Thoratec® Ventricular Assist Device (VAD) System
Premarket Approval (PMA) Application Supplement P870072/S5

SUMMARY of SAFETY and EFFECTIVENESS

Thoratec Laboratories Corporation
6035 Stoneridge Drive
Pleasanton, California 94588

I. GENERAL INFORMATION

Device Generic Name:	Ventricular assist device
Device Trade Name:	Thoratec® Ventricular Assist Device System
Applicant's Name and Address:	Thoratec Laboratories Corporation 6035 Stoneridge Drive Pleasanton, California 94588
PMA Application Number:	P870072/S5
Date of Notice of Approval to the Applicant:	May 21, 1998

This device was originally approved on December 20, 1995 for use as a bridge to transplantation for cardiac transplant candidates who were in imminent risk of dying before donor heart procurement, and who were dependent on, or had an incomplete response to, continued vasopressor support.

The sponsor has submitted this supplement to expand the clinical indications to include post-cardiotomy myocardial recovery. These are patients who have had a technically successful open heart operation but are unable to be weaned from cardiopulmonary bypass. Data to support this new indication are provided in this summary. The preclinical test results were presented in the original application, and are not repeated here. For more information on the data which were used to support the original indication, the summary of safety and effectiveness for the original PMA should be referenced. Written requests for copies can be obtained from the Dockets Management Branch (HFZ-305), Food and Drug Administration, 12420 Parklawn drive, rm. 1-23 Rockville, MD 20857, under Docket #97M-0136.

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II. INDICATIONS FOR USE

The Thoratec® Ventricular Assist Device is indicated for:

Bridge to transplant patients who meet all of the following criteria:

1. Candidate for cardiac transplantation.
2. Imminent risk of dying before donor heart procurement.
3. Dependence on, or incomplete response to, continued vasopressor support.

Post-cardiotomy recovery patients who are unable to be weaned from cardiopulmonary bypass.

III. CONTRAINDICATIONS

Uncontrolled hemorrhage.

Central nervous system damage resulting in fixed and dilated pupils.

IV. WARNINGS/PRECAUTIONS

See labeling for warnings and precautions.

V. DEVICE DESCRIPTION

Refer to the Summary of Safety and Effectiveness for the original PMA application.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional medical therapy, including the use of pharmacologic agents and/or the intraaortic balloon pump (IABP), is employed to assist in maintaining heart pumping function for patients who have difficulty in weaning from cardiopulmonary bypass. Patients have also been supported by extracorporeal membrance oxygenators (ECMO) pending recovery of myocardial function.

VII. MARKETING HISTORY

Marketing of the Thoratec® VAD for post-cardiotomy recovery outside the U.S. began in 1983, with introduction of the device in Switzerland. The device has since been marketed for both bridge to transplant and post-cardiotomy recovery in the following countries: Argentina, Australia, Austria, Belgium, Brazil, Canada, France, Germany, India, Israel, Italy, Korea, Mexico, Norway, Japan, Spain, Taiwan R.O.C., and the United Kingdom. The device has not been withdrawn from marketing for any reason.

VIII. ADVERSE EVENTS

Adverse events were collected for all patients enrolled in the clinical study of the device, which included 60 post-cardiotomy patients at 18 medical centers. Twenty-nine patients described in Section XI, Description of Clinical Studies, formed the Primary Data Cohort for the analyses of safety and efficacy. The frequency of each of nine critical adverse events that occurred during the period of VAD support in the clinical trials is presented in Table 1, ordered by decreasing frequency in the Primary Data Cohort. Although the frequency of death was 52%, the expected mortality in the study patient population (post-cardiotomy patients unable to be weaned from cardiopulmonary bypass after exhausting pharmacological and/or intraaortic balloon pumping therapy) is about 100%.

Table 1. Critical adverse events by category, while on VAD support, all Thoratec VAD post-cardiotomy recovery patients (n=60).

EVENT CATEGORY	Primary Data Cohort (n=29)			Other Post-cardiotomy Data (n=31)		
	# Events	# Pts	% Pts	# Events	# Pts	% Pts
Cardiovascular dysfunction (e.g. any single event of hypo- or hypertension, arrhythmias, RV failure)	28	21	72%	32	20	65%
Renal dysfunction (e.g. dialysis, any single creatinine >1.5× high normal)	18	18	62%	21	21	68%
Bleeding (e.g. excessive CT drainage, DIC, tamponade, hematuria)	25	18	62%	7	22	71%
Hepatic dysfunction (e.g. any single total bilirubin >3× high normal, cholecystitis)	17	17	59%	14	13	42%
Reoperation (for any cause - e.g. hemostasis, cannula reposition, tracheostomy, cholecystectomy)	27	16	55%	14	11	35%
Death	15	15	52%	19	19	61%
Infection (e.g. any positive culture, purulent discharge)	18	13	45%	20	14	45%
Thromboembolism (e.g. all autopsy evidence of any organ infarction; stroke, TIA)	14	11	38%	20	13	42%
Hemolysis (e.g. any single plasma free hemoglobin >3× high normal after 24 hr)	9	9	31%	11	11	35%

A variety of other adverse events were noted during the studies including:

- Mechanical dysfunction
- Thrombocytopenia
- Neurological dysfunction
- Respiratory dysfunction
- Pleural effusions
- Pancreatitis

Note:

Bleeding can be due to surgical- and device-related reasons at the cannulation sites or arterial anastomoses, or it can occur due to coagulopathy.

The need for reoperation may result from excessive bleeding, right ventricular failure requiring RVAD insertion, VAD inflow problems requiring cannula repositioning, etc.

There was evidence that the VAD produces some hemolysis, with plasma free hemoglobin after 2 weeks of pumping averaging = 18 ± 9 mg/dL. Blood transfusions may be required for patients who have excessive bleeding or hemolysis.

Infection can also occur at the cannulation sites, around the monitoring lines, or in the blood, urinary tract, or respiratory tract. There was no apparent pattern of organisms or source.

Neurological dysfunction may result from pre-existing hypoxic brain injury (for example, from pre-VAD cardiac arrest or hypotension), or events during the VAD period such as cerebral hemorrhage, drug-related side effects, and cerebral hypoperfusion.

