platinum/Iridium |

| Component | Material Description |
|---|---|
| **Shaft** | Vestamid 75D<br>Pebax 72D, 63D, 40D<br>33% Bismuth subcarbonate ($BiO_2CO_3$)<br>Blue color |

Biocompatibility testing was conducted on finished 9F Freezor catheters designed with materials identical to the 7F Freezor catheters. Catheters were sterilized with ethylene oxide and tested in accordance with ISO 10993 and FDA Blue Book Memorandum G95-1, "Use of International Standard ISO 10993." The catheter is classified as short duration, direct blood path, and externally communicating per ISO 10993-1. The table below summarizes the biocompatibility test results.

**Table 5: Biocompatibility Testing**

| Tests | Results |
|---|---|
| **Cytotoxicity**:<br>ISO elution, L-929 cells, 48 hours | The MEM test extracts showed no evidence of causing cell lysis or toxicity. The MEM test extracts were not cytotoxic and met the requirements of the test. The negative controls, the reagent controls and the positive controls performed as anticipated. |
| **ISO Sensitization:**<br>in guinea pig (Maximization method); saline and cottonseed oil extracts | Under the conditions of the study, the SC and CSO test articles extracts showed no evidence of causing dermal contact sensitization in the guinea pig. |
| **ISO Acute Intracutaneous Reactivity**<br>in rabbit; saline and cottonseed oil extracts | Under the conditions of the study, there was no mortality or evidence of significant systemic toxicity from the extracts injected intracutaneously into rabbits. The primary irritation index characterization for the extracts was negligible. |
| **ISO Acute Systemic Toxicity**<br>in mouse; saline and cottonseed extracts | Under the conditions of the study, there was no mortality or evidence of significant systemic toxicity from the extracts. Each test article extract met the requirements of the test. |
| **Material Mediated Pyrogen**<br>in rabbit | Under the conditions of the study, the total rise of rabbit temperatures during the 3-hour observation period was within acceptable USP limits. The extract was judged non-pyrogenic. |
| **Hemolysis**<br>in rabbit blood | Under the conditions of the test, the mean hemolytic index for the test article extract was 0%. The test article extract was non hemolytic. The negative and positive controls performed as anticipated. |
| **Complement Activation**<br>In normal human serum | Under the conditions of this assay, the test article extract indicated activation of 17.741 ng/ml. As a point of reference, this was 9% of the normalized C3a concentration produced by latex, the positive reference material. The low control, serum controls, positive control, and reference control materials performed as anticipated. |
| ***In vivo* Thromboresistance**<br>in dog (Venous implant) | Under the conditions of the assay the device was found to be resistant to thrombus formation |

All results passed. As a result, the testing demonstrated that the Freezor® is biocompatible for its intended placement and duration of use.

## 9.3 SHELF LIFE TESTING

Microbial barrier testing to confirm catheter sterility and performance testing to confirm catheter functionality was conducted on packaged Freezor® Catheters that had undergone real-time and accelerated aging. Testing results support a 2-year expiration date for the device.

## 9.4 ANIMAL TESTING

Preclinical testing of the Freezor® Catheter and CryoConsole System in animals established sufficient feasibility and safety of the device in ablating endomyocardial tissue to allow the initiation of human studies of the device. Animal testing was performed in over 275 dogs.

The animal testing demonstrated that the system:

- passed through the vascular system and could be positioned accurately at desired intracardiac locations;
- created controlled ablation lesions in myocardium;
- created lesions with a persistent effect up to 1 month in follow-up;
- reversibly interfered with the cardiac conduction physiology (cryomapping);
- detected electrical signals from atrial and ventricular sources;
- caused minimal thrombogenesis;
- ablated within the coronary sinus and pulmonary veins without evidence of venous or arterial stenosis at up to 1-month follow up.

## 10.0 SUMMARY OF CLINICAL STUDIES

### 10.1 STUDY DESIGN

The Freezor® Catheter and CryoConsole System was evaluated in a clinical study for the treatment of supraventricular tachycardias (SVT). The study was designed as a nonrandomized, single-arm, multicenter study to assess the safety and effectiveness of the device used percutaneously in the treatment of AVNRT, AVRT and refractory AF in subjects acting as their own controls.

