P990046

Summary of Safety and Effectiveness Data
ATS Open Pivot® Bileaflet Heart Valve

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SUMMARY of SAFETY and EFFECTIVENESS DATA
ATS Open Pivot® Bileaflet Heart Valve

1. GENERAL INFORMATION

Device Generic Name:	Replacement Heart Valve
Device Trade Name:	ATS Open Pivot® Bileaflet Heart Valve Aortic Models 500FA and 501DA, and Mitral Models 500DM and 501DM
Applicant's Name and Address:	ATS Medical, Inc. Suite 105 3905 Annapolis Lane Minneapolis, MN 55447
PMA Application Number:	P990046
Date of Notice of Approval to the Applicant:	OCT 13 2000

2. INDICATIONS FOR USE

The ATS Open Pivot® Bileaflet Heart Valve is indicated for the replacement of diseased, damaged, or malfunctioning native or prosthetic aortic or mitral valves.

3. DEVICE DESCRIPTION

The ATS Open Pivot® Bileaflet Heart Valve is a low profile bileaflet valve consisting of pyrolytic carbon orifice ring and leaflets.

The prosthesis consists of an orifice housing two mirror image leaflets. The low profile of the prosthesis results from the bileaflet design where the pivot areas are located entirely within the orifice ring, which minimizes the overall height of the valve. Pivot guides located on the inner circumference of the orifice ring control the range of leaflet motion. The pivot geometry consists of arc-shaped notches at either end of each leaflet and spherical protrusions at four places on the orifice. Each leaflet rotates around two opposing spheres. The inflow and outflow stops are adjacent to each sphere on the orifice, which limit the rotation of the leaflets. There are no recesses or cavities in the pivot area. In the closed position, the plane of each leaflet forms a nominal angle of 25° relative to the plane of the orifice ring. In the fully open position, the plane of each leaflet forms a nominal angle of 85° relative to the plane of the orifice ring.

The leaflets consist of pyrolytic carbon coated over a graphite substrate. The graphite substrate is impregnated with 20% tungsten for radiopacity. The orifice consists entirely of pyrolytic carbon.

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The valve sewing cuff is constructed of double velour polyester fabric and is mounted on the orifice using a titanium stiffening ring and secured with two titanium lock rings and a lock wire. This method of sewing cuff attachment to the orifice allows for rotation of the sewing cuff *in situ,* during surgical placement. The sewing cuff of mitral sizes 29, 31, and 33 mm contains a polytetrafluoroethylene (PTFE) liner inside the double velour polyester fabric.

The ATS Open Pivot® Bileaflet Heart Valve is available in the aortic and mitral configurations in two sewing cuff styles, the Standard and Advanced Performance (AP) styles. The AP model, with a reduced cuff, is a supra-annular configuration of the Standard model. The ATS Open Pivot® Bileaflet Heart Valve Standard model is available in sizes 21 through 29 mm in the aortic position (Model 500FA), and sizes 29 through 33 mm in the mitral position (Model 500DM). The ATS Open Pivot® Bileaflet Heart Valve AP model is available in sizes 18 through 26 mm in the aortic position (Model 501DA), and sizes 26 and 28 mm in the mitral position (Model 501DM).

4. CONTRAINDICATIONS

The ATS Open Pivot® Bileaflet Heart Valve is contraindicated in patients unable to tolerate anticoagulation therapy.

5. WARNINGS AND PRECAUTIONS

5.1. Warnings

- FOR SINGLE USE ONLY.
- Avoid damaging the prosthesis. Only handle the prosthesis with the accessories provided by ATS Medical. Touching of the valve with gloved fingers or any surgical instrument may cause damage to the valve surface not seen with the unaided eye that may lead to accelerated valve structural deterioration or leaflet escape, or serve as a nidus for thrombus formation.
- Do NOT pass a catheter through the prosthesis as this may cause valvular insufficiency, disc dislodgment, or catheter entrapment.
- Do NOT apply force to the leaflets, attempt to change the position of the leaflets, or remove a leaflet.

6. PRECAUTIONS

6.1. Precautions Prior to Use

- Do NOT use the ATS Open Pivot® Bileaflet Heart Valve if the prosthesis has been dropped, damaged, or mishandled in any way. Should the valve be damaged during implantation or removal from the package, do not use for implantation.

- Do NOT use the ATS Open Pivot® Bileaflet Heart Valve if the tamper evident seal is broken, or if the expiration date has elapsed.

- Do NOT resterilize any ATS Open Pivot® Bileaflet Heart Valve.

6.2. Precautions During Use

- Use only the ATS Medical Valve Sizer to select the proper valve size as other sizers may result in improper valve selection.

- When seating the valve, ensure that no suture material or anatomic structures interfere with leaflet motion. The valve's rotation capability may be helpful in avoiding abnormal residual pathology that could interfere with leaflet motion.

7. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative forms of treatment include medical therapy with drugs or surgical treatments such as annuloplasty or valvuloplasty with or without the use of implantable materials (i.e., annuloplasty rings, sutures). When the patient requires replacement of his/her native or previously placed prosthetic valve, the option of choosing a mechanical or biological valve exists. The choice of replacement valve depends upon factors that include the patient's age, preoperative conditions, cardiac anatomy, and ability to tolerate long term anticoagulation therapy.

8. MARKETING HISTORY

The ATS Open Pivot® Bileaflet Heart Valve is distributed in Argentina, Australia, Austria, Belgium, Brazil, Canada, China, Croatia, France, Germany, Greece, India, Israel, Italy, Japan, South Korea, Lebanon, Mauritius, Mexico, Morocco, Netherlands, Norway, Portugal, Russia, South Africa, Spain, Switzerland, Tunisia, Turkey, United Kingdom, and Yugoslavia.

The ATS Open Pivot® Bileaflet Heart Valve has not been withdrawn from the market in any country for any reason.

9. ADVERSE EVENTS

A multi-center, non-randomized, prospective, international clinical study was conducted of patients implanted with the ATS Open Pivot® Bileaflet Heart Valve. In this study, 685 patients had isolated aortic valve replacement (AVR), 280 patients had isolated mitral valve replacement (MVR), and 35 patients had double valve replacement (DVR) where both the aortic and the mitral valves were replaced with an ATS Open Pivot® Bileaflet Heart Valve. The study was conducted between 1994 and 1999. Patients were evaluated pre-operatively, intra-operatively, and post-operatively at discharge, at 3-6 months, at 1 year, and annually thereafter. Adverse events were captured throughout the post-operative period.

The adverse event rates were based on 965 patients at 20 centers. The cumulative follow-up was 1323 patient-years with a mean follow-up of 1.4 years (range 0 to 5 years).

A total of 56 deaths occurred during the study. Twenty (20) of these deaths were characterized as valve-related. The causes of valve-related deaths were endocarditis (2 patients), paravalvular leak (1 patient), thromboembolism (3 patients), anticoagulant-related hemorrhage (10 patients), and unknown (4 patients).

9.1. Observed Adverse Events

Table 1 shows the observed adverse events for early events (≤ 30 days), the linearized rates for late events (>30 days post-operatively), and the actuarial adverse event rates at one and five years post-operatively.

Table 1: Observed Adverse Events for AVR and MVR

	Early Events % of pts. (N)	Late Events %/pt-yr. (N)	Actuarial Freedom by Kaplan-Meier 1 Year [95% CI]	5 years [95% CI]
Aortic Valve Replacement, All patients implanted: N= 685, Cumulative Follow-up= 866.4 patient years				
Deaths (all causes)	2.04% (14)	2.77% ± 1.06% (24)	.9735 [± .01]	.9031 [± .05]
Death (valve-related/unexplained)	0.58% (4)	1.15% ± 0.74% (10)	.9817 [± .01]	.9539 [± .03]
Anticoagulant-Related Hemorrhage (All)	4.67% (32)	1.96% ± 0.91% (17)	.9781 [± .01]	.9340 [± .04]
Anticoagulant-Related Hemorrhage (Major)	3.21% (22)	1.27% ± 0.76% (11)	.9878 [± .01]	.9473 [± .04]
Thromboembolism (All)	1.75% (12)	2.08% ± 0.93% (18)	.9733 [± .01]	.9283 [± .05]
Permanent Neurological Events	0.88% (6)	0.69% ± 0.60% (6)	.9920 [± .01]	.9706 [± .04]
Transient Neurological Events	0.88% (6)	1.39% ± 0.78% (12)	.9812 [± .01]	.9564 [± .03]
Valve Thrombosis	0.00% (0)	0.00% ± 0.00% (0)	1.000 [± .00]	1.000 [± .00]
Perivalvular Leak (All)	0.15% (1)	0.46% ± 0.52% (4)	.9966 [± .00]	.9898 [± .01]
Perivalvular Leak (Major)	0.15% (1)	0.12% ± 0.33% (1)	.9983 [± .00]	.9983 [± .00]
Endocarditis	0.00% (0)	0.35% ± 0.46% (3)	.9960 [± .01]	.9908 [± .01]
Hemolysis	0.00% (0)	0.00% ± 0.00% (0)	1.000 [± .00]	1.000 [± .00]
Structural Dysfunction	0.00% (0)	0.00% ± 0.00% (0)	1.000 [± .00]	1.000 [± .00]
Nonstructural Dysfunction	0.00% (0)	0.00% ± 0.00% (0)	1.000 [± .00]	1.000 [± .00]
Reoperation	0.15% (1)	0.35% ± 0.46% (3)	.9961 [± .01]	.9914 [± .01]
Explant	0.00% (0)	0.23% ± 0.41% (2)	.9978 [± .00]	.9931 [± .01]

