U.S. FOOD AND DRUG ADMINISTRATION

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CIRCULATORY SYSTEM DEVICES ADVISORY PANEL

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MEETING

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FRIDAY,
NOVEMBER 30, 2007

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The meeting convened at 8:00 a.m. at the Gaithersburg Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, Maryland, Warren Laskey, M.D., Acting Panel Chairperson, presiding.

PANEL MEMBERS PRESENT:

WARREN K. LASKEY, M.D., Acting Panel Chairperson
RICHARD L. PAGE, M.D., Voting Member
JOHN C. SOMBERG, M.D., Voting Member
EUGENE H. BLACKSTONE, M.D., Consultant
MICHAEL J. DOMANSKI, M.D., Consultant
HENRY EDMUNDS, M.D., Consultant
NORMAN S. KATO, M.D., Consultant
PATRICIA A. KELLY, M.D., Consultant
JoANN LINDENFELD, M.D., Consultant
BARRIE MASSIE, M.D., Consultant
SHARON-LISE NORMAND, Ph.D., Consultant
CYNTHIA TRACY, M.D., Consultant
THOMAS VASSILIADES, Consultant
MARCIA S. YAROSS, Industry Representative
KAREN R. RUE, Consumer Representative

FDA PARTICIPANTS:

JAMES P. SWINK, Panel Executive Secretary

BRAM ZUCKERMAN, M.D., Director, Division of Cardiovascular Devices

CHUL AHN, Ph.D., Cardiovascular & Ophthalmic Device Branch, Division of Biostatistics, CDRH

ERIC CHEN, M.S., CDRH/ODE/DCD

ILEANA PIÑA, M.D., Case Western Reserve, Consultant to FDA

JULIE SWAIN, M.D.

DALE R. TAVRIS, M.D., M.P.H., Epidemiology Branch, Division of Postmarket Surveillance, Office of Surveillance and Biometrics

SPONSOR PRESENTERS:

LAURA DAMME, R.N., M.P.H., Senior Director, Clinical Affairs, Thoratec Corporation

GERALD J. HEATLEY, M.S., Senior Manager, Clinical Data Systems, Thoratec Corporation

DONALD A. MIDDLEBROOK, Vice President, Corporate Regulatory Affairs and Quality Assurance, Thoratec Corporation

LESLIE W. MILLER, M.D., Washington Hospital Center and Georgetown University Hospital

FRANCIS D. PAGANI, M.D., Ph.D., Director, Heart Transplant Program, University of Michigan Hospital

RALPH PETRUCCI, Ed.D., Drexel University
STEVEN H. REICHENBACH, Ph.D., Senior Director, New Technology Development, Thoratec Corporation

STUART RUSSELL, M.D., Johns Hopkins Hospital

PUBLIC HEARING SPEAKERS:

SALINA GONZALES
ROGER-GUY FOLLY
JANNA KINTZLEY

DAVID C. NAFTEL, Ph.D., University of Alabama at Birmingham, on behalf of INTERMACS

ROBERTA C. BOGAEV, M.D., Texas Heart Institute at St. Luke's Episcopal Hospital

T A B L E O F C O N T E N T S

P R O C E E D I N G S

8:00 a.m.

Call to Order

CHAIRMAN LASKEY: Good morning. I'd like everyone to take their seats, please. Thank you. I'd like to call this meeting of the Circulatory System Device Panel to order.

My name is Warren Laskey, the Chairperson of this panel for today. I am the Chief of Cardiology at the University of New Mexico School of Medicine. If you've not already done so, please sign the attendance sheets that are on the tables by the doors.

If you wish to address the panel during the one of the open sessions, please provide your name to Ms. Andry Williams at the registration table.

If you're presenting in any of the open public sessions today, and have not previously provided an electronic copy of your presentation to FDA, please arrange to do so with Ms. Williams.

I note for the record that the voting members present constitute a quorum as required by 21 C.F.R. Part 14. I would also like to add that the panel participating in the meeting today has received training in FDA device law and regulations.

I'd like to remind all to please put the cell phones or beepers on silence as a courtesy. Mr. Swink, our Executive Secretary for the Circulatory System Device Panel, will make some introductory remarks.

Conflict of Interest/Deputization

MR. SWINK: The Food and Drug Administration is convening today's meeting of the Circulatory System Devices Panel of the Medical Devices Advisory Committee, under the authority of the Federal Advisory Committee Act of 1972.

With the exception of the industry representative, all members and consultants of the panel are special government employees, or regular federal employees from other agencies,

and are subject to federal conflict of interest laws and regulations.

The following information on the status of this panel's compliance with federal ethics and conflict of interest laws are covered by, but not limited to, those found at 18 U.S.C. Section 208, and Section 712 of the Federal Food, Drug and Cosmetic Acts, are being provided to participants in today's meeting and to the public.

FDA has determined that members and consultants of this panel are in compliance with federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special government employees who have potential financial conflicts, when it is determined that the agency's need for a particular individual's service outweighs his or her potential financial conflict of interest.

Under Section 712 of the FT&C Act, Congress has authorized FDA waivers to special

government employees, or regular government employees with potential financial conflicts when necessary, to afford the committee essential expertise.

Related to the discussions of today's meetings, members and consultants of this panel who are special government employees have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their spouses or minor children, and for purposes of 18 U.S.C. Section 208, their employers.

These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties and primary employment.

Today's agenda involves the discussion of a pre-market approval application for the Heartmate II Left Ventricular Assistance System, sponsored by a

Thoratec Corporation. This system is intended for use as a bridge to transplantation and cardiac transplant candidates at risk of imminent death from non-reversible left ventricular failure.

The device is intended for use both inside and outside the hospital. This is a particular matters meeting, during which specific matters related to this PMA will be discussed.

Based on the agenda for today's meeting, and all financial interests reported by the panel's members and consultants, no conflicts of interest waivers have been issued in accordance with 18 U.S.C. Section 208 and 712 of the FT&C Act.

A copy of this statement will be available for review at the registration table during this meeting, and will be included as part of the official transcripts.

Marsha S. Yaross, Ph.D., is serving as the industry representative, acting on

behalf of all related industry, and is employed by Biosense Webster, Incorporated, a Johnson and Johnson company.

We would like to remind members and consultants that if the discussion involved any other products or a firm that's not already on the agenda, for which the FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and their exclusion will be noted for the record.

FDA encourages all other participants to advise the panel of any financial relationships that they have with any firms at issue. Thank you.

I will now read the appointment to temporary voting status for the panel.

Pursuant to the authority granted under the Medical Devices Advisory Committee charter of the Center for Devices and Radiological Health, dated October 27th, 1990, and as amended August 18th, 2006, I appoint the

following individuals as voting members of the Circulatory System devices panel for the duration of this meeting on November 30th, 2007.

Joann Lindenfeld, Michael J. Domanski, Eugene H. Blackstone, Henry Edmunds, Norman Kato, Thomas Vassiliades, Sharon-Lise Normand, Patricia Kelly and Cynthia Tracy.

For the record, these individuals are special government employees and are consultants to this panel under the Medical Devices Advisory Committee. They have undergone the customary conflict of interest review and have reviewed the material to be considered at this meeting.

In addition, I appoint Warren K. Laskey, M.D., to act as temporary chairperson for the duration of this meeting. This was signed by Daniel G. Schultz, M.D., Director, Center for Devices of Radiological Health, and dated November 16th, 2007.

I will now read the appointment to

temporary voting status for Dr. Massie. Pursuant to the authority granted under the Medical Devices Advisory Committee charter of the Center for Devices and Radiological Health, dated October 27th, 1990 and as amended August 18th, 2006, I appointed Barrie M. Massie, M.D., as a temporary voting member of the Circulatory System Devices Panel for the duration of this meeting on November 30th, 2007.

For the record, Dr. Massie serves as a consultant to the Cardiovascular and Renal Drugs Advisory Committee of the Center for Drug Evaluation and Research. He's a special government employee who has undergone the customary conflict of interest review, and has reviewed the materials to be considered at this meeting.

This was signed by Randall Lutter, Ph.D., Deputy Commissioner for the Policy, dated November 22nd, 2007. Before I turn the meeting back over to Dr. Laskey, just a few

general announcements.