Thromboembolism can also occur from the VAD, cannulae, natural heart chambers, or arteries. Embolism may result in stroke, pulmonary or other non-cerebral organ infarction, leg ischemia, or other vascular obstruction. Continuous anticoagulation with heparin or warfarin is recommended.

IX. NON-CLINICAL LABORATORY STUDIES

Non-clinical laboratory studies presented in the summary of safety and effectiveness for the original PMA for the bridge to transplant indication for use (PMA P870072) are equally applicable to use of the VAD for post-cardiotomy recovery.

X. RELIABILITY

Reliability data presented in the summary of safety and effectiveness for the original PMA for the bridge to transplant indication for use (PMA P870072) are equally applicable to use of the VAD for post-cardiotomy recovery.

XI. DESCRIPTION OF CLINICAL STUDIES

A. Study Design

The use of the Thoratec VAD for post-cardiotomy myocardial recovery was studied in an international, multi-center clinical trial. In the United States the study was conducted in compliance with the Investigational Device Exemption (IDE) regulations. A detailed study protocol was followed by all U.S. centers with specific subject inclusion and exclusion criteria, and data collection requirements for hemodynamics, hematology, blood chemistry and adverse events.

The purpose of the study was to demonstrate that the Thoratec VAD provided adequate hemodynamic support to permit myocardial recovery with survival of patients who were unable to be weaned from cardiopulmonary bypass. Adequate hemodynamic support was defined as a VAD flow index of at least 2.0 L/min/m^2. Myocardial recovery was determined by the ability to wean the patient from VAD support. Survival was evaluated at two points, hospital discharge, and survival at one year after weaning from VAD support.

B. Patient Selection

Two hundred fifteen patients were enrolled at 46 medical centers in 13 countries from March 1982 to December 1996 evaluating use of the Thoratec VAD System pending myocardial recovery. However, only sixty post-cardiotomy patients received the device in its final configuration at eighteen investigational sites in the United States as part of the IDE study sponsored by Thoratec Laboratories Corporation. The analyses of safety and effectiveness were performed on a primary data cohort of 29 patients who met all study entrance criteria.

The 29 patients included in the primary data cohort met the following criteria:

1. Male or female aged 15 to 69.
2. Technically successful open heart operation.
3. Normal steps taken to discontinue cardiopulmonary bypass.
4. Failed to wean from cardiopulmonary bypass after exhausting pharmacological and/or intraaortic balloon pump (IABP) therapy.

Thirty-one patients were excluded from the primary data cohort for failure to meet entrance criteria:

1. Inability to wean from cardiopulmonary bypass after cardiac transplantation (n=16).
2. Cardiac failure outside of the operating room after initial successful weaning from cardiopulmonary bypass (n=8).
3. Not effectively supported; i.e. death in operating room (n=3).
4. Age greater than 69 years (n=2).

5. Active systemic infection (n=1).
6. Technically unsuccessful operation (n=1).

C. Patient Demographics

Baseline information for the primary data cohort is presented in the following tables: Table 2. Baseline Demographic and Clinical Characteristics, Table 3 Baseline Hemodynamic Summary, and Table 4. Baseline Hematology and Blood Chemistry.

Table 2. Baseline Demographic and Clinical Characteristics, Primary Data Cohort (N=29), mean ± s.d. (range)

Age (years)	52 ± 8 (38 - 66)
Weight (kg)	83 ± 17 (50 - 127)
Body surface area (BSA-m^2)	1.97 ± 0.24 (1.37 - 2.46)
Gender: Male Female	23 (79%) 6 (21%)
Preoperative Diagnosis[1]: Coronary Artery Disease Myocardial Infarction Valvular Disease Hypertensive Cardiomyopathy	 26 (90%) 14 (48%) 5 (17%) 1 (3%)
Original Cardiac Operation[1]: CABG Valve replacement Other	 26 (90%) 5 (17%) 3[2] (10%)
Emergent cardiac operation	12 (41%)
Prior Cardiac Operations	9 (31%)
Perioperative Myocardial Infarction	4 (14%)
NYHA Class: I or II III IV Unknown	 8 (28%) 4 (14%) 15 (52%) 2 (7%)
LVEF	0.46 ± 0.2
Pre-VAD cardiac arrest	10 (34%)
VAD support type: BVAD LVAD	 15 (52%) 14 (48%)

[1]Percentages add to greater than 100% due to multiple diagnoses and operative procedures in some patients.

2 Aortic arch replacement (2); ventricular aneurysmectomy (1)

Table 3. Baseline Hemodynamic Summary, Primary Data Cohort (N=29), mean ± s.d. (range)

Cardiac Index ($L/min/m^2$)	1.52±0.52 (0.4 - 2.8) n=16
LAP or PCWP (mm Hg)	24.9±7.3 (12 - 41) n=21
RAP (mm Hg)	15.0±4.5 (7 - 23) n=15
MAP (mm Hg)	54.0±11.4 (40- 80) n=14
SAP (mm Hg)	67.4±14.7 (30 - 90) n = 24
PAP (mm Hg)	26.9±6.7 (13 - 34) n = 11

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SAP (mm Hg)	67.4±14.7 (30 - 90) n = 24
PAP (mm Hg)	26.9±6.7 (13 - 34) n = 11

Table 4. Baseline Hematology and Blood Chemistry, Primary Data Cohort (N=29).

	mean ± s.d. (range)	
Creatinine (mg/dl)	1.32±0.54 (0.4 - 3.0)	n = 25
Blood Urea Nitrogen BUN (mg/dl)	20.3±8.8 (7 - 44)	n = 24
Total Bilirubin (mg/dl)	0.79±0.50 (0.1 - 2.1)	n = 16
Lactic Dehydrogenase LDH (I.U.)	420±454 (101 - 1620)	n = 18
Serum Glutamic Oxaloacetic Transaminase SGOT (I.U.)	243±454 (8 - 1452)	n = 16
Plasma Free Hemoglobin (mg/dl)	52.5±38.8 (25 - 79.9)	n = 2
Fibrinogen (mg/dl)	240±110 (115 - 395)	n = 7
Fibrin Split Products FSP (mg/dl)	25±0 (25)	n = 2
White Cell Count (1000s/mm^3)	9.6±3.8 (4.8 -18.6)	n = 23
Hematocrit (%)	38.9±6.8 (19.5 - 47.6)	n = 22
Platelet Count (1000s/mm^3)	239±77 (71 - 439)	n = 23
Prothrombin Time PT (sec)	21.2±25.3 (11.3 - 121)	n = 19
Partial Thromboplastin Time PTT (sec)	39.0±19.6 (22 - 90)	n = 21