Notes:

1. Cumulative probability of freedom from event estimate at the end of the interval (Pc) is based on the Kaplan-Meier method.
2. The 95% confidence interval bound for the cumulative freedom rate at the end of the interval = 1.96 X SE, where SE is the standard error estimate of the cumulative probability of freedom from study heart valve related or unexplained event estimate calculated using Greenwood's formula.
3. The actuarial hazard rate estimates are calculated at the midpoint of each interval.
4. The 95% confidence interval bound for the hazard rate at the midpoint of each interval = 1.96 X SE, where SE is the standard error estimate of the hazard rate estimate at the midpoint of the interval.

Table 1: Observed Adverse Events for AVR and MVR - continued

	Early Events % of pts. (N)	Late Events %/pt-yr. (N)	Actuarial Freedom by Kaplan-Meier 1 Year [95% CI]	5 years [95% CI]
Mitral Valve Replacement, All patients implanted: N=280, Cumulative Follow-up= 374.7 patient years				
Deaths (all causes)	1.79% (5)	3.47% ± 1.88% (13)	.9814 [± .02]	.8099 [± .11]
Death (valve-related/unexplained)	0.71% (2)	1.07% ± 1.19% (4)	.9831 [± .02]	.9342 [± .07]
Anticoagulant-Related Hemorrhage (All)	3.21% (9)	0.53% ± 0.95% (2)	.9958 [± .01]	.9673 [± .06]
Anticoagulant-Related Hemorrhage (Major)	3.21% (9)	0.53% ± 0.95% (2)	.9958 [± .01]	.9673 [± .06]
Thromboembolism (All)	3.21% (9)	4.00% ± 2.00% (15)	.9534 [± .03]	.8589 [± .09]
Permanent Neurological Events	1.79% (5)	0.80% ± 1.08% (3)	.9910 [± .01]	.9807 [± .02]
Transient Neurological Events	1.43% (4)	3.20% ± 1.82% (12)	.9621 [± .03]	.8758 [± .09]
Valve Thrombosis	0.00% (0)	0.53% ± 0.95% (2)	.9947 [± .01]	.9866 [± .02]
Perivalvular Leak (All)	0.71% (2)	1.07% ± 1.19% (4)	.9819 [± .02]	.9819 [± .02]
Perivalvular Leak (Major)	0.36% (1)	0.53% ± 0.95% (2)	.9915 [± .01]	.9915 [± .01]
Endocarditis	0.36% (1)	0.53% ± 0.95% (2)	.9957 [± .01]	.9861 [± .02]
Hemolysis	0.00% (0)	0.53% ± 0.95% (2)	.9952 [± .01]	.9814 [± .03]
Structural Dysfunction	0.00% (0)	0.00% ± 0.00% (0)	1.000 [± .00]	1.000 [± .00]
Nonstructural Dysfunction	0.00% (0)	0.00% ± 0.00% (0)	1.000 [± .00]	1.000 [± .00]
Reoperation	0.71% (2)	1.07% ± 1.19% (4)	.9874 [± .01]	.9697 [± .03]
Explant	0.36% (1)	0.53% ± 0.95% (2)	.9959 [± .01]	.9783 [± .03]

Notes:

1. Cumulative probability of freedom from event estimate at the end of the interval (Pc) is based on the Kaplan-Meier method.
2. The 95% confidence interval bound for the cumulative freedom rate at the end of the interval = 1.96 X SE, where SE is the standard error estimate of the cumulative probability of freedom from study heart valve related or unexplained event estimate calculated using Greenwood's formula.
3. The actuarial hazard rate estimates are calculated at the midpoint of each interval.
4. The 95% confidence interval bound for the hazard rate at the midpoint of each interval = 1.96 X SE, where SE is the standard error estimate of the hazard rate estimate at the midpoint of the interval.

9.2. Potential Adverse Events

Adverse events potentially associated with the use of prosthetic heart valves (in alphabetical order) include:

- cardiac arrhythmias
- death
- leaflet entrapment (impingement)
- endocarditis
- hemolysis
- hemorrhage, anticoagulation-related
- leak, transvalvular or perivalvular
- prosthesis thrombosis
- structural deterioration
- valve thromboembolism

10. SUMMARY OF NONCLINICAL STUDIES

10.1. Bench testing

In vitro studies were performed for the ATS Open Pivot® Bileaflet Heart Valve as recommended in the FDA's *Draft Replacement Heart Valve Guidance* (1994).