Transcripts of today's meeting will be available from Neal Gross and Company. Information on this at the front desk. Information on purchasing videos of today's meeting can be found at the table outside the meeting room.

Presenters to the panel who have not already done so should provide FDA with a hard copy of the remarks, including overheads. I would like to remind everyone that members of the public and the press are not permitted around the panel area, beyond the speaker's podium.

The press contact for these meetings are Karen Riley. She's standing over here, and I request that reporters wait to speak with FDA officials until after the panel meeting. Thank you.

Panel Introductions

CHAIRMAN LASKEY: Good morning, again. At this meeting, the panel will be

making a recommendation to the Food and Drug Administration on the pre-market application, PMA P060040, Thoratec Heartmate II Left Ventricular Assist System.

The Heartmate II Left Ventricular Assist System is intended for use as a bridge to transplantation and cardiac transplant candidates at risk of imminent death from non-reversible left ventricular failure.

The Heartmate II LVAS is intended for use both inside and outside the hospital. Before we begin, I'd like to ask our panel members who are generously giving their time today, and other FDA staff seated at this table, to introduce themselves.

Please state your name, area of expertise, your position and affiliation, and we will begin with Dr. Zuckerman.

DR. ZUCKERMAN: Thank you. Bram Zuckerman, Director, FDA Division of Cardiovascular Devices. I'd also like to make a short comment for both the panel members and

the speakers today.

I was told by the AV people that for optimal recording, people need to remember to really speak into the microphone about six inches away. Apparently, we had problems with the recording yesterday.

DR. VASSILIADES: Tom Vassiliades, cardiovascular surgeon at Emory University School of Medicine in Atlanta.

DR. KELLY: Patricia Kelly, cardiac electrophysiologist, in practice in Missoula, Montana.

DR. MASSIE: Barrie Massie, University of California at San Francisco at San Francisco VA, heart failure cardiologist in my clinical work.

DR. KATO: Norman Kato, cardiothoracic surgery in private practice, Los Angeles, California.

DR. NORMAND: Sharon-Lise Normand. I'm a professor of Health Care Policy and Biostatistics in the Harvard Medical School

and the Harvard School of Public Health in Boston.

DR. SOMBERG: John Somberg, professor of Medicine and Pharmacology, Rush University, Chicago.

DR. EDMUNDS: I'm Hank Edmunds, cardiothoracic surgeon is my major and a minor in Hematology. I'm at the University of Pennsylvania.

MR. SWINK: James Swink, Executive Secretary for the Circulatory Systems Devices Panel.

DR. PAGE: Richard Page. I'm a cardiologist and an electrophysiologist. I'm head of Cardiology at the University of Washington in Seattle.

DR. BLACKSTONE: Eugene Blackstone, head, Clinical Research, Department of Thoracic Cardiovascular Surgery, Cleveland Clinic.

DR. LINDENFELD: JoAnn Lindenfeld. I specialize in heart failure and

transplantation at the University of Colorado at Denver.

DR. DOMANSKI: Mike Domanski. I am an interventional cardiologist and Chief of the Ethrothrombosis and Coronary Artery Disease Branch at the National Heart, Lung and Blood Institute.

DR. TRACY: Cindy Tracy. I'm the Associate Director of the Division of Cardiology and the Director of Cardiac Services at George Washington University, and I'm an electrophysiologist.

DR. YAROSS: Marcia Yaross, Vice president, Clinical Quality, Regulatory and Health Policy at Biosense Webster in Diamondback, California and industry representative to the panel.

MS. RUE: Karen Rue with Griswold Special Care from Lafayette, Louisiana. I'm a consumer representative.

CHAIRMAN LASKEY: Thank you all, and congratulations, we're still on time. So

I'd like to make that one of the prevailing themes of the day.

We will proceed with the open public hearing portion of our meeting. Both the Food and Drug Administration and the public believe in a transparent process for information-gathering and decision-making.

To ensure such transparency at the open public hearing session of the Advisory Committee meeting, FDA believes it is important to understand the context of any individual's presentation.

For this reason, FDA encourages you at the open public hearing or industry speaker at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with the sponsor, its product and if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging or other expenses in

connection with your attendance at the meeting.

Likewise, FDA encourages you at the beginning of your statement to advise the committee if you do not have any such financial relationships.

If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

Currently, there are three scheduled speakers for the morning session: Salina Gonzales, Roger-Guy Folly and Janna Kintzley, and if we can have the first step forward.

1st Public Hearing - Testimony

MS. GONZALES: Hello. My name is Salina Gonzales. I have no financial interest in Thoratec. They are reimbursing me for the cost of travel to this meeting.

I am a second grade teacher from San Antonio, Texas. I am here to share my

testimony on given a second chance to live because of the Heartmate II. In July of 2006, I went from a healthy mother and teacher to a person diagnosed with congestive heart failure.

Heart failure does not run in my family, and it is unknown how I went into this state of condition so quickly. I was told that my heart was very enlarged, and my heart muscle was extremely weak. Everything that was stated coincided with how I felt.

I could not walk up a short flight of stairs without becoming severely short of breath. I could not carry my 18 month-old son at the time in or out of the car without being completely weak or need to gasp for air.

I had so much pain in my abdomen that I could barely eat or sleep. After hearing the worst, that my heart was in its final stages and I was dying, I was introduced to one more opportunity that would help me survive. It was the Heartmate II.

This was my only hope of life, that would give me one more chance to watch my only child grow up with a mother. In October 2006, the pump was successfully implanted in my heart. I recovered day by day, and after a month I was discharged from the hospital.

My second month after the surgery, I was able to walk on the treadmill from five minutes a day to 30 minutes a day. On my third month, I was able to increase my time to an hour at an incline. Six months later, I was able to return to the profession I love, which is teaching.

To this day, I've had my pump for a year and two months. It is an honor to be here and personally thank each and every one of you who was part of the decision of allowing a clinical trial, because I would not be here today if it wasn't for you.

I am forever grateful for allowing an LVAS to be implanted in me. You have let me celebrate life, teaching and raising a

child. Thank you for giving me the joy of letting me watch my son turn three years old this past week, and thank you for letting me give him the love from a mother.

If I was near death and now I am here alive and well because of the technology, sophistication and invention of this pump, I think anyone else deserves this hope that can restore their lives completely. Thank you.

CHAIRMAN LASKEY: Thank you.

MR. FOLLY: Good morning. My name is Roger-Guy Folly. I have no financial interest in this corporation. They are reimbursing me for my trip to this conference today.

My history is a history of sickness. I have a very large heart for more than 20 years. I had a pacemaker and a defibrillator implanted for many years, and I think that since last year, those devices have been passe. My heart was becoming weaker and weaker.

I could not walk. I could not speak longer, and I was coughing all the time. I was almost known at the ambulance, by the ambulance staff people who were taking me always to the emergency room almost every week.

When I go to the emergency room, I will have some Lasix, some oxygen and maybe stay in the hospital for two or three days, and come back home I will be okay.

Three days later, I may be going again back to the emergency room at the Washington Hospital Center. Until my cardiologist, Dr. Watkins, suggested to me to go see Dr. Miller and his team about this LVAS. I went. They explained to me what it meant, and questions asked and answered.

After I decided to go ahead with the implant. I was confident that this would save my life, this would save my energy. When I was in the hospital, I was implanted with the device in June of this year, and I spent

two months in the hospital.

I came home and first of all, I was afraid that I couldn't walk upstairs. I did. I was surprised that I walked upstairs without any trouble, without getting out of breath.

Following the advices that I was given by the hospital staff, I started walking every day. Every day I walk for about five miles and come back home when the weather permits.

But generally, I don't have any of these same times of getting out of breath as I used to. LVAS is a good device. It's a device which gives you a break waiting for maybe a heart transplant.

Even though it is a little bit bulky, it is saving a lot of lives, including mine. I have to thank all the people that participated in developing the concept, the doctors, the nurses and all the people that contributed in putting together the device.

I hope that it will become known in the public, because right now I don't think it's very well known. It will become known in the public, so a lot of people can know that they have, when they have an enlarged heart and they have this situation of heart problem, they know they can go to this device and have some time to leave before they get a heart to be implanted in them.