D. Criteria for BVAD Placement

Adequate right ventricular function is essential for the successful utilization of left ventricular assist devices, to provide sufficient blood flow through the pulmonary circulation to the left side of the heart. A right ventricular assist device is used in addition to a left ventricular assist device (in other words, biventricular assist) when right heart failure prevents adequate circulation of blood, generally when the blood flow index is less than 1.8 L/min/m^2 with a central venous pressure greater than 20 mmHg. Biventricular support is also indicated in patients with potentially lethal arrhythmias, which could result in death during univentricular support. An RVAD was implanted prophylactically in patients considered at high risk for right heart failure.

Outside of the primary data cohort, several patients with isolated right heart failure required an isolated right ventricular assist device.

E. VAD Placement and Cannulation Sites

Fifteen of the 29 patients (52%) in the Primary Data Cohort received biventricular devices and 14 received LVADs (Figure 1). Left atrial cannulation, either via the LA appendage or interatrial groove, was favored over LV apical cannulation.

Figure 1. Frequencies of BVAD, LVAD, RVAD and location of LVAD inflow cannulation, Primary Data Cohort (n=29).

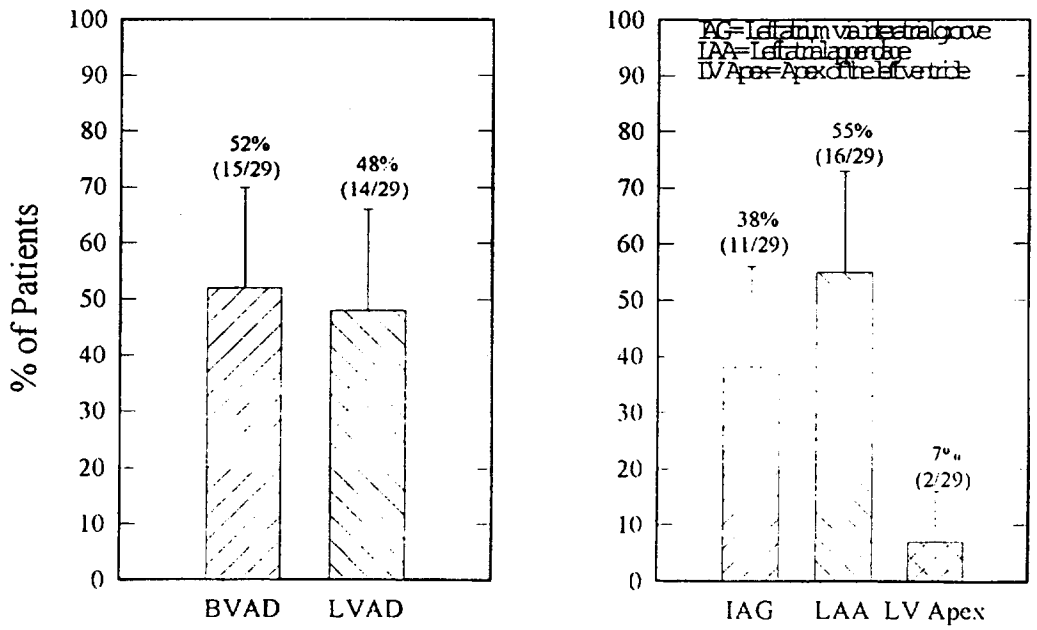


Table 5. Left heart cannulation sites, Primary Data Cohort (n=29)

LVAD CANNULATION SITE	BVAD	LVAD	OVERALL
Interatrial groove	4 (27%)	7 (50%)	11 (38%)
Left atrial appendage	9 (60%)	7 (50%)	16 (55%)
Left ventricular apex	2 (13%)	0 (0%)	2 (7%)
Total VAD patients	15 (52%)	14 (48%)	29

XII. RESULTS

A. Effectiveness

Effectiveness was demonstrated by the restoration of hemodynamic function, the ability to wean the patient from VAD support, survival to hospital discharge and survival to one year after weaning from VAD support.

Table 6. Principal Effectiveness Outcomes, Post-cardiotomy Myocardial Recovery Support

	Thoratec Primary Data Cohort (N=29)		Thoratec Other Postcardiotomy Data (N=31)	
	No. of Patients	% [95% CI]	No. of Patients	% [95% CI]
Hemodynamic Function Restored (VAD index ≥2.0 L/min/m²)	22	76% [60 - 91%]	18	58% [41 - 75%]
Survival to Weaning	14	48% [30 -67%]	12	39% [22 - 56%]
Survival to Discharge	10	34% [17 -52%]	5	16% [3 - 29%]
Survival to One Year	8	28% [11 - 44%]	5	16% [3 - 29%]

Hemodynamic parameters are presented over time in Table 7 and in Figures 2 through 4 for LVAD flow index, arterial pressures, and atrial pressures. These figures show that hemodynamic function was significantly improved, as

demonstrated by increases in blood flow index and mean arterial pressure, and a decrease in left atrial pressure. LVAD flow index increased to 2.2±0.3 L/min/m^2 (averaged across both LVAD and BVAD patients) after one day of VAD support, compared to the average pre-VAD implant cardiac index, 1.5±0.5 L/min/m^2 (Table 7). LVAD flow index (averaged across both LVAD and BVAD patients) ranged from 2.1 to 2.5 L/min/m^2 throughout the period of VAD support. The average left atrial pressure decreased from 25 to 15 mm Hg after one day of VAD support, and to 12 mm Hg after 7 days (Figure 4). Mean arterial pressure increased from 54 to over 80 mm Hg throughout most of the period of VAD support (Figure 3).