10.1.1. Biocompatibility Studies

Selected short-term tests recommended in the Tripartite Biocompatibility Guidance for Medical Devices document have been conducted on material used in the ATS Open Pivot® Bileaflet Heart Valve and accessories.

Biocompatibility tests were performed according to the requirements of ISO 10993-1, with the exception of carcinogenicity and hemocompatibility testing. Carcinogenicity testing was determined to be unnecessary since the test devices demonstrated no mutagenic potential at the levels at or above those intended for clinical use. Hemocompatibility evaluation was determined in animal implant studies. See Section 10.2. All studies were performed in accordance with FDA Good Laboratory Practices Regulation (21 CFR Part 58). A matrix of tests performed and the corresponding results is provided in Table 2.

Table 2: Biocompatibility Studies Testing Results

Test Performed	Test Objective	Samples: Control	Samples: Test article	Results
In Vitro Inhibition of Cell Growth	Assess the effect of an extract of the material on the normal growth of cells in culture.	Negative control: Extract only Positive control: Known toxic material	ATS Open Pivot Bileaflet Heart Valve	Non-inhibitory to cell growth
USP Systemic Toxicity	Assess the systemic effect of a material extract in mice.	Negative control: Normal Saline and cottonseed oil	ATS Open Pivot Bileaflet Heart Valve	All mice normal. Non-toxic
Hemolysis	Assess the hemocompatibility of an extract of the device.	Negative control: Normal Saline Positive control: Known hemolytic material.	ATS Open Pivot Bileaflet Heart Valve	Mean hemolysis = 0%
Genotoxicity-Gene Mutation	Assess the mutagenicity of carbon components with extracts of Saline and DMSO.	Negative controls: Normal Saline and DMSO.	Carbon Components	Extracts were non-mutagenic.
Rabbit Implantation 7 days	Assess implantation effects.	3 USP control strips and 3 sections of test article per rabbit	Carbon Components	Macroscopic reaction was not significant as compared to the negative control implant material.

Table 2: Biocompatibility Studies Testing Results - continued

Rabbit Implantation 90 days	Assess implantation effects.	3 USP control strips and 3 sections of test article per rabbit	Carbon Components	Macroscopic reaction was not significant as compared to the control.
Cytotoxicity	Assess the effect of an extract on the normal growth of cells in culture.	Negative Control: MEM, Positive Control Known material	Accessories	Non-cytotoxic
Sensitization-Guinea Pig Maximization	Assess the potential of a material to produce sensitization when material saline and cottonseed oil extracts are exposed to the test animal.	Negative control: Normal Saline and cottonseed oil	Accessories	No evidence of causing delayed dermal contact sensitization in the guinea pig.
Acute Systemic Toxicity - USP 22 Mouse Injection	Assess the systemic effect of material extract in mice.	Negative control: Normal Saline and cottonseed oil.	Accessories	All mice normal. Non-toxic
Hemocompatibility	Assess the affect of an extract on blood.	Normal Saline extract	Accessories	Non-hemolytic
Pyrogenicity USP 22	Assess the pyrogenicity of an extract	Non-pyrogenic Saline	Accessories	Non-pyrogenic

10.1.2. Hydrodynamic Performance

In vitro hydrodynamic performance studies of the ATS Open Pivot® Bileaflet Heart Valve were completed according to test recommendations outlined in FDA's *Draft Replacement Heart Valve Guidance* (1994) and ISO 5840 *Cardiovascular Implants-Cardiac Valve Prostheses.* Commercially available mechanical valves were used as controls. All test and control valves were final production samples. A matrix of the hydrodynamic tests is provided in Table 3.

Table 3: Hydrodynamic Performance Testing and Results

Test performed	**Sample Size: Control**	**Sample Size: ATS Open Pivot® Bileaflet Heart Valve**	**Results**
Steady Forward Flow Pressure Drop	3 valves of each size (19, 23, and 31 mm)	3 valves of each size (16/19, 18/2, 20/23, 22/25, 24/27, 26/29, and 28/31/33 mm)	The test results revealed that steady flow pressure drop is approximately the same in both the aortic and mitral positions and consistent with results reported in the literature.
Steady Backflow leakage Testing	1 each 23 mm	3 valves of each size (16/19, 18/2, 20/23, 22/25, 24/27, 26/29, and 28/31/33 mm)	The leakage rate of the test valves was less than the control valve.
Pulsatile Flow Pressure Drop	3 each 19, 23, and 31 mm	3 valves of each size (16/19, 18/2, 20/23, 22/25, 24/27, 26/29, and 28/31/33 mm)	Results were comparable to the control valve.