I thank you very much for your attention.

CHAIRMAN LASKEY: Thank you.

MS. KINTZLEY: Good morning. I want to thank you for the opportunity to share my story with you today. As a matter of full disclosure, I have no financial interests in Thoratec, other than their reimbursement of the costs of travel to this meeting.

I believe I am uniquely talk about living with the Heartmate II, since I am on my second Heartmate II pump, and have participated in two separate hospitals'

program. Let me explain.

Two years ago, I was a completely healthy 35 year-old wife and mother of three small girls. I had recently had a physical and everything was normal.

On February 19th of 2006 while returning home from the store from our house in Oak Harbor, Washington state, I began experiencing extreme shortness of breath and tightness in my chest and hands.

I arrived home to fall unconscious in my husband's arms. I came to and was taken by ambulance to Whidbey Island Naval Hospital. After three hours of observation, I was told I had suffered a panic attack and was sent home with Valium.

Three days later, it all happened again, this time with jaw pain. Fortunately, the friend who was with me had been a cardiac nurse and recognized the symptoms. Upon arriving at the Naval Hospital, it was determined immediately that my heart was

failing, and the call was made to life-flight me to Bellingham, Washington.

I went directly to the cath lab, where a balloon pump was implanted, which stabilized me temporarily. After two days in ICU with no progress being made, the cardiologist there had the foresight to realize that I needed to be transported to a hospital with FAD and transplant capabilities.

That afternoon, I was life-flighted across the state of Washington to Sacred Heart Medical Center in Spokane, into the care of Drs. Timothy Icenogle and David Sandler.

After three days in ICU, my organs were showing signs of failure. So the decision was made to operate and implant a ventricular assist device.

Due to my smaller body frame, the Heartmate XVE was not an option. My only hope was with the Heartmate II. My family moved from Oak Harbor to Spokane while I recovered. I spent 12 days in ICU, then several weeks in

the hospital.

Following the surgery, there was some hope that my heart would recover on its own. Nearly three months after the initial surgery, an evaluation was done and it was decided that my ejection fraction was estimated at 40 percent.

The decision was made to ex-plant the pump. It was evident within hours after surgery that my native heart was insufficient and struggling. Two days later, I went back in and a second Heartmate II was implanted.

I remained in ICU another nine days and repeated the process of recovery. Because there was no naval base in Spokane to which my husband could transfer, the Navy allowed us to transfer to Annapolis, Maryland, where Keith, my husband, could teach at the Naval Academy, and I could continue under the care of Johns Hopkins Hospital.

Despite having endured all of this, most days I still find it hard to believe it

ever happened. Today, I feel fantastic. I am again the mother and wife I once was. I simply am one who needs to change batteries every few hours.

I am strong and happy, and my quality of life is phenomenal. I volunteer in my daughter's school and take part in several church groups. I even hope to go back to teaching high school in several years, which was always my original plan once the girls were all older.

This past summer, we bought a house and I've helped paint more rooms than I care to mention. The medical demands of this pump are minimal, and I have monthly clinic visits and echocardiograms at the hospital, and an INR check every other week.

In addition to the high quality of life the Heartmate II has afforded me, I am extremely thankful for the Heartmate II, because being O positive with a PRA of well above 80 percent, I fully expect to wait a

long time for a compatible heart.

It is extremely comforting that this pump is capable of sustaining me until that time. The most important thing this pump is doing is giving me time with my husband and three daughters.

It is humbling to think that if this had all occurred five years ago, the life I am living today would not be possible. Thank you.

CHAIRMAN LASKEY: Thank you. We will now proceed to the sponsor presentation for the Heartmate II LVAS.

I would like to remind public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific request of the panel.

We will now begin with the sponsor presentation.

Sponsor Presentation

MR. MIDDLEBROOK: Good morning. My

name is Donald A. Middlebrook. I am the Vice President of Corporate Regulatory Affairs and Quality Assurance, and a full-time employee of Thoratec Corporation, the sponsor of the PMA we will be reviewing this morning.

Before we begin our formal presentation, I would just like to take this opportunity to thank all of the FDA Advisory Panel members and FDA reviewers for the hard work and time invested in preparing for today's meeting.

I'd also like to give thanks to all of the Thoratec presenters and experts here with me this morning, and to all of the Thoratec employees who have worked very hard for the past decade to bring this life-saving technology to this important point in time.

This is an outline of the presentation we will be making to you this morning.

After I conclude brief opening remarks, we will provide you with some

information about the device, the technology behind it and the mechanisms of action. We will then move into the study, the clinical trial itself for the Heartmate II, and we'll provide you with information on the study design, the clinical management of the trial while it was underway, and the statistical considerations that we baked into the trial design.

From there, we will move into the summary of the outcome data, the patient population, the clinical outcomes, device safety, the secondary inputs of quality of life, functional status, neurocognitive assessment, and we will end with a few brief closing remarks.

These are the Heartmate II presenters. In addition to myself, Steve Reichenbach, Laura Damme and Gerry Heatley from Thoratec Corporation will provide information on the device, the trial design and the statistics that were considered in the

trial.

Dr. Leslie Miller from Washington Hospital Center and George Washington University Hospital, and Dr. Frank Pagani from the University of Michigan Hospital, will provide the bulk of the clinical outcome data.

We also brought along a number of experts here this morning. This is the list of those experts. Dr. Bill Holman from the University of the Alabama, who is a member of the Data Safety Monitoring Board.

Dr. Ralph Petrucci from Drexel University, who is a neurocognitive expert, also served as a core lab for us during the clinical trial.

Dr. Val Jeevanandam from the University of Chicago was a member of the Clinical Events Committee. We have Vic Poirier here with us from Thoratec, who can answer any questions that may come up on the Heartmate II or the ex-plant analysis we conducted.

Dr. Stuart Russell from Johns Hopkins Hospital, who is a Heartmate II investigator; Susan Wright from the University of Michigan, who is a VAD coordinator; and finally Dr. David Naftel from the University of Alabama, who is here to help us with questions you may have regarding the post-market study, or the INTERMACS registry which we will be using to collect that data.

A little bit about Thoratec. The company was founded in 1976. We merged with Thermocardiosystems in February 2001 to form what is now known as Thoratec Corporation.

Our primary product focus is cardiac assist devices. We have 1,200 employees worldwide. We are the world's leader in the cardiac assist device arena. We have four PMA-approved VADS.

We have conducted six clinical trials for ventricular assist devices, and we have over 12,000 VADS implanted in patients, including over a 1,000 Heartmate II's,

considering both our European commercial experience and patients enrolled in the clinical trial here in the United States.

This is a slide of the clinical regulatory chronology for the Heartmate II. There's a lot of information here, but there's a few key points I want to make.

In February of 2005, the Heartmate II pivotal study was approved by the FDA and the study began. In May of 2006, just a short 15 months after we initiated the study, the pivotal study enrollment was complete with 133 patients enrolled.

This pace of enrollment for this device is a record for our company, and I believe it to be a record pace of enrollment for this technology and the history of this technology.

We followed those 133 patients, until we had at least six months of follow-up on those patients. We conducted an analysis and we rolled that up into an original PMA,

which we submitted in December of 2006 to the FDA.

In April of 2007, FDA issued a deficiency letter to us, and we met with them face to face to review that letter on May 1st, 2007, our Day 100 review meeting. From that meeting, we agreed to some re-analysis, which we did complete, and we submitted that back to the FDA in July 2007.

I think it's also important to point out that between May of 2006 and September of 2007, there have been four continuous access approvals, for a total of an additional 280 patients.

I think both the fact that we have 280 additional CAP patients and the pace of enrollment, speaks to the clinical acceptance of this device, by both the users and their patients.

I also should point out that in November of 2005, the device received authorization for a C marking. It allowed us

to market the device in Europe, and there have been over 300 implants since that time in Europe.

I'd like to now turn the podium over to Steven Reichenbach, who will provide a device overview.

DR. REICHENBACH: I'm Steve Reichenbach. I'm the Senior Director of New Technology Development at Thoratec. I'm also a full-time employee at Thoratec.