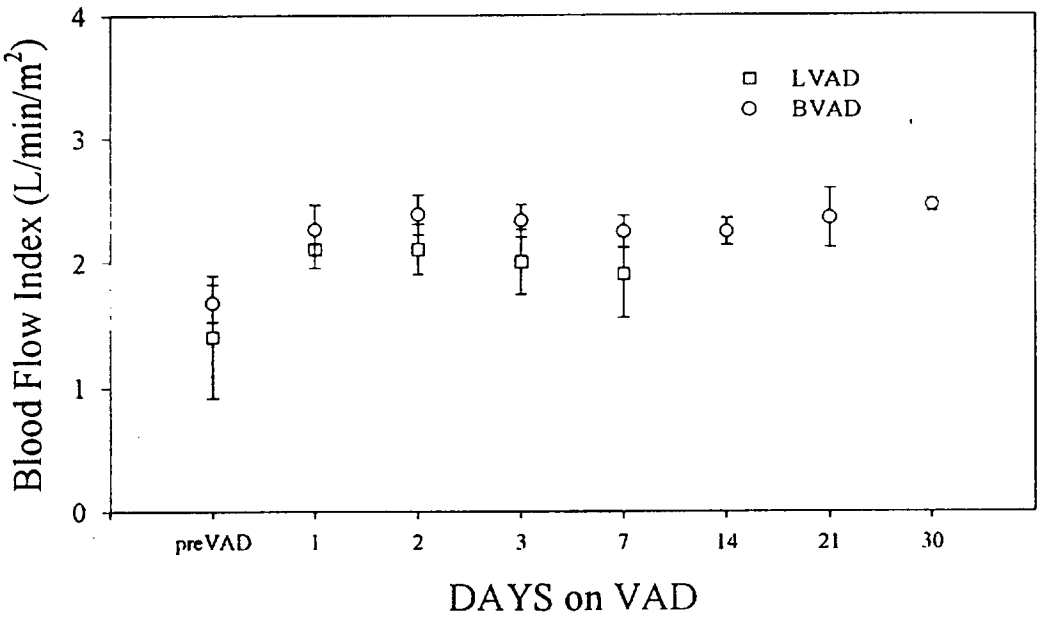
The median duration of VAD support in the Thoratec Primary Data Cohort was six (6) days, ranging from 1 to 80 days, with a mean duration of 12 days.

Table 7. Comparison of hemodynamic effectiveness variables, baseline and one day after VAD implantation (POD1), Primary Data Cohort (N=29).

	Baseline (pre-VAD) values			Average value on POD1		
Hemodynamic Parameter	Mean	Std. Dev.	N	Mean	Std. Dev.	N
Mean arterial pressure (mmHg)	54	11.4	14	78	7.7	24
Left Atrial filling pressure (mmHg)	25	7.3	21	15	4.4	15
Blood flow index (l/min/m^2)	1.5[1]	0.52	16	2.2[2]	0.3	25

[1] Pre-VAD cardiac index, averaged across both LVAD and BVAD patients
[2] LVAD flow index, averaged across both LVAD and BVAD patients

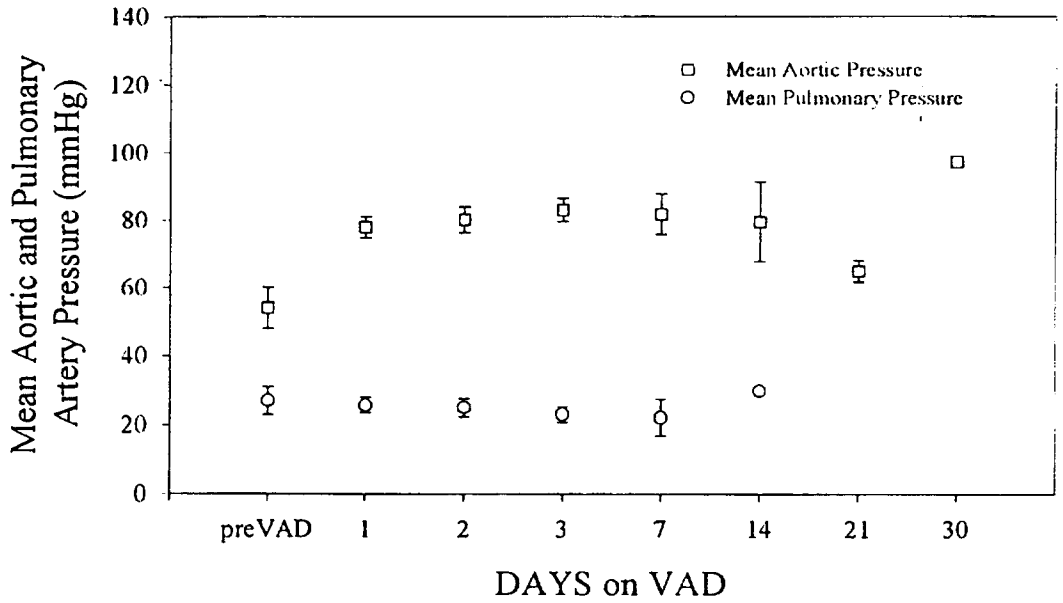
Figure 2. Cardiac index (CI) before, and VAD flow index after VAD implantation for BVAD (n=15) and LVAD (n=14) patients, mean ± 1.5 SEM, L/min/m^2, Primary Data Cohort (N=29). VAD flow index[c] measurement obtained by dividing VAD drive console display (L/min) by patient BSA (m^2).