Table 3: Hydrodynamic Performance Testing and Results - continued

Pulsatile Flow Regurgitation	3 each 19, 23 and 31 mm	3 valves of each size (16/19, 18/2, 20/23, 22/25, 24/27, 26/29, and 28/31/33 mm)	Results were comparable to the control valve.
Laser Doppler Anemometry	1 each size 27 mm	1 each size 27 mm	Similar flow patterns were observed with the test and control valves. The highest turbulent shear stress for the ATS valve was measured to be 25.2 Pa with the corresponding values for the control 45 Pa.
Flow Visualization	N/A	1 each size 19 and 27 mm	There were no adverse flow characteristics observed with test valves.
Verification of the Bernoulli Relationship	N/A	1 each size 19, 23, 27, and 31 mm	Transvalvular pressure drops determined by Doppler ultrasound showed good correlation.

10.1.3. Structural Performance

In vitro structural performance studies of the ATS Open Pivot® Bileaflet Heart Valve were performed in accordance with testing recommendations outlined in FDA's *Draft Replacement Heart Valve Guidance (1994)* and ISO 5840 *Cardiovascular Implants- Cardiac Valve Prostheses.* Commercially available valves were used as controls in those studies that require concurrent testing. All control and reference valves were final production samples. A matrix of the structural performance tests performed is provided in Table 4.

Table 4: Structural Performance Testing and Results

Test performed	**Sample Size: Control**	**Sample Size: ATS Open Pivot® Bileaflet Heart Valve**	**Results**
Material characterization testing - carbon coated graphite	N/A	Carbon-coated graphite specimen	Crack initiation fracture toughness (K_c) values between 1.00 to 2.59 MPa/m; worst case Paris law coefficients for fatigue crack growth rates were $da/dN=56.5 (\text{delta } K)^{63}$ in units of m/cycle; worst case crack growth rate of $da/dt=2.7 \times 10^{-9}K^{75}$
Material characterization testing - pyrolytic carbon	N/A	Pyrolytic carbon specimen	Crack initiation fracture toughness (K_c) value of 1.0MPa/m; worst case fatigue crack growth rates were $da/dN=4141 (\text{delta } K)^{88.9}$ in units of m/cycle; worst case crack growth rate of $da/dt=21.36 \times 10^{-7}K^{13.8}$

Table 4: Structural Performance Testing and Results - continued

Accelerated Wear Testing	2 each 31 mm	10 each 31 mm	The magnitude of leaflet depth wear varied on the tester used. For the two sets of ATS valves, the average inflow leaflet wear depths were 34.8 microns and 59.1 microns. For the corresponding control valves, average inflow wear depths were 32 and 47.2 microns.
Stress Analysis	N/A	19 and 31 mm sizes	Worse case stresses were used in fracture mechanics formulae to calculate the critical crack size at fracture. Paris law fatigue crack growth computations were used to calculate the initial length of cracks that would grow to critical size in 100 years or less at 72 bpm.
Fatigue Lifetime Determination	N/A	19 and 31 mm sizes	A proof test was designed by fracture mechanics methods to ensure valves placed in service at 200 mmHg systolic pressure will survive at least 100 years at 72 bpm
Dynamic Failure Mode	1 each 31 mm	6 each 31 mm	The test suggested the ultimate failure mode is fracturing of either the orifice or the leaflet at the point of contact between the major radius of the leaflet and orifice. Failures did not occur until loading conditions were greater than 780 mmHg. No failures occurred in the pivot regions.
Sewing Ring Integrity Testing	N/A	1 each standard and AP valves	Cuff push-off force was >100 lbs for all sizes except size 16. Size 16 valve tested in excess of 50 lbs before fixturing difficulties ended the test.
Leaflet Escape Testing	1 each 19, 21, 23, 29, and 31	3 each size standard valves and 3 each size AP valves	Minimum load to leaflet escape is 29.6 lbs and comparable to control valves.
Leaflet Impingement Testing	Literature	Minimum 3 each size Standard and AP valves	Minimum load to impingement 5 lbs compared to 3.5 lbs for literature control valve.

10.2. Animal testing

Animal studies were conducted in compliance with Good Laboratory Practices. Ten (10) juvenile sheep underwent mitral valve replacement with either a size 23 mm ATS Open Pivot® Bileaflet Heart Valve (n=8) or a 23 mm commercially available valve (n=2). Parameters evaluated included ease of surgical implantation, assessment of valve-related deaths, hemodynamic performance, and pathological impact following 150 days implantation. There were no surgical complications and no technical failures. All animals underwent angiography and sacrifice after 150 days post-operatively or greater. Blood abnormalities were not detected. Angiography analysis demonstrated normally functioning valves with minimal regurgitation and small transvalvular pressure gradients. Pathological evaluation of the 10 surviving animals revealed all implant devices functioning fully at autopsy. Paravalvular leaks detected in animals implanted with the ATS Open Pivot® Bileaflet Heart Valve or the control valves were attributed to surgical technique.