The Heartmate II represents really the next step in the advancement of Thoratec's ventricular assist device systems. All of our devices, or all of our approved devices, certainly provide an effective means of circulatory support.

The earlier devices, shown on the left-hand panel, tied the patient to a fairly large console. This resulted in the patient being tethered and having very limited mobility. They also kept the patients in the hospital.

With the development of portable pneumatic drivers, the patients were able to be more mobile. They're also able to be discharged home. However, they still are required to bring that driver with them.

The next step for us was really our wearable electric system, such as the Heartmate XVE. These devices allowed the patient much more mobility and a return to a fairly normal lifestyle.

This device has been clinically very well-accepted, and generally used for many bridge to transplant patients, and many consider it a standard of care for that indication. In addition, there's been over 4,000 implants worldwide with that device.

The one thing about the XVE is that it's a fairly large electromechanical device that has to be implanted. The Heartmate II represents the next step for the technology.

This provides a much smaller pump, applicable for a broad range of patients,

while still providing the support needed and also was designed for long-term durability.

The Heartmate II system consists of an implanted blood pump that pumps blood in parallel with the natural left ventricle, taking blood from the LVA packs and returning it to the ascending aorta. A percutaneous lead, connected from the pump, exits the skin and connects to an externally-worn electronic controller.

This controller provides information for the patient, as well as controlling the pump. The system itself is powered by external batteries.

The key attributes of the Heartmate II system really is its mechanism of pumping the blood. The pulsatile pumps, the XVE system, employs a fairly advanced orthomechanical actuator and a pusher plate to propel the blood.

It also has inflow and outflow valves that are used to maintain a

unidirectional flow through the pump.

In contrast, the Heartmate II utilizes a continuous flow rotary pump. This utilizes a single rotating part to propel the blood through the system. This pump does not require valves because of that.

The design of this rotary pump is that of an axial flow device. It has the single rotating component. This component is supported on each end by blood-washed bearings. These bearings are hydrodynamic, and that leads to very long-term durability.

The resultant pump design is very small. Its displaced volume is 64 milliliters. It's much small than the pulsatile XVE pump, being approximately one-seventh the size and one quarter of the weight of that device. It's also designed to fit in a wide range of patients.

Not having valves lends to its potential for long term durability. In addition, the operation is extremely quiet and

virtually silent to people standing near the patient or the patients themselves.

In addition, because this pump does not have a blood pumping chamber, there's no need for venting and the percutaneous lead was made substantially smaller. The Heartmate II lead is 40 percent smaller than the existing XVE lead.

While the size difference between these pumps is quite obvious, there are a number of similarities. First of all, the flow capacity of the pumps are the same. Both provide up to ten liters of flow for the patient.

The outflow conduits are also similar, in that they're both constructed from woven polyester graphs and anastomosis to the ascending aorta. The inflow cannula are also similar.

They both employ a textured titanium inlet, that's held to the LV with the identical sewing ring for both devices, and

they both use a flexible section on the cannula to allow for anatomic positioning as well as for any anatomical motion or movement.

The device can be powered in two different configurations. One is battery power. This is the typical configuration, where the patients carry batteries with them and they can go about their daily activities.

The other configuration is a tethered operation. This is typically used for night time, where power, AC power can be obtained from a wall outlet.

Now the controller and the pump of the Heartmate II are unique to that system. However, the other power handling components, these external components, are shared with the XVE.

So being shared with the XVE, there's been a substantial history with these components, and they've been out clinically for a number of years.

It goes beyond the power handling

components, but certainly includes the battery and battery charging systems, backup power supplies, monitors and displays that are used for programming as well as obtaining information from the system.

There are a number of soft accessories that the patients use and wear, to carry the external components of the system.

As with any new device, much has been learned during the clinical trial. We've used this experience to make improvements to the device. The inflow cannula on the pump has been made more robust from this experience. Also, we have made changes to the sterile packaging, to facilitate handling in the operating room.

We've also made a number of changes to the controller and a number of improvements. The bulk clip on this controller has been made more robust.

There's been a number of software upgrades to provide additional features and

functionality. In addition, the percutaneous connector has been improved, and the perc lead itself has been made more robust.

In terms of pump reliability, the core of the system has been very good, and the experience has been good between bench testing and the clinical experience.

On the bench, we've had 15 pumps running for more than 37 years' cumulative time, with the longest pump running nearly five years. There's been no failures with that experience.

The clinical trial has been similar, in that there's been no failures. In the pivotal trial, with 126 patients, we've had over 61 cumulative patient years of support at this point, and there's been no failures with that experience.

The longest implanted patient in the pivotal trial has been 1.8 years. It should be noted, though, that we do have two patients in the pilot trial that are now out

over three years of support. Now I'd like to hand it over to Laura Damme, who will give an overview of the clinical study.

MS. DAMME: I'm Laura Damme, Senior Director of Clinical Affairs, and I'm an employee of Thoratec. I'll be providing you an overview of the study and its management.

The study was designed to evaluate the safety and effectiveness of the Heartmate II as a bridge to cardiac transplantation in patients in end stage heart failure who had imminent risk of death.

The study was designed as a prospective, single arm non-randomized study that required 133 patients. The primary study end point was survival to transplantation or 180 days of LVAD support while remaining listed at Status 1A or 1B.

This success rate was compared to an objective performance criteria, or OPC, that was based on Thoratec's bridge data. Gerry Heatley will be providing further

information on the OPC in his presentation.

A number of secondary end points were also collected in the study, as pre-specified in the study protocol.

These included adverse events, functional status, as measured by NYHA, six minute walk and activity score, quality of life as measured by the Minnesota Living with Heart Failure questionnaire and the Kansas City Cardiomyopathy questionnaire.

Clinical reliability, as evidenced by malfunctions and failures; reoperations; neurocognitive evaluations that were performed at a subset of sites; 30-day and one year post-transplant survival.

A total of 279 patients were enrolled in the study between March 2005 and March of 2007. In addition to the 133 patients that were required in the study protocol, 146 patients were enrolled under a continued access protocol or CAP.

The patients enrolled under CAP

were followed under the same identical protocol as the study patients. During our 100-day meeting with the FDA, FDA had requested that the small BSA patients be analyzed separately, therefore leaving 126 patients in the primary study cohort.

The small BSA patients from the original cohort were combined with the small BSA patients from the CAP cohort, giving us a total of 15 small BSA patients, and leaving 138 patients in the CAP cohort.

Not all of these patients have been followed to the study's specified end point of outcome, or are being followed for 180 days. 58 of the CAP patients have been followed for 180 days.

Ten of the small BSA patients have been followed for 180 days, and all of the 126 primary study cohort patients have been followed for 180 days.

In the presentation today, you will see data presented on various cohorts.

Baseline information will be presented on the entire population. The 126 primary study cohort patients; the 15 small BSA patients, and the 138 CAP patients.

The primary and secondary end points will be presented on these patients that have reached study end point. These patients also represent the first 194 consecutive patients that have been enrolled in the bridge study, and Thoratec proposes to use these patients as our labeling cohort.

The labeling cohort will also be presented in today's presentation.

The 279 patients were enrolled at 33 U.S. sites. These sites are a representative sample of our values or community. There are 279 patients are presented here. This is enrollment per site and you will see this on the next two slides.

As I indicated, this is enrollment per site per cohort. Almost 60 percent of the sites enrolled more than five patients. There

were five sites that were high enrollers that enrolled 15 patients are more; 42 percent of the sites enrolled from six to 14 patients, and 42 percent of the sites enrolled five or less patients.

Regarding study management, as sites were evaluated and assessed to become one of the Heartmate II study sites, they were assessed for their qualifications.

The elements that we assessed included a site's experience with the Heartmate XVE; there's a site's resources for data collection; and also a site's data management capabilities.

Once a site was identified as a Heartmate II site, the staff underwent surgical and protocol training. All data and site management was performed by Thoratec.

As indicated in the protocol, there were two independent oversight committees. These included a Clinical Events Committee that adjudicated all the adverse events and

deaths. The committee members consisted of four physicians with varying specialties, and their names can be seen listed on the slide.

In addition, there was a Data Safety Monitoring Board that reviewed adjudicated study data, as well as study compliance and management every six months.