#### 10.1.1 Study Endpoints

The endpoints for the study were as follows:

- procedural safety - defined by the absence of serious complications associated with the use of the investigational device within seven days of the ablation procedure; and
- acute procedural success - defined as the absence of recurrence and non-inducibility of sustained SVT at the end of the procedure.
- chronic success - defined as no recurrence of sustained SVT at follow-up.

Safety was analyzed for each diagnostic group and overall by calculating the proportion and exact two-sided 95% confidence intervals for acute major complications, and the upper bound was compared to an historically determined safety objective performance criterion (OPC) as described in the FDA guidance, "*Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Guidance for Industry* (July 1, 2002).

The OPCs from the guidance document are as follows:

**Table 6: Acceptable Endpoint Criteria Based on Medical Literature**

| Study Endpoint | Target Value | 95 % Confidence Bound |
|---|---|---|
| Acute Success | > 95% | ≥ 85% |
| Chronic Success | > 90% | ≥ 80% |
| Major Complications | < 2.5% | ≤ 7% |

The OPCs were determined by the FDA to be an adequate goal, lower bound, for the pooled population of patients with AVNRT, AVRT and atrial fibrillation with a rapid ventricular response.

After treatment, the subjects remained hospitalized per hospital procedure under continuous electrocardiogram monitoring, and post procedure assessments were performed. Subsequent follow-up was scheduled at 1 week (telephone interview), at 1 and 3 months (clinic visits) and at 6 months (telephone interview) after the procedure.

## 10.2 DESCRIPTION OF SUBJECTS

A total of 166 subjects were enrolled in the study. Of the 166 enrolled subjects, final diagnoses were AVNRT, 102 (61%); AVRT, 51 (31%); AF, 12 (7%); and 1 subject with a non-protocol arrhythmia [atrial tachycardia (AT)]. Of these 166 enrolled subjects, 164 were treated with cryoablation and constitute the intent-to-treat (ITT) population.

## 10.3 DEMOGRAPHICS

The study population consisted of 53 (32%) men and 113 (68%) women. Patient demographics for the study are shown in the table below:

**Table 7: Summary of Demographic Data of Enrolled Subjects (n=166)**

| Diagnosis | Number of Subjects | Age (yr) | Sex n (%) |
|---|---|---|---|
| AVNRT | 103 | 50 ± 15 | M: 31 (30)<br>F: 72 (70) |
| AVRT | 51 | 39 ± 13 | M: 18 (35)<br>F: 33 (65) |
| AF | 12 | 73 ± 11 | M: 4 (33)<br>F: 8 (67) |
| Overall | 166 | 48 ± 16 | M: 53 (32)<br>F: 113 (68) |

AF, atrial fibrillation; AVRT, atrioventricular reentrant tachycardia;

## 10.4 CRYOABLATION PROCEDURE DATA

The treatment of SVT utilizing the Freezor® Catheter can be achieved by using the cryomapping function prior to cryoablation of the targeted substrate or by proceeding directly with the ablation of the targeted substrate without cryomapping. The table below describes the cryoablation procedural information.

**Table 8: Cryoablation Procedure Data**

| Parameter | Mean ± SD (Range) | Subjects (n) |
|---|---|---|
| Cryoablation attempts | 1230 times | 164 |
| Cryoablation attempts/patient | 7.5 ± 6.6 (1 – 36) | 164 |
| Fluoroscopy duration (min) | 24.9 ± 24.0 (1 – 115) | 162 |
| Total EPS procedure duration (min) | 265.2 ± 120.8 (115 – 920) | 164 |

## 10.5 SAFETY RESULTS

Device safety was evaluated via an assessment of the acute major complication rate for the SVT population and compared to the objective performance criterion for safety. Eight (8) acute major complications (AMCs) were reported in 7/166 patients (4.2%, upper bound 8.5%). The clinical study safety results exceeded the safety objective performance criteria of 2% with an upper bound of 7.5%. Three of these AMCs occurred in the 103 AVNRT patients (2.9%).