10.3. Sterilization and Shelf life

The ATS Open Pivot® Bileaflet Heart Valve is terminally sterilized using steam to a sterility assurance level (SAL) of at least 10^{-6}. Product is quarantined until sterility is verified. Revalidation of this process is performed annually.

Resterilization and cleaning of accessory components (sizers) was validated using an artificial soil inoculated with *B. stearothermophilus*. The cleaning method achieved a > 4 log reduction of spores. Terminal sterilization of the accessories using steam yielded a SAL of at least 10^{-6}.

Both packaging and product integrity studies were conducted to ensure that the shelf life for the package and product is maintained for a minimum of three years. These studies consisted of real-time and accelerated aging.

10.4. Magnetic Resonance Imaging (MRI) Testing

The ATS Open Pivot® Bileaflet Heart Valve has been shown to be safe when tested using MR systems operating with shielded static magnetic field strengths of 1.5 Tesla or less. However, the testing may cause significant MRI image artifacts or distortion. This phenomenon produced no harmful effects to the patient.

11. SUMMARY OF CLINICAL STUDIES

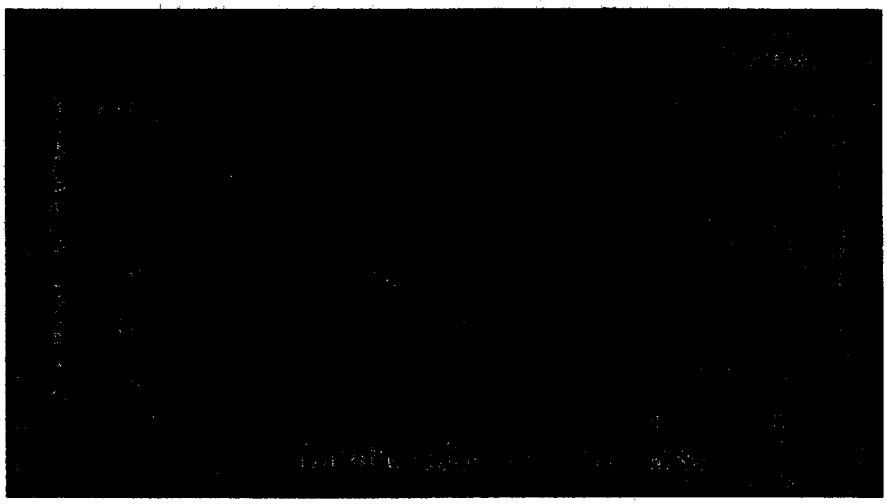
The safety endpoints captured in the prospective studies were complications. The safety results are provided in Table 1 above. Effectiveness endpoints were New York Heart Association (NYHA) functional classification and echocardiographic assessments. Preoperative and operative patient demographics are presented below, followed by the effectiveness results.

Table 5: Patient Characteristics

All patients implanted, N = 965, 1323 patient-years

Description of Patients	Aortic Valve N = 685 (70.98%)	Mitral Valve N = 280 (29.02%)
Age at implant in years		
0-9	5 (0.7%)	6 (2.1%)
10-19	4 (0.6%)	0 (0.0%)
20-29	11 (1.6%)	2 (0.7%)
30-39	33 (4.8%)	14 (5.0%)
40-49	72 (10.5%)	31 (11.1%)
50-59	142 (20.7%)	52 (18.6%)
60-69	238 (34.7%)	107 (38.2%)
70-79	155 (22.6%)	62 (22.1%)
80 & over	25 (3.6%)	6 (2.1%)
Gender		
Male	460 (67.2%)	120 (42.9%)
Female	225 (32.8%)	160 (57.1%)
Etiology of valve disease		
Stenosis	541 (79.0%)	118 (42.1%)
Insufficiency	330 (48.2)	210 (75.0%)
Mixed	205 (29.9%)	63 (22.5%)
Other	12 (1.8%)	12 (4.3%)

Figure 1: Number of Patients by Implant Location over Time
All patients implanted, N=965



Year	0	1	2	3	4	5
Total Patients	965	624	331	135	92	2
Aortic Patients	685	436	231	93	58	2
Mitral Patients	280	188	100	42	34	0

Table 6: Number of Patients Implanted and Maximum Number of Patients with Hemodynamic Data at > 6 Months Follow-Up
By implant location and valve size, n[1] = 493, N=965

Implant Location	Valve size (mm)							
	16/19	18/21	20/23	22/25	24/27	26/29	28/31/33	Total
Aortic (N/n)	23/9	100/61	202/108	206/113	111/70	39/32	4/4	685/397
Mitral (N/n)	0/0	3/1	5/4	3/2	23/8	71/39	175/106	280/160
Total (N/n)	23/9	103/62	207/112	209/115	134/78	110/71	179/110	965/557