Flow Index (L/min/m^2)[c]	DAYS ON VAD															
	Pre-VAD[a]		1[b]		2[b]		3[b]		7[b]		14[b]		21[b]		30[b]	
	BVAD	LVAD	BVAD	LVAD	BVAD	LVAD	BVAD	LVAD	BVAD	LVAD	BVAD	LVAD	BVAD	LVAD	BVAD	LVAD
Mean	1.7	1.4	2.3	2.1	2.4	2.1	2.3	2.0	2.2	1.9	2.3	-[d]	2.3	-[d]	2.5	-[d]
Median	1.7	1.4	2.2	2.1	2.3	2.1	2.3	2.1	2.3	1.9	2.2	-	2.4	-	2.4	-
SD	0.21	0.70	0.40	0.24	0.31	0.34	0.26	0.43	0.18	0.39	0.15	-	0.24	-	0.04	-
N	8	8	14	11	13	11	13	11	5	5	5	-	4	-	2	-
Min	1.2	0.4	1.4	1.6	1.8	1.3	1.8	0.9	2.0	1.6	2.1	-	2.1	-	2.4	-
Max	1.9	2.8	2.9	2.5	2.9	2.6	2.7	2.6	2.4	2.6	2.4	-	2.6	-	2.5	-
2.0 SEM	0.15	0.49	0.21	0.15	0.17	0.20	0.14	0.26	0.16	0.35	0.13	-	0.24	-	0.05	-

a. Last patient cardiac index obtained from PA catheter; obtained intraoperatively.
b. Multiple daily measurements (generally at least 3) averaged over 24 hour period.
c. LVAD flow index for BVAD and LVAD patients.
d. No LVAD patients were supported for longer than 11 days.

Figure 3. Mean aortic (MAP) and pulmonary arterial (PAP) pressures before and after VAD implantation, mean ± 2.0 SEM, mm Hg, Primary Data Cohort (n = 29). Aortic pressure measurements obtained from either arterial pressure line or pressure cuff, pulmonary pressure measurements obtained from PA catheter; lines pulled after patients stabilized.



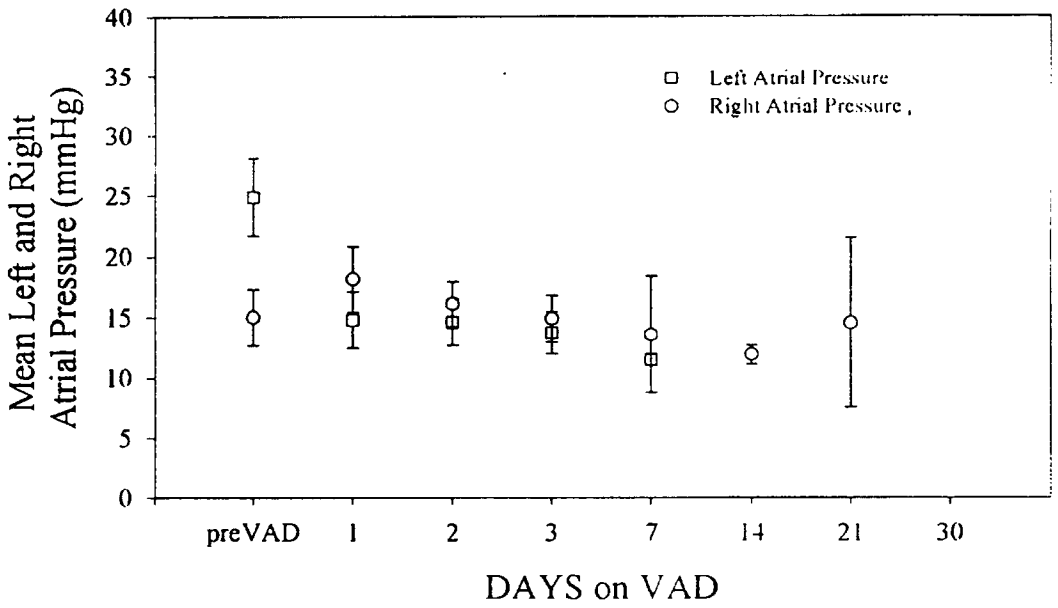
Mean Arterial Pressure (mm Hg)	DAYS ON VAD															
	Pre-VAD[a]		1[b]		2[b]		3[b]		7[b]		14[b]		21[b]		30[b]	
	MAP	PAP	MAP	PAP	MAP	PAP	MAP	PAP	MAP	PAP	MAP	PAP	MAP	PAP	MAP	PAP
Mean	54	27	78	26	80	25	83	23	82	22	80	30	65	-	97	-
Median	53	30	78	24	81	24	83	23	81	23	78	30	65	-	97	-
SD	11.4	6.7	7.7	5.6	9.1	5.8	8.5	4.8	9.0	4.7	13.1	0	2.2	-	0	-
N	14	11	24	23	22	20	23	19	9	3	5	1	2	-	1	-
Min	40	13	62	15	63	16	68	14	64	17	64	30	63	-	97	-
Max	80	34	94	36	97	36	99	30	93	26	93	30	67	-	97	-
2.0 SEM	6.1	4.1	3.2	2.3	3.9	2.6	3.5	2.2	6.0	5.4	11.8	0	3.2	-	0	-

Notes:

a. Last value measured at time of decision to implant VAD.

b. Multiple daily measurements (generally at least 3) averaged over 24 hour period.

Figure 4. Left and right atrial pressures before and after VAD implantation, mean ± 2.0 SEM, mm Hg, Primary Data Cohort (N = 29). Left atrial pressures derived from direct atrial sampling or the pulmonary catheter, right atrial pressures derived from CVP catheter. Vascular lines in use until patients stabilized.



Mean Atrial Pressure (mm Hg)	DAYS ON VAD															
	Pre-VAD[a]		1[b]		2[b]		3[b]		7[b]		14[b]		21[b]		30[b]	
	LAP	RAP	LAP	RAP	LAP	RAP	LAP	RAP	LAP	RAP	LAP	RAP	LAP	RAP	LAP	RAP
Mean	25	15	15	18	15	16	14	15	12	14	-	12	-	15	-	-
Median	24	15	14	17	15	16	13	15	12	10	-	12	-	15	-	-
SD	7.3	4.5	4.4	5.5	3.5	3.9	3.2	4.0	0.5	6.4	-	0.6	-	4.9	-	-
N	21	15	15	21	14	20	14	19	3	7	-	2	-	2	-	-
Min	12	7	7	8	8	7	8	9	11	7	-	12	-	11	-	-
Max	41	23	27	31	21	22	20	24	12	25	-	12	-	18	-	-
2.0 SEM	3.2	2.3	2.3	2.4	1.9	1.7	1.7	1.8	0.5	4.8	-	0.8	-	7	-	-

Notes:

a. Last value measured at time of decision to implant VAD

b. Multiple daily measurements (generally at least 3) averaged over 24 hour period

B. Safety

Adverse events were collected for all 29 patients in the Primary Data Cohort. A comparison of adverse event rates between the bridge to transplant and post-cardiotomy myocardial recovery study primary data cohorts showed no significant differences in incidence, other than for death, which was higher in the recovery study. The frequency of nine critical adverse events that occurred during the period of VAD support in the clinical trials is presented in Table 8 below.