There were five DSMB members, four physicians and one statistician, and again their names are listed on the slide.

I will now turn the podium over to Gerry Heatley.

DR. HEATLEY: Thank you, Laura. My name is Gerry Heatley. I'm the senior manager of Clinical Data Systems, Thoratec Corporation.

I'm a full-time employee of Thoratec Corporation. I'm going to be speaking briefly about our study design and some statistical considerations.

As Laura has indicated, the Heartmate II study was a prospective single

arm study that compared the Heartmate II to objective performance criteria.

The study was designed to be an non-inferiority study, in that the Heartmate II would be considered a success if it performed as good or better than the OPC.

The null hypothesis for the trial was that the success rate of the Heartmate II is less than or equal to 65 percent, which represents the OPC success rate of 75 percent, with a non-inferiority margin of ten percent.

The alternate hypothesis is that the success rate of the Heartmate II is greater than 65 percent. 133 patients were needed to achieve a power of 80 percent, and the Heartmate II would be considered non-inferior to the OPC if the one-sided lower 95 percent confidence interval is greater than 65 percent.

The OPC was developed using historic Thoratec data on implantable VADS, and these included the Heartmate IP, the

Heartmate VE, and the Thoratec IVAD. For trial efficiency, Thoratec proposed a definition of success as survival to transplant or 180 days of support, as our experience has shown that the use of a more traditional end point of transplant rate alone has resulted in very long follow-up times.

We believe our data supports the use of 180 days as an acceptable performance standard for bridge patients. 70 percent of our historic patients reach outcome by 180 days post-implant, and 73 percent of the patients that are ongoing at 180 days are ultimately transplanted.

180 days of support also represents about twice the median support time for bridge patients.

Now this slide summarizes some of the data that was used in developing our OPC. The data sources include previous bridge to transplant clinical trials, as well as some data from our device tracking registries. A

portion of this data has been published in peer reviewed literature.

Over 2,000 patients who were implanted with an LVAD were evaluated, and these patients were implanted over about an eight year period.

Overall, 75 percent of the patients either were transplanted or had survived for 180 days, and this became our success rate in our proposed OPC.

It's important to point out that this success rate does not include the transplant listing status of the patient at 180 days. Neither our clinical trials nor our device-tracking registries collect information on the listing status of patients, either prior to implant or at 180 days. So that data was not available for us to evaluate.

The data does include, however, patients with body surface areas less than 1.5 meters square. Although the overall success rate is 75 percent, there is year to year

variation in this success rate, and this was the basis for our non-inferiority margin.

Finally, no Heartmate II patients who were studied in our feasibility trial or European bridge to transplant patients, were evaluated as we developed our OPC.

Now in proposing an end point that included a discrete time point, Thoratec understood that there may be patients who are ongoing and supported at 180 days, who are no longer medically eligible for transplant.

It was Thoratec's goal, and we believe the FDA's goal, to identify patients who are doing well at 180 days as successes, and exclude patients who are languishing on the device.

To that end, Thoratec proposed a study end point of 180 days of support, with no irreversible contraindication to transplant, or survival to transplant as its end point. This was our initially proposed end point in our first protocol.

FDA did not approve this end point. The FDA stated that they felt it was qualitative, would be difficult to interpret the data, and recommended that we amend the end point to 180 days of support, while remaining transplant listed status 1A or 1B.

Thoratec agreed to this, and the study's end point became survival to transplantation, or 180 days of LVAD support while remaining listed as Status 1A or 1B.

Now this end point allows patients who are transplanted after 180 days to be considered trial successes, regardless of their 180 day transplant listing. Also, patients who are explanted from the device due to myocardial recovery are considered study successes.

Now as we began to analyze the data in preparation for our PMA submission, it became apparent that this listing requirement for patients who are ongoing at 180 days was accurately identified for patients who are

doing poorly on a device's failures.

These included three patients with medical conditions their clinicians considered to be irreversible.

Now about six months later, FDA asked us to update our outcome data, and at that point, all three of these patients had expired on support.

There was also one patient who was extremely deconditioned. Their clinician felt that this patient was no longer medically eligible for transplant.

During our re-analysis of the data, this patient was still ongoing on support, but was removed from the transplant list.

The listing requirement also had an unanticipated, unexpected result of counting ten patients who are thriving on support at 180 days as failures. Four patients were not listed 1A or 1B, because they preferred to remain on VAD support rather than accept the cardiac transplant.

At the time of our re-analysis, two of the patients had a change of heart and were not transplanted. One patient was not status 1A or 1B while being evaluated for myocardial recovery. This patient was also transplanted in our follow-up analysis.

Two patients were not 1A-1B, while they experienced medical conditions their clinicians considered to be reversible. In our follow-up analysis, one of these patients was now transplanted. The other was ongoing and now listed 1B.

Finally, three patients were not listed 1A or 1B while they experienced compliance issues, which included some substance abuse problems.

In our follow-up analysis, one of these patients was now weaned with myocardial recovery. The other two are ongoing, not listed while they resolved their compliance problems.

Now please keep these patients in

mind. Referring to these four irreversible patients and ten reversible patients further in my talk, Dr. Pagani will be discussing them in his presentation.

We discussed these unanticipated effects with the FDA at our 100-day meeting, and at that time the FDA suggested that Thoratec could provide some adjunctive data to support our claim that the ten reversible patients were similar to patients that were listed 1A-1B, and therefore should not be considered study failures.

Thoratec provided the FDA some adjunctive analysis, which included these ongoing patients' quality of life and functional class status at six months, and also some follow-up survival data.

Our analysis indicates that these ongoing patients at 180 days basically fall into two general groups. Those patients that remain transplant-eligible, which include 15 patients that are ongoing, listed 1A-1B study

successes, and those ten patients I described that are not listed 1A or 1B due to reversible reasons, and a second group of patients who are now transplant-ineligible, due to irreversible medical conditions.

This graph kind of summarizes some of the adjunctive data we've provided to the FDA. In this graph, I'm comparing those four irreversible patients to the ten reversible patients.

When we look to see how many patients had been supported for least one year on VAD support, which is twice the end point specified in the study, all ten of the reversible patients had achieved at least a year of support, compared to only one of the irreversible patients.

In our follow-up outcome analysis that we provided to the FDA, nine of the ten reversible patients were either remaining ongoing on support, had been transplanted, or had been weaned off the device due to

myocardial recovery. Only one of the irreversible patients was still ongoing.

Eight of the ten reversible patients were able to achieve a six minute walk test at six months of 200 meters or greater. None of the irreversible patients could walk 200 meters at six months.

An independent assessor judged all ten of the reversible patients to be at New York Heart Association Class 1 or 2 at six months, versus only one of the irreversible patients.

Now obviously we're dealing with very small numbers of patients here. We can't draw any statistical conclusions. But it's interesting that the data does suggest that these patients are falling into two groups: one that is clearly benefitting on the device, and another that's languishing.

When we compare these patients to the ongoing patients who are listed 1A or 1B at 180 days, what we find is that the

reversible patients are very similar to the success patients, in terms of their NYHA status at 180 days, and also in the results of their six minute hall walk test at 180 days, in both groups very different from the patients who are languishing on the device.

When we look at quality of life at six months, the reversible patients are actually doing a little better than the patients who are successes, and much better than the patients who are irreversible.

This is the Minnesota Living With Heart Failure score. Lower scores mean better quality of life. The Kansas City Cardiomyopathy score, a higher score means greater quality of life.

Now again, we're dealing with very small numbers of patients. We can't do a statistical analysis that would produce any kind of meaningful results. But we do think that the data suggests that these reversible patients are more similar to patients who have

achieved study success, than patients who are languishing on the device.

Based on this adjunctive data, we've provided FDA with an alternate analysis of our end point, where we define success as 75 percent survival to transplant or 180 days of support, with no irreversible contraindications to transplant.

Now this is a post hoc analysis, but it also represents the initial OPC we proposed to the FDA. We believe this analysis is consistent with the historic data that we used in developing the OPC, which as you will recall, did not include a listing status.

We believe it is also consistent with the FDA literature-based performance goal, which also does not include listing status.