Eighty-seven (52%) of the 166 safety subjects evaluated in this study reported one or more AEs. Device-related AEs were reported for 11 (7%) of the 166 enrolled subjects. The table below summarizes this information per patient arrhythmia type:

**Table 9: Subjects with Adverse Events (n=166)**

| Adverse Event Type | AVNRT (n = 103) | AVRT (n = 51) | AF (n = 12) | All subjects (n = 166) |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | n (%) |
| adverse event | 52 (50) | 29 (57) | 6 (50) | 87 (52) |
| serious adverse event | 8 (8) | 6 (12) | 6 (50) | 20 (12) |
| acute major complication | 3 (3) | 4 (8) | 0 (0) | 7 (4.2) |
| death | 0 (0) | 0 (0) | 1 (8) | 1 (0.6) |

The AMCs consisted of: pulmonary embolism, prostatitis secondary to Foley catheter placement, thrombus in IVC after cryoablation and RF ablation, subtotal RCA occlusion with MI in a patient after failed cryoablation and RF ablation of left sided pathway, sheared introducer for diagnostic catheter, pericardial perforation by diagnostic catheter requiring pericardiocentesis, deep venous thrombophlebitis, and thrombus formation on diagnostic catheter requiring removal of catheter. One patient died 4 months post-procedure. This death was not considered related to the study device or procedure

## 10.6 Effectiveness Results: Acute Procedural Success and Long-Term Clinical Success

Device effectiveness was evaluated via an assessment of the rates of acute procedural success and long-term (3-month) clinical success. One hundred sixty four (164) intent-to-treat subjects had a cryoablation catheter activated in a cardiac chamber, and 136 (83%, 95%CI 76% – 88%) of these subjects demonstrated acute procedural success at the end of the EP procedure. Acute success of the device system did not successfully reach the objective performance criteria of 95% lower bound 85%.

Long term clinical success conditional on acute success (freedom from recurrence) was achieved in 122/134 patients (91%, 95%CI 85%-95%). When acute success was not achieved with cryoablation, RF ablation was attempted resulting in an overall acute success rate of 161/166 patients (97%, 95%CI 93%-99%).

The table below summarizes the acute procedural and long-term clinical success in the ITT patient population, per diagnostic group.

**Table 10: Acute Procedural Success and Long-Term Clinical Success (ITT)**

| Diagnosis | N | Acute Procedural Success N (%, lower bound CI %) | Long Term Clinical Success* % (lower bound CI %) |
|---|---|---|---|
| **AVNRT** | 103 | 94 (91, **82**) | 93% (85)* |
| **AVRT** | 49 | 34 (69, **51**) | 88% (69)* |
| **AF** | 12 | 8 (67, **29**) | 75% (28)* |
| **Overall** | 164 | 136 (83, **76**) | 91% (85) |

*Bonferroni adjusted confidence interval

10.7 CRYOMAPPING

Cryomapping effect was demonstrated in 64% (87/135) of subjects attempted. One AVNRT subject had a cryomapping related adverse event (transient AV block lasting 25 seconds which resolved completely without treatment). See Table 9 below for a summary of cryomapping effect and related adverse events.

**Table 1: Summary Data for Cryomapping Effect and Related Adverse Events (ITT Subjects; n=164)**

| Diagnosis | ITT Subjects who had Cryomapping Attempts* n (%) | ITT Subjects with Effective Cryomaps** n (%) | ITT Subjects with Cryomapping- related AEs n (%) |
|---|---|---|---|
| **AVNRT #** | 86 / 102 ( 84%) | 66 / 86 (77%) | 1 / 86 (1.1%) |
| **AVRT** | 38 / 49 ( 78%) | 18 / 38 (47%) | 0 / 38 ( 0%) |
| **AF** | 10 / 12 ( 83%) | 3 / 10 (30%) | 0 / 10 ( 0%) |
| **AT** | 1 / 1 (100%) | 0 / 1 ( 0%) | 0 / 1 ( 0%) |
| **Overall** | 135 / 164 ( 82%) | 87 / 135 (64%) | 1 /135 (0.7%) |

\# Excluding subject 0915 with AT

* The number of intent-to-treat subjects who had one or more cryomapping attempts.