Table 8. Critical adverse events by category, while on VAD support

EVENT CATEGORY	Bridge to Transplant (n=71)			Post-cardiotomy Myocardial Recovery (n=29)		
	# Events	# Pts	% Pts	#Events	# Pts	% Pts
Death	22	22	31%	15	15	52%
Cardiovascular dysfunction (e.g. any single event of hypo- or hypertension, arrhythmias, RV failure)	90	55	77%	28	21	72%
Hepatic dysfunction (e.g. any single total bilirubin >3× high normal, cholecystitis)	40	40	56%	17	17	59%
Renal dysfunction (e.g. dialysis, any single creatinine >1.5× high normal)	38	38	54%	18	18	62%
Bleeding (e.g. excessive CT drainage, DIC, tamponade, hematuria)	54	36	51%	25	18	62%
Hemolysis (e.g. any single plasma free hemoglobin >3× high normal after 24 hr)	36	36	51%	9	9	31%
Infection (e.g. any positive culture, purulent discharge)	50	35	49%	18	13	45%
Reoperation (for any cause - e.g. hemostasis, cannula reposition, tracheostomy, cholecystectomy)	51	32	45%	27	16	55%
Thromboembolism (e.g. all autopsy evidence of any organ infarction; stroke, TIA)	27	20	28%	14	11	38%

C. Causes of Death

The most frequent cause of death in the Primary Data Cohort was due to five cases of central nervous system (CNS) damage. Three patients never regained conciousness after the original open heart operation. CNS damage in the other two patients was attributed to device-related embolism.

Table 9. Causes of Death While on VAD Support, Post-cardiotomy Myocardial Recovery

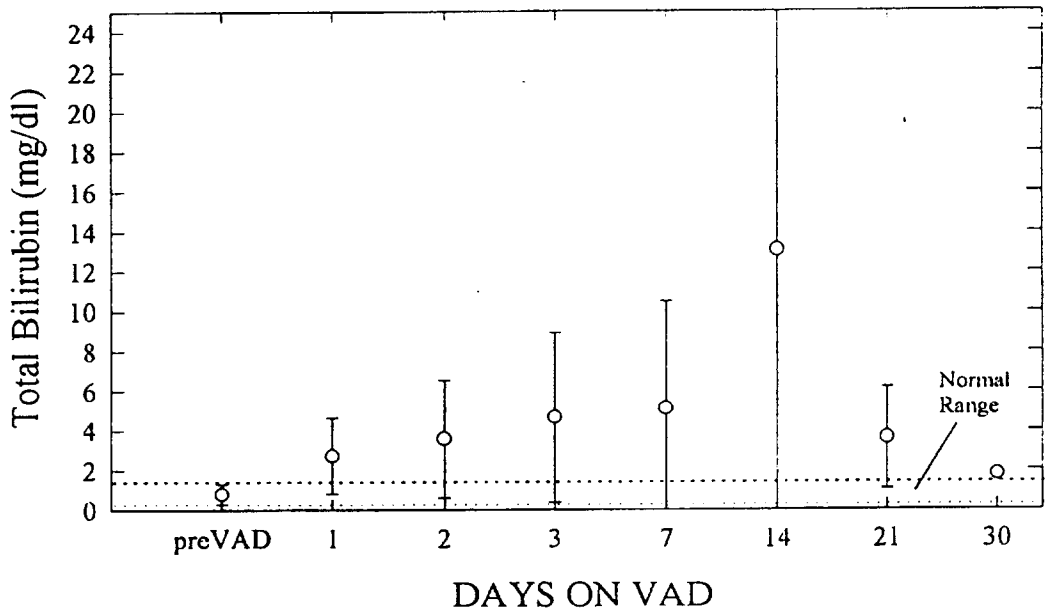
	Primary Data Cohort (N=29)			Other Postcardiotomy Data (N=31)			
Category	BVAD	LVAD	Total	BVAD	LVAD	RVAD	Total
Multi-organ Failure	2	2	4	5	1	3	9
Neurological	2	3	5	3	0	1	4
Sepsis	4	0	4	0	1	0	1
Bleeding	0	2	2	1	1	0	2
Respiratory	0	0	0	2	0	1	3
All causes	8	7	15	11	3	5	19

D. Impact on the body

Blood chemistry results were generally outside of normal ranges, but consistent with the underlying clinical condition of these patients. Blood trauma, determined from measurements of plasma free hemoglobin, hematocrit and platelet count during the period of VAD support, is not significantly different from that reported in the Summary of Safety and Effectiveness for bridging to cardiac transplantation.

Laboratory parameters indicative of end organ support: total bilirubin, blood urea nitrogen, creatinine, and plasma free hemoglobin, are presented in Figures 5 to 8.