This definition accurately identifies patients who are languishing on the device as failures, and we believe it's more representative of the dynamic nature of

clinical practice, where we're seeing patients moving from Status 1 to Status 7 and back, based on the patient's medical-social conditions or preferences.

In the data we are about to present you, Thoratec will present the pre-specified analysis as described in the protocol.

But we will also present our alternate analysis and some actuarial analysis that you can use as additional data when you consider if this device is effectively supporting patients to transplant.

I'll now turn the podium over to Dr. Miller, who will describe our patient population.

DR. MILLER: Good morning. I'm Dr. Leslie Miller. I'm the chief of Cardiology at the Washington Hospital Center and Georgetown University. I was a principal investigator in this trial, but I have not in the past nor do I currently have stock or financial interest in Thoratec.

This beginning of the data will be to review the patients enrolled in this trial. I'd like to overview the slides, as you'll see it in this format through most of the rest of the data presentation.

I'll be presenting to you the data on the entire 279 patients who are enrolled as of March of this year.

They include the primary cohort in the pivotal trial, the extension of access to using this device while the data was being reviewed, the continuous access protocol, 138 patients, and those small patients as detailed by Laura Damme, who were pre-specified with a body surface area of less than 1.5 meters squared.

These patients represent a very typical population of those being listed for heart transplantation and undergoing heart transplantation today. That's based on a comparison of the UNOS ISHLT database registry, which shows that the average age

today in 2006 was 53 to 54 years of age, very similar between the primary and CAP cohort, slightly younger in the small patient cohort.

The etiology interest over the last five years has declined, such that in 2006, only 39 percent of patients had an ischemic etiology, very consistent between the primary and CAP cohort; slightly lower in the small patient cohort.

The gender for the last 30 years has been 80 percent male, 20 percent female undergoing heart transplantation. They're reflective of the groups in the primary and CAP cohort.

But importantly, in the small patient cohort, 13 of 15 of those subjects were females, which reflects the increased access to this technology with the new smaller pumps.

The size of the patients is described here as median in range, and you can see nearly identical between the two primary

and CAP cohorts, both in body mass index and estimated body surface area. They are by definition significantly lower in the small patient cohort.

This data again, by median and range, is shown in graphic form here, and I think you can see the similarities and the ranges between the ages in the three cohorts described, but quite a difference in the body mass index, total body weight and body surface area.

I draw your attention to the range of weight that was observed in this trial, and this pump was able to effectively support patients as low as 40 kilograms, and as high as nearly 140 kilograms. So nearly all patients can be equally accommodated by this pump.

The baseline and the dynamics in this cohort describe a very ill population. This is an average ejection fraction of 16 percent, nearly identical across all three

cohorts, but reminds you that by definition these are all UNOS Status 1A patients, and therefore inotrope-dependent.

Twenty-five percent of the patients in the primary cohort were all more than one inotrope at the time, and 40 percent of the patients were on intra-aortic balloon pump. So a very ill, advanced heart failure population.

You see the dynamics are obtained while they were on this intravenous drug support, and shows a very significant reduction in cardiac index, elevation in filling pressures on the left and right side, with pulmonary capillary wedge pressures as shown, and central venous pressure reflecting right ventricle filling.

The systolic blood pressure was reduced in all three cohorts, but the observation is that the data is consistent across all three cohorts presented.

There are a number of baseline

biochemistries. What we've chosen to show you here is renal and hepatic function. The average creatinine is as shown here, and reflects mild to moderate renal insufficiency, perhaps even moreso, even though the value is slightly lower in the small cohort, but given their small body size reflects an even lower renal function and pre-renal azotemia.

Similarly, mild to moderate increase in serum bilirubin and transaminases, most particularly elevated in the small cohort.

One of the surrogate markers of poor prognosis and advanced heart failure is serum sodium, and you see here levels of significant reduction serum sodium, and particularly in the small patient cohort, again verifying the severity of illness across all three cohorts.

This data is again shown as medians and range, and I think you get a sense of the tremendous variability and the severity of

illness in these patients, with creatinines up to over three, significant elevations in these other parameters. There's a lower spread in the serum sodium.

The cardiovascular history is also reflective of patients with advanced heart failure, and particularly the common finding of arrhythmia as both atrial and ventricular. In this particular group of patients, ventricular arrhythmia has occurred in nearly half of the patients.

Ventricular pacing was also present in a majority of the patients, and nearly half of these patients had failed biventricular pacing and required mechanical support.

Typical of patients with advanced heart failure, nearly three-quarters of the patients had an internal defibrillator in place at the time of the operation. It is of note that there was a relatively high percentage of pre-existing experience with stroke that occurred in these patients, fairly

similar across all three cohorts, reflective of the common finding of atrial fibrillation, poor ventricular function, apical clots and so forth.

So in summary, this is very sick population, that's consistent with end stage heart failure and listing for transplantation and not different because of their need for mechanical support. These data are very consistent across all three cohorts, in terms of clinical variables, laboratory and hemodynamic findings.

I'll turn the microphone over to Dr. Pagani, who will present the outcome data.

DR. PAGANI: My name is Frank Pagani. I'm a cardiac surgeon and Director of the Heart Transplant Program and Center for Circulatory Support at the University of Michigan. I have no past or present financial interest in Thoratec.

I will review with you the surgical considerations for the trial and anti-

coagulation management. The primary end point analysis, secondary end point analysis and the proposed label cohort.

The surgical implant technique for the Heartmate II pump is the same implant technique as the Heartmate XVE, which represents the current standard of care.

The surgical implantation for the Heartmate II pump allows a shorter cardiopulmonary bypass time as compared to the Heartmate XVE pump.

The pump is a smaller size and therefore the preperitoneal pocket required for pump implantation is smaller, as well as the easier process to prime and de-air the pump.

No unique surgical challenges have been identified in small body size patients, and importantly, 30-day mortality for the Heartmate II trial was observed to be one-half that for the Heartmate VE trial, and we'll review more of that data later.

A recommended anti-coagulation protocol was developed for the trial and consisted of early intravenous heparin anti-coagulation, followed by initiation of anti-platelet therapy on post-operative Day 2 to 3.

Intravenous heparin anti-coagulation was converted to oral warfarin therapy on post-operative Day 3 to 5, following removal of thoracostomy tubes.

Patients who have a contraindication or do not tolerate anti-coagulation therapy should not undergo implantation of the Heartmate II, and this should be included in the labeling.

Our review of the primary end point analysis. Treatment success, as you recall, was for the pre-specified end point analysis, was defined as survival to transplant, or survival at 180 days of LVAD support while remaining listed for heart transplantation at UNOS Status 1A or 1B.

Using the pre-specified analysis,

67 percent of patients were defined as treatment successes, with a lower confidence limit of 60 percent, on an analysis that was performed as of March 16th, 2007.

For the CAP cohort with 58 patients with end points, 66 percent of patients were defined as treatment successes, with a lower confidence limit of 55 percent. For the patients in the small body size cohort, 70 percent of patients were defined as a treatment success, with a lower confidence limit of 46 percent.

As requested by the FDA, a further data analysis, a more recent data analysis was performed on September 14th, 2007. At that time period, there was increase in the number of successful end points, number of successful patients of 71 percent, with a lower confidence limit of 64 percent.

This was due to five patients in the primary cohort, who were previously considered not successful outcomes because

they were not actively listed at Status 1A or 1B, who subsequently underwent heart transplantation and were defined as successful outcomes in the primary cohort with the updated analysis, thus reducing the number of patients that were termed not successful outcomes, who were listed at 180 days or not listed at 1A or 1B.

A Kaplan-Meier survival analysis was performed for the Heartmate II primary cohort, as displayed in the blue. This survival analysis was compared to 280 patients supported by the Heartmate VE device, which represents the standard of care.

These 280 patients also represent the final labeling cohort for the PMA submission for the Heartmate VE device. Importantly, these data demonstrate an equivalent or trend towards improved survival for the Heartmate II device, as compared to the Heartmate VE device.

Again importantly, what we noticed

or observed during this trial was a significant reduction in 30-day mortality for the Heartmate II device, as compared to the Heartmate VE device.

A Kaplan-Meier survival analysis was performed for the CAP cohort, and compared to the primary cohort and to the Heartmate VE device.