** The number of cryomapped intent-to-treat subjects who had one or more effective cryomaps

Cryomapping effect occurred in 164 of 812 (20%) cryomapping attempts in the 87 subjects with one or more effective cryomaps. Of 164 effective cryomaps, 102 were converted directly to cryoablation without intervening warming to assess reversibility. Of the remaining 62 effective cryomaps: 49 (80%) were immediately reversible upon warming, 9 (14%) reversed within 1 – 6 minutes after warming, and 4 (6%) were cryoablated within 4 – 21 minutes after an effective cryomap, without evidence of reversibility prior to cryoablation.

Subjects with effective cryomaps had a significantly higher acute procedural success rate overall when compared to subjects without an effective cryomap (94% v. 70%), but this trend was not significant in the AVNRT group (94% v. 89%).

## 11.0 CONCLUSIONS DRAWN FROM THE STUDIES

The pre-clinical testing demonstrates that the Freezor® Catheter will maintain its mechanical and electrical integrity and that the patient-contacting materials should be biocompatible under the proposed conditions of use. The animal testing established the performance of the device with regard to catheter maneuverability and ability to create focal lesions and supported initiation of human studies of the device.

Clinical evaluation of the Freezor® Catheter and Console System demonstrated that the device is reasonably safe and effective for the cryoablation of the conducting tissues of the heart in the treatment of patients with atrioventricular nodal reentrant tachycardia (AVNRT). Clinical evaluation of the device system demonstrated that the cryomapping feature is reasonably safe for its intended use, but was not demonstrated to be effective.

## 12.0 PANEL RECOMMENDATION

At an advisory meeting held on March 6, 2003, the Circulatory System Devices Advisory Panel recommended that Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System be approved, subject to submission of and approval by the Center for Devices and Radiological Health (CDRH) of a post-approval study. This post-approval study would evaluate the rate of AV block due to the device. The panel also recommended that the indication of cryomapping not be approved.

## 13.0 CDRH DECISION

CDRH evaluated the clinical study results, as documented in Section 10.0 above, in terms of both the overall patient population and individual study groups. As described above, the sponsor sought approval for one specific patient subgroup (AVNRT). Accordingly, CDRH primarily considered the effectiveness information for the AVNRT subgroup in order to characterize the effectiveness of the device for this patient population. CDRH considered the safety information for the overall patient population because safety issues for the overall patient population would be applicable to the AVNRT subgroup.

Acute procedural and long term clinical success for the AVNRT group (lower bound 95% confidence interval) was 82 and 85%, respectively. This compares to 85% and 80% for the lower bound of the OPCs established for the overall patient population. Procedural safety for the AVNRT group was 2.9%, as compared to the OPC of 7% for the overall patient population.

As described in Section 12.0 above, the Circulatory System Devices Advisory Panel recommended approval of the device system for the AVNRT subgroup, the indications for use proposed by the sponsor.

In consideration of the panel's recommendation and its own evaluation of study data, CDRH determined that the OPCs designated for the overall study population should not be used to

evaluate the safety and effectiveness of the device in the AVNRT subgroup. As a result, the device system for the proposed indication was evaluated on its merits, as CDRH qualitatively considered the device risk-benefit profile. Thus, based on this assessment and the recommendation from the CDRH advisory panel, CDRH determined that the sponsor demonstrated reasonable assurance of safety and effectiveness for the above device and indications.

CDRH determined that the cryomapping feature should be enabled for use in the approved device and that adequate instructions for its use should be included in device labeling. In addition, the labeling should include a warning to indicate that the effectiveness of the cryomapping feature has not been established. The applicant agreed to conduct a post approval study to collect safety data on unintentional heart block in AVNRT patients. The purpose of this study is to confirm the rate previously observed.

CDRH inspection determined the manufacturing facility to be in compliance with the device Quality System Regulation (Part 820). CDRH issued an approval order on April 17, 2003.

## 14.0 APPROVAL SPECIFICATIONS

- Direction for Use: See the labeling (Instructions for Use).
- 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.