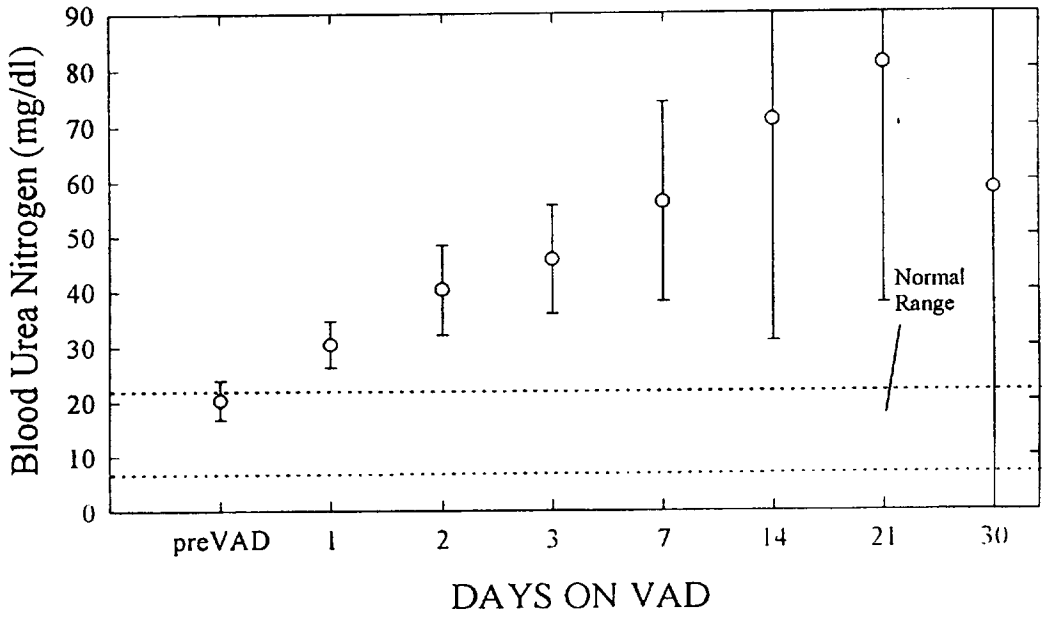
Figure 5. Total bilirubin before and after VAD implantation, mean ± 2.0 SEM, mg/dl, Primary Data Cohort (N=29).



Total Bilirubin (mg/dl)	DAYS ON VAD							
	Pre-VAD[a]	1[b]	2[b]	3[b]	7[c]	14[c]	21[c]	30[c]
Mean	0.8	2.7	3.6	4.7	5.1	13.1	3.6	1.8
Median	.65	2.5	2.8	3.1	2.8	8.7	3.4	1.8
SD	0.50	1.90	2.97	4.26	5.39	14.09	2.55	0
N	18	22	18	17	12	4	4	1
Min	0.1	0.5	0.6	0.7	0.7	1.5	0.8	1.8
Max	2.1	8.7	12.3	17.4	16.17	33.4	6.9	1.8
2.0 SEM	0.24	0.81	1.40	2.07	3.11	14.09	2.55	0

Notes:
a. Last value measured; generally within 24 hours prior to VAD implant.
b. Generally, single daily measurement; multiple daily measurements averaged over 24 hour period.
c. Average of 3 daily means for days n-1, n, and n+1.

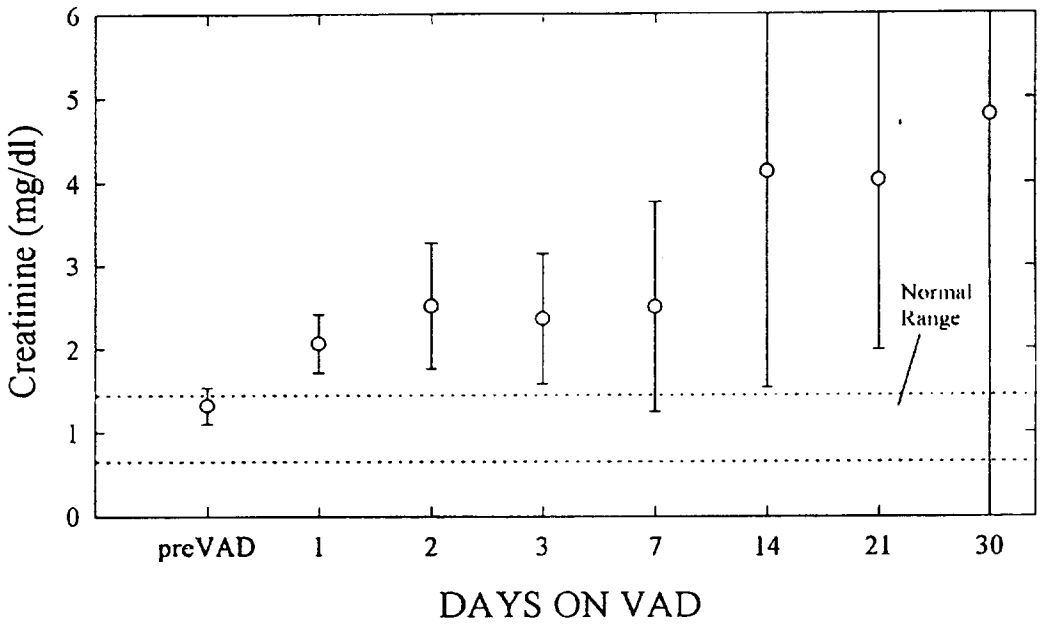
Figure 6. Blood urea nitrogen before and after VAD implantation, mean ± 2 0 SEM, mg/dl, Primary Data Cohort (N=29).



Blood Urea Nitrogen (mg/dl)	DAYS ON VAD							
	Pre-VAD[a]	1[b]	2[b]	3[b]	7[c]	14[c]	21[c]	30[c]
Mean	20	30	40	46	56	71	81	59
Median	19	28	40	44	50	90	96	59
SD	8.8	10.5	18.6	23.2	33.9	44.8	43.3	50.2
N	24	25	21	22	14	5	4	2
Min	7	14	17	17	16	15	20	23
Max	44	54	83	114	146	112	112	94
2.0 SEM	3.6	4.2	8.1	9.9	18.1	40.0	43.3	71

Notes:
a. Last value measured; generally within 24 hours prior to VAD implant.
b. Generally, single daily measurement; multiple daily measurements averaged over 24 hour period.
c. Average of 3 daily means for days n-1, n, and n+1.