This analysis demonstrates an equivalent or a continuing trend, with improvement in survival for the CAP cohort, with increasing clinical experience.

I will now review the alternate analysis end point. As you recall, our rationale for providing an alternate analysis end point was that we believed that the pre-specified end point was too restrictive, requiring a listing at 1A and 1B, and was not representative of all possible successful outcomes, and did not reflect the dynamic nature of heart transplant listing.

Using an alternate analysis for the

primary cohort of 126 patients, 75 percent of patients was defined as treatment successes, with a lower confidence limit of 68 percent.

For the CAP cohort of 58 patients, 78 patients were defined as treatment successes, with a lower confidence limit of 69 percent.

For the small body size cohort, 80 percent of patients were defined as treatment successes, with a lower confidence limit of 59 percent.

I will review secondary end points now. The median duration of support time was 116 days for the study, with a cumulative support time of 61 patient years. The median length of stay for the indexed hospitalization at pump implant was 25 days.

Eighty-four percent of patients were discharged from the hospital. 74 percent were discharged on LVAD support. Ten percent of patients underwent heart transplantation during the indexed hospitalization, and were

discharged following heart transplantation.

Sixty percent of patients discharged were readmitted to the hospital. However, the percent of support time outside the hospital was 75 percent.

I'll review causes of death. Sepsis was the leading cause of death in the primary cohort, and is reflective of the ill nature of this group of patients.

Other causes of death included multi-organ failure, stroke, device-related deaths, right heart failure, anoxic brain injury, bleeding and other causes of death.

Review of the CAP cohort causes of death are similar to the primary cohort of causes of death, and similar to -- actually no observed deaths in the small body size cohort.

We are also presenting all patients in the Heartmate II trial. These include patients that have not achieved study end points, and these causes of death are similar in frequency and distribution to each of the

cohorts.

Serious adverse events for patients included bleeding requiring surgery, which was the leading serious adverse event, occurring in 29 percent of patients.

Other serious adverse events included stroke, local infection, sepsis, percutaneous lead infection and pump pocket infection. The distribution of frequencies of serious adverse events were similar for the CAP cohort of 58 patients, and also similar to the small body size cohort.

Other serious adverse events included other neurological events, deep venous thrombosis and pulmonary embolism, device thrombosis, right heart failure, cardiac arrhythmia, respiratory failure, renal failure and hemolysis.

Again, the frequency and distribution of serious adverse events for this group was similar for the CAP cohort and the small body size cohort.

Serious confirmed malfunctions occurred in six percent of patients in the primary cohort. The majority of these were internal components.

For the CAP cohort, seven percent of patients experienced serious confirmed malfunction, again the majority of these being internal components. In the small body size cohort, the majority were all external components.

LVAD replacement was required in four percent of patients in the primary cohort. There was three LVAD-related deaths or 2.4 percent in the primary cohort. These were similar to what was observed in the CAP cohort. There was no LVAD-related deaths or LVAD replacement in the small body size cohort.

Again, reviewing for all patients entered in the trial, including those who had not reached primary end points, the percentages of those requiring LVAD

replacement in LVAD-related deaths is the same.

Importantly, no purely mechanical pump failures were noted during the trial in any group.

57 percent of patients required reoperation in the first 30 days following LVAD implant for the primary group. This reflects the critically ill nature of this group of patients. The majority of reoperations were related to bleeding.

This distribution of reoperations was similar for the CAP cohort, and also for the small body size cohort.

The smallest patient enrolled in the trial had a body surface area of 1.3 meters squared. Fifteen of 279 patients or five percent of the study population were small body size. This is not a new population, and a similar percentage was seen in other Thoratec VAD trials.

The majority of the small body size

patients are women, and the small patients appear to tolerate the pump equally well, and appear to have similar outcomes and similar rates of adverse events.

The similar results support our extrapolation of data from the primary study cohort, to small body surface area patients.

I'd like to review the proposed labeling cohort now. The proposed labeling cohort represents the first 194 patients enrolled in the study, and consists of the 126 primary study cohort, the 58 CAP cohort, and ten small body size cohort patients.

All patients have reached a study end point, and this represents the most complete dataset from the study, and represents the longest follow-up and we believe the most appropriate data summary for clinicians and patients.

This is our graphical representation of results from each of the cohorts for the pre-specified end point and

the alternate end point. As you can see from these data, each of the study cohorts have similar outcomes.

There is no inferior or superior results in any study cohort that would influence bias or interpretation of data from the proposed labeling cohort, and we believe that the proposed labeling cohort is reflective of the outcomes from the individual cohorts.

For the alternate analysis, the same observations apply. However, with the alternate analysis, significant -- we have reached the level of the 65 percent, with the alternate analysis.

Using the proposed labeling cohort with the pre-specified analysis, 67 percent of patients were defined as a treatment success, with a lower confidence limit of 61 percent.

Using the pre-specified analysis updated to a September 14th, 2007 analysis, 70 percent of patients were defined as a study

success, with a lower confidence limit of 65 percent.

Using the alternate analysis as of March 16th, 2007, 76 percent of patients were defined as a treatment success, with a lower confidence limit of 61 percent, surpassing the lower confidence limit of greater than 65 percent.

A Kaplan-Meier survival analysis was performed for the proposed labeling cohort, and compared to the 280 patients supported by the Heartmate VE. Again, remember that this 280 patients represents the final labeling cohort for the PMA submission for the Heartmate VE.

There is a significant improvement in survival by lab rank analysis for the Heartmate II, compared to the Heartmate VE, which represents the current standard of care.

A comparison of serious adverse events was performed between the proposed 194 patients in the proposed labeling cohort, and

compared to the 280 patients on the VE cohort. Only definitions with similar -- only serious events with similar definitions between the two trials were used for comparison.

When you compare the incidents or rates of serious adverse events for stroke, other neurological events, bleeding requiring surgery, percutaneous lead infection and right heart failure requiring a right ventricular assist device, there was a significant reduction in each of the serious adverse events.

When displayed graphically as a relative risk, there was a significant favor of reduction in relative risk favoring the Heartmate II device for stroke, other neurological events, bleeding requiring surgery, percutaneous lead infection and right heart requiring right ventricular assist device.

Transplant survival between the primary cohort and proposed labeling cohort

was similar at 30 days and one year post-transplant.

Survival at 30 days was 97 percent. Survival at one year was 83 percent.

These survival figures are consistent with data from national registries.

In summary, the pre-specified primary cohort analysis did not meet the OPC. They missed the OPC by one percentage point, a representation of two patients.

An alternative analysis of the primary cohort exceeded the OPC, 68 percent, versus the lower confidence limit of greater than 65 percent.

The Kaplan-Meier survival analysis favorably compares to the current standard of care, which is the Heartmate Vented Electric Device. In a significant proportion of the population, the use of the device would provide clinically significant results, and the data clearly demonstrates reasonable assurance of efficacy.

Adverse events are within acceptable norms, given the critically ill nature of the population of patients that are being operated upon. No new risks were identified.

No pure mechanical pump failures were identified in the study, and the proposed labeling cohort demonstrates significant improvement in the five comparable adverse events relative to the Heartmate VE.

The indication for use should be the same as the approved bridge to transplant ventricular assist devices. Importantly, the decision to implant the device should be based on an individualized assessment of the body habitus, and not an arbitrary body surface area limit.

It should include a contraindication for patients that do not tolerate anti-coagulation, and we recommend utilizing the proposed labeling cohort dataset, as it represents the largest and most

complete dataset. Thank you. I'll turn the podium over to Dr. Miller.

DR. MILLER: Thank you. There is a very appropriate focus on the outcomes of adverse events and survival. But from the beginning of the trial, we were very interested in the ability of these devices to improve functional capacity and quality of life. I'll review that data for you now.

We employed five different metrics to assess the quality of life and functional capacity. Shown first here in the primary cohort only is the six minute walk distance.

You see how impaired these patients were at baseline, and how rapidly they improved their functional capacity in six minute walk distance, portrayed here in meters walked during the six minutes.

There was a substantial difference between baseline in as early as 30 days, and a continued improvement in this primary cohort by six months.