Note:
1. n = number of patients with hemodynamic data; N = number of patients implanted

Table 7: Number of Patient-Years by Implant Location and Valve Size
By implant location and valve size, all patients implanted, N = 965

Implant Location	Valve size (mm)								
	16/19	18/21	20/23	22/25	24/27	26/29	28/31	33	Total
Aortic	15.7	159.3	275.0	255.6	150.1	61.1	7.4	0	924.2
Mitral	0	2.2	4.8	2.4	17.6	99.8	97.7	174.0	398.5
Total	15.7	161.5	279.8	258.0	167.7	160.9	105.1	174.0	1322.7

Table 8: Effectiveness Outcomes, Functional New York Heart (NYHA) Classification

NYHA Class	Pre-op		1 Year (11-14 Months)		2 Year (23-26 Months)		3 Year (35-38 Months)		4 Year (47-50 Months)	
	n/N[1]	%	n/N	%	n/N	%	n/N	%	n/N	%
Aortic Valve Replacement, N = 685										
I	4/685	0.6%	399/431	92.5%	205/231	88.7%	85/94	90.4%	53/58	91.4%
II	267/685	38.9%	25/431	5.8%	20/231	8.7%	7/94	7.4%	5/58	8.6%
III	340/685	49.6%	1/431	0.2%	1/231	0.4%	0/94	0%	0/58	0%
IV	68/685	9.9%	1/431	0.2%	1/231	0.4%	0/94	0%	0/58	0%
Missing	6/685	0.9%	5/431	1.2%	4/231	1.7%	2/94	2.1%	0/58	0%
Mitral Valve Replacement, N = 280										
I	0/280	0%	158/182	86.8%	78/100	78.0%	33/42	78.5%	28/34	82.4%
II	74/280	26.4%	19/182	10.4%	19/100	19.0%	8/42	19.0%	5/34	14.7%
III	155/280	55.4%	3/182	1.6%	2/100	2.0%	1/42	2.4%	1/34	2.9%
IV	45/280	16.1%	0/182	0%	0/100	0%	0/42	0%	0/34	0%
Missing	6/280	2.1%	2/182	1.1%	1/100	1.0%	0/42	0%	0/34	0%

Note:
1. N = all values reported; n = number in subgroup

Table 9: Effectiveness Outcomes – Hemodynamics, Valvular Regurgitation

Valvular Regurgitation	Early[1] % patients, n/N[3]	Late[2] % patients, n/N[3]
Aortic Valve Replacement, N = 685		
No Regurgitation	41.4%, 244/590	34.8%, 119/342
Trivial Regurgitation	57.6%, 340/590	64.6%, 221/342
Mild Regurgitation	1.0%, 6/590	0.6%, 2/342
Moderate Regurgitation	0%, 0/590	0%, 0/342
Severe Regurgitation	0%, 0/590	0%, 0/342
Mitral Valve Replacement, N = 280		
No Regurgitation	60.7%, 128/211	60.5%, 78/129
Trivial Regurgitation	37.4%, 79/211	38.0%, 49/129
Mild Regurgitation	1.9%, 4/211	1.6%, 2/129
Moderate Regurgitation	0%, 0/211	0%, 0/129
Severe Regurgitation	0%, 0/211	0%, 0/129

Notes:
1. Early post-operative evaluation conducted at 30-days post-implantation or hospital discharge.
2. Late post-operative evaluation = 11-14 months post-implantation.
3. N = all values reported; n = number in subgroup

Table 10: Effectiveness Outcomes – Hemodynamics, Mean Pressure Gradient and Effective Orifice Area