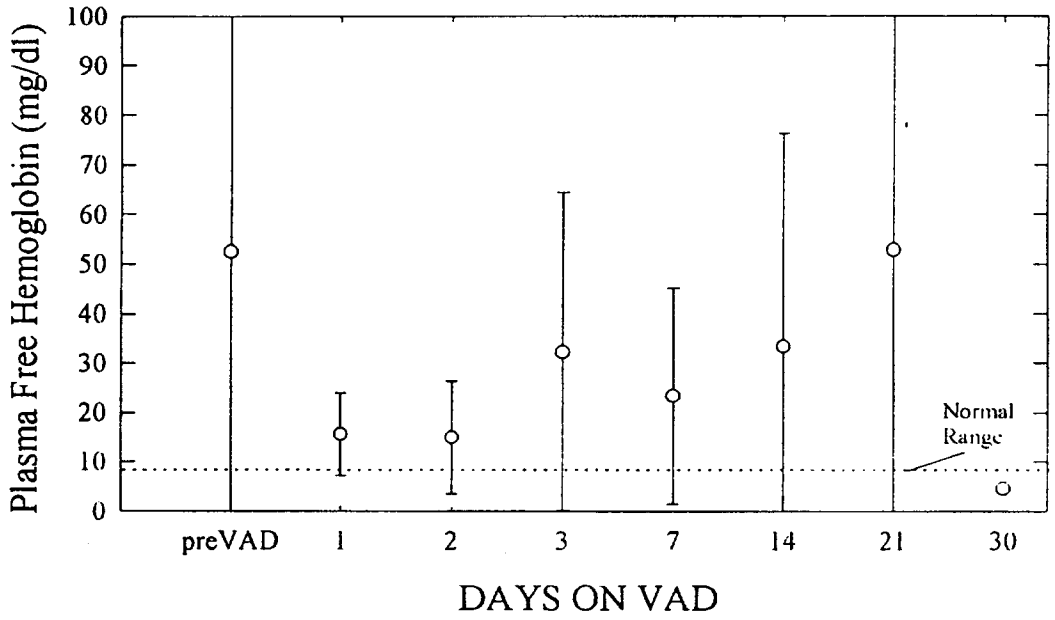
Figure 7. Creatinine before and after VAD implantation, mean ± 2.0 SEM, mg/dl, Primary Data Cohort (N=29).



Creatinine (mg/dl)	DAYS ON VAD							
	Pre-VAD[a]	1[b]	2[b]	3[b]	7[c]	14[c]	21[c]	30[c]
Mean	1.3	2.1	2.5	2.4	2..5	4.1	4.0	4.8
Median	1.2	2.0	2.1	1.6	1.6	5.5	4.1	4.8
SD	0.54	0.88	1.75	1.84	2.37	2.91	2.29	4.24
N	25	25	21	22	14	5	5	2
Min	0.4	1.0	0.7	0.5	0.4	0.7	1.7	1.8
Max	3.0	4.3	7.2	8.6	9.4	7.2	6.4	7.8
2.0 SEM	0.22	.04	.76	0.79	1.26	2.61	2.05	6.00

Notes:
a. Last value measured; generally within 24 hours prior to VAD implant.
b. Generally, single daily measurement; multiple daily measurements averaged over 24 hour period.
c. Average of 3 daily means for days n-1, n, and n+1.

Figure 8. Plasma free hemoglobin before and after VAD implantation, mean ± 2.0 SEM, mg/dl, Primary Data Cohort (N=29).



Plasma Free Hemoglobin (mg/dl)	DAYS ON VAD							
	Pre-VAD[a]	1[b]	2[b]	3[b]	7[c]	14[c]	21[c]	30[c]
Mean	52.5	15.6	15.0	32.2	23.4	33.4	52.9	4.6
Median	52.5	11.9	5.7	8.7	14.0	15.6	17.4	4.6
SD	38.8	16.9	20.6	53.2	26.7	37.1	62.5	-
N	2	16	13	11	6	3	3	1
Min	25.0	0.9	1.6	3.0	0.0	8.6	16.2	-
Max	79.9	69.0	64.0	171.0	69.6	76.0	125.0	-
2.0 SEM	54.9	8.4	11.4	32.1	21.8	42.8	72.1	-

Notes:
a. Last value measured; generally within 24 hours prior to VAD implant.
b. Generally, single daily measurement; multiple daily measurements averaged over 24 hour period.
c. Average of 3 daily means for days n-1, n, and n+1.

E. Evaluation for Gender Bias

The gender distribution of the Primary Data Cohort was 79% (23/29) male and 21% (6/29) female. The male predominance is similar to the male predominance for the incidence of, and death rates from coronary heart disease as reported by the Framingham Heart Study (Murabito, 1995) and the American Heart Association (1997).

Gender was not a significant factor associated with either survival to weaning from VAD support, or survival to discharge. Forty-eight percent (11/23) of the males and 50% (3/6) of the females were weaned from VAD support. Thirty-nine percent (9/23) of the males and 17% (1/6) of the females were discharged alive from the hospital.

F. Conclusions Drawn from the Studies

The results presented in the original PMA demonstrated that the Thoratec Ventricular Assist Device (VAD) System performed reliably, and that the device is biocompatible, sterile, and non-pyrogenic. Those results support a conclusion that the Thoratec VAD is safe for human use.

The present clinical study provides reasonable assurance that the device effectively reduces the workload of the heart, to allow myocardial recovery in some patients unable to be weaned from cardiopulmonary bypass after successful open heart operations. The data acquired during this multi-center study show that the Thoratec VAD is effective in restoring and maintaining patient hemodynamics, with improvements in the survival rate of post-cardiotomy patients who are unable to be weaned from cardiopulmonary bypass. Furthermore, analysis of the data indicates the Thoratec VAD is equally effective in both males and females.

The complication rate (adverse events) is acceptable and is comparable to the Thoratec VAD bridge to transplant study.

These data demonstrate that in the study patient population, the benefits of the Thoratec VAD System justified the risks. Further, the data support reasonable safety and effectiveness when used for a post-cardiotomy population to provide circulatory support pending myocardial recovery in patients unable to be weaned from cardiopulmonary bypass.

XIII. PANEL RECOMMENDATION

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

XIV. FDA DECISION

FDA issued an approval order on May 21, 1998.

FDA performed an inspection and found the applicant in compliance with the Quality System Regulation (21 CFR Part 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling

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

Postapproval Requirements and Restrictions: See approval order.