By comparison, if you look at the published meta-analysis on the improvement derived from biventricular pacing trials, it averaged between 40 and 50 meters, and we're showing you here an improvement of over 300 meters.

When you compare side by side the labeling cohort and the primary cohort, I think you can see that this trend of significant improvement over time was consistent across all three cohorts.

A second metric for looking at functional improvement was the assessment of New York Heart Association Class 1 or 2, limited functional limitations. Again, all patients were Class 4 at the time of the operation and enrollment in the trial.

You can see that by one month, nearly two-thirds of the patients had achieved the New York Heart Association Class 1 or 2, and a continued improvement over time, such that by six months, nearly all of the patients

had achieved a Class 1 or 2 functional capacity.

These observations were true not only in the primary cohort, but were very similar across the three cohorts in the labeling group.

The third was a gross look at patient activity as assessed by the patient, and percentage improvement was described on the Y axis.

I think you can see the very limited functional capacities of patients at baseline, and a continual improvement across time, consistently across all the patients in the primary cohort, and again a consistent improvement of all patients in the proposed labeling cohort, showing a very consistent improvement of functional capacity across the three metrics that were employed in this trial in all three cohorts.

We used two tools commonly employed in heart failure patients to assess their

quality of life, shown here initially as the Kansas City cardiomyopathy questionnaire. This tool uses an improvement in quality of life as an improvement in score.

This is a very low baseline, reflecting a very poor quality of life in these patients, and an almost unprecedented improvement, a doubling in the value of this score to 60 by six months in these patients.

You can see that there is a 50 percent improvement as early as 30 days following a major operation in the self-assessed quality of life by the Kansas City tool.

That data was in the primary cohort, but it was very impressive on how nearly identical the scores were across all three cohorts and the proposed labeling cohort. So very consistent data across all three study groups.

Finally, the Minnesota Living With Heart Failure was the second comparison of

quality of life.

In contrast to the Kansas City cardiomyopathy score, where an increasing score reflects improvement with the Minnesota Living With Heart Failure questionnaire, a high score in the beginning improvement reflects a reduction in the score, again very similar, a very significant reduction as early as 30 days and an improvement in their quality of life, a very significant reduction and overall improvement in the primary cohort.

Much like the Kansas City cardiomyopathy questionnaire, you can see that there was very consistent data across this cohort.

One of the most challenging and most important issues in mechanical support would be the assessment of neurocognitive function, if there were any adverse consequences to placement of this type of device, particularly this change in our entire understanding, moving from pulsatile support

now to continuous flow.

Eleven of the twenty-six participating sites were engaged in performing neurocognitive tests, and they occurred in 64 patients in the primary cohort, a total of 83 assessments.

The patients were evaluated one month, which was to determine what we refer to as their baseline, and then an opportunity to reassess their neurocognitive function at three and six months post-op.

Due to the number of patients who were transplanted who were ill, or who actually refused participation in a follow-up tests, there were very few patients who had impaired tests.

What we can say from the data is that there was no evidence of neurocognitive decline in these patients at three and six months post-op. There were, however, significant improvements at these time points, in both auditory and visual memory scores.

These trends continued in the proposed labeling cohort, in addition to the primary cohort.

So in summary, I think that we've demonstrated a very consistent improvement in multiple health status measures of quality of life and functional capacity, including New York Heart Association functional class, six minute walk, patient activity score and the two metrics for quality of life.

There was really extraordinary consistency across all three study cohorts. The trends in neurocognitive seen were supportive of the improvements seen in quality of life and functional capacity, and did show this improvement in auditory and digital memory.

But importantly, there was no evidence of any neurocognitive decline in this study. I'll turn the podium back over to Don Middlebrook.

MR. MIDDLEBROOK: Thank you, Les,

and thanks to all of the Thoratec presenters for that excellent presentation. I'm going to wrap things up with a few closing remarks here.

In regards to the post-market considerations for the Heartmate II, Thoratec has developed a comprehensive plan to ensure that our commercial Heartmate II experience is equal or better than what we've seen during the clinical trial.

The plan includes a rigorous, well-defined training and education program. This consists of a day and a half off-site training, both didactic and includes an animal lab. We also have comprehensive labeling for the Heartmate II users, a user handbook and a user manual and a patient handbook.

We also do device tracking in accordance with 21 C.F.R. Part 821. We have a worldwide service tracking database. So all of the hardware and axillary components that you saw Steve present, that are used in

conjunction with the pump itself, are tracked for service.

We also report MDRs and user facility reports are reported, in compliance with 21 C.F.R. Part 803. We also have anticipated in our PMA and proposed to the FDA a robust post-market study, using the INTERMACS registry. I want to talk a little bit more about that.

The post-market study that we have proposed for the Heartmate II utilizes the interagency registry of mechanical-assisted circulation support, INTERMACS for short.

This is a VAD-specific registry developed for the use of tracking the performance of VADS in a commercial setting. It was developed in partnership between the NHLBI, the FDA, CMS, clinicians and industry including Thoratec was involved in the development of this important registry.

The study we are proposing utilizes the INTERMACS registry, and our primary

objective for the study is to assess patient outcomes.

We are also tracking secondary objectives that include adverse events, clinical reliability, quality of life, reoperations, a neurocognitive evaluation and one year post-explant evaluation.

I also want to point out that all of the data requirements that were determined and baked into the INTERMACS registry were determined by leading authorities and experts in these devices, to be all that really is necessary to be colleted, to characterize the performance of a ventricular assist device in a commercial setting.

With regards to the Heartmate II labeling, a couple of points I want to make here. The indications for use that we have proposed for this device and the proposed labeling are identical to the indications for use that are in the improved ventricular assist devices for all VADS, for bridge to

transplantation.

There's no differences. We've not added anything or subtracted anything. That's not only the Thoratec devices but all the devices currently approved for bridge to transplantation.

We are encouraging the FDA to consider the proposed labeling cohort that we have provided, because it really is the largest and most complete dataset from this study, with 194 patients having at least 180 days of follow-up. We think that's really most appropriate for the user community.

We also recommend that the small patients, with a body surface area of less than 1.5, not be excluded from the labeling, because we believe the data that we have presented here can be extrapolated to those small patients.

In summary, from a clinical trial perspective, again, this is the largest dataset, with 279 patients, that has been

submitted in support of an implantable VAD PMA. As I mentioned earlier, the pace of trial enrollment is unparalleled in the history of this technology.

From a safety perspective, the Heartmate II adverse event rates compare favorably to previous devices studied, including the Heartmate VE, in adverse events with definitions that could be compared.

The 30-day perioperative mortality is ten percent. That's half of what we've seen with the Heartmate VE and the bridge to transplant studies they have performed.

The Heartmate II results show consistent and predictable product performance across all the cohorts that we have analyzed and presented to you here this morning.

From an effectiveness standpoint, the Heartmate II provides similar survival benefit, as other PMA-approved devices in this critically ill patient population, despite support durations that are two to five times

longer than these other devices.

The Heartmate 2 30 day post transplant survival is 97 percent and one year post-transplant survival is 83 percent. I think that speaks to the clinical utility of this device.

In conclusion, these data demonstrate a reasonable assurance that the Heartmate II is safe and effective, by all clinical measures evaluated, including survival, adverse events, functional status, neurocognitive function and quality of life.

I want to thank all of the panel members for their time and attention. That concludes our presentation.

CHAIRMAN LASKEY: I'd like to thank the sponsor for a very concise and complete presentation of the data set. Does anyone on the panel have a question or questions for the sponsor, keeping in mind that we reserve that right this afternoon to ask the sponsor questions also.

Finally, if anyone has extensive questions for the sponsor, you might want to get that on the floor now, so we can respond more completely this afternoon. We're doing well on time, so hopefully we can have the early phase of the questioning. Dr. Lindenfeld, yes.

DR. LINDENFELD: You've shown us comparisons between the Heartmate II and the XVE. Could we see a demographic comparison of those two groups? I just would like to see age, ejection fraction, all the basic things that predict outcomes.

If we can't do it right this minute, I think we need to see that later. You've shown us that they're comparable results, but we need to see that they are comparable demographics.

MR. MIDDLEBROOK: We don't have it handy, but we will pull that together for you and present that to you.

DR. LINDENFELD: It's hard to