Endpoint	Early[1] n/N[3], mean ± SD (min, max)	Late[2] n/N, mean ± SD (min, max)
Aortic Valve Replacement, N = 685		
Mean Gradient (mm Hg)		
16/19mm	15/23, 25.8 ± 5.1 (10.5, 49.0)	9/23, 20.2 ± 2.8 (15.0, 26.6)
18/21mm	87/100, 18.7 ± 1.7 (2.4, 42.0)	61/100, 18.0 ± 1.6 (7.0, 36.0)
20/23mm	181/202, 14.3 ± 0.8 (2.6, 37.0)	107/202, 13.1 ± 0.8 (5.1, 30.1)
22/25mm	187/206, 12.8 ± 0.8 (2.6, 29.5)	112/206, 11.1 ± 0.8 (3.2, 26.0)
24/27mm	102/111, 10.0 ± 0.7 (1.8, 22.0)	70/111, 8.0 ± 0.8 (1.3, 16.7)
26/29mm	38/39, 9.2 ± 1.1 (3.5, 18.0)	32/39, 7.8 ± 1.1 (2.0, 13.0)
28/31mm	3/4, 3.0 ± 0.7 (2.6, 3.8)	4/4, 5.1 ± 3.3 (1.4, 9.3)
Effective Orifice Area (cm^2)		
16/19mm	11/23, 1.1 ± 0.2 (0.7, 1.8)	8/23, 1.2 ± 0.3 (0.8, 1.9)
18/21mm	81/100, 1.5 ± 0.1 (0.8, 3.7)	60/100, 1.5 ± 0.1 (0.7, 3.4)
20/23mm	165/202, 1.7 ± 0.1 (0.8, 6.6)	102/202, 1.7 ± 0.1 (0.9, 3.7)
22/25mm	173/206, 2.0 ± 0.1 (1.1, 4.0)	103/206, 2.1 ± 0.1 (1.0, 4.9)
24/27mm	97/111, 2.4 ± 0.2 (1.1, 4.8)	65/111, 2.5 ± 0.2 (1.5, 4.9)
26/29mm	34/39, 3.0 ± 0.3 (1.4, 4.7)	28/39, 3.1 ± 0.4 (1.4, 5.4)
28/31mm	3/4, 2.8 ± 0.8 (2.0, 3.4)	3/4, 3.1 ± 1.6 (1.6, 4.5)
Mitral Valve Replacement, N = 280		
Mean Gradient (mmHg)		
16/19mm	0	0
18/21mm	0/3	1/3, 6.0 (6.0, 6.0)
20/23mm	3/5, 5.3 ± 3.6 (3, 9)	4/5, 4.6 ± 0.9 (4.0, 6.0)
22/25mm	1/3, 10.0 (10, 10)	2/3, 5.4 ± 4.7 (3.0, 7.8)
24/27mm	15/23, 4.4 ± 0.9 (2.3, 7.9)	8/23, 4.5 ± 0.9 (2.4, 6.2)
26/29mm	66/71, 3.7 ± 0.4 (1.5, 10.0)	39/71, 3.7 ± 0.7 (1.3, 9.9)
28/31/33mm	154/175, 3.5 ± 0.3 (0.7, 9.0)	106/175, 3.1 ± 0.2 (0.3, 7.3)
Effective Orifice Area (cm^2)		
16/19mm	0	0
18/21mm	0/3	1/3[4]
20/23mm	3/5, 2.9 ± 0.6 (2.3, 3.3)	3/5, 1.6 ± 0.3 (1.3, 1.8)
22/25mm	1/3, 1.6 (1.6, 1.6)	2/3, 1.8 ± 0.5 (1.5, 2.0)
24/27mm	15/23, 3.3 ± 0.5 (1.8, 5.2)	8/23, 2.9 ± 0.9 (1.6, 5.7)
26/29mm	63/71, 3.3 ± 0.2 (1.6, 5.0)	38/71, 2.8 ± 0.3 (1.0, 4.6)
28/31/33mm	140/175, 3.0 ± 0.2 (1.3, 7.6)	95/175, 2.9 ± 0.2 (1.5, 7.4)

Notes:

1. Early post-operative evaluation conducted at 30-days post implantation or hospital discharge.
2. Late post-operative evaluation = 11-14 months post implantation
3. N= all values reported; n = number in subgroup
4. Echo confirmed valve function.

11.1. Description of Patients and Analysis for Gender Bias

A gender bias was not found in the ATS Open Pivot® Bileaflet Heart Valve clinical study. Of the 965 patients, 60% (580/965) were male and 40% (385/965) were female. This gender distribution is consistent with incidence of patients presenting for valve replacement. The results of analysis for morbidity/mortality by gender were not significant following valve replacement.

12. CONCLUSIONS DRAWN FROM THE STUDIES

The results from pre-clinical laboratory studies performed on the ATS Open Pivot® Bileaflet Heart Valve for biocompatibility testing, hydrodynamic performance testing, and structural performance testing demonstrate that this device is suitable for long-term implant.

The animal studies show that the ATS Open Pivot® Bileaflet Heart Valve is safe for valve replacement.

The clinical studies submitted in the PMA provide scientific evidence that the ATS Open Pivot® Bileaflet Heart Valve is safe and effective for the replacement of native or prosthetic aortic or mitral valves.

13. PANEL RECOMMENDATIONS

In accordance with the provisions of section 510(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Device Panel, a FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

14. FDA DECISION

FDA issued an approval order on OCT 13 2000.

The applicant's manufacturing and control facilities were inspected on September 13, 1999, and the facilities were found to be in compliance with the Good Manufacturing Practices (GMP) regulation.

15. APPROVAL SPECIFICATIONS

Direction for Use: See Final Draft Labeling (Instructions for Use).

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the Final Draft Labeling (Instructions for Use).

Post-approval Requirements and Restrictions: See Approval Order.