SUMMARY OF SAFETY AND EFFECTIVENESS DATA
SJM Biocor® Valve and SJM Biocor® Supra Valve

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1. General Information

Device Generic Name:	Replacement Heart Valve
Device Trade Name(s):	SJM Biocor® Valve aortic sizes 21, 23, 25, and 27 mm and mitral sizes 27, 29, 31, and 33 mm SJM Biocor® Supra Valve aortic valve sizes 19, 21 and 23 mm
Applicant's Name and Address:	St. Jude Medical, Inc. One Lillehei Plaza St. Paul, MN 55117
PMA Application number:	P040021
Date of Notice of Approval to the Applicant:	AUG - 5 2005

2. Indications for Use

The SJM Biocor® valve is intended as a replacement for a diseased, damaged, or malformed aortic or mitral native heart valve. It may also be used as a replacement for a previously implanted aortic or mitral prosthetic heart valve.

The SJM Biocor® Supra valve is intended as a replacement for a diseased, damaged, or malformed native aortic heart valve. It may also be used as a replacement for a previously implanted aortic prosthetic heart valve.

3. Device Description

3.1 SJM Biocor® Valve

The SJM Biocor® valve is a triple composite bioprosthetic heart valve manufactured from selected porcine aortic valve cusps. The cusps are matched for optimum leaflet coaptation and hemodynamics. Only cusps devoid of the septal muscle bar are utilized in the fabrication of the valve. Following tissue fixation, the tissue is mounted onto a polyester covered flexible acetal copolymer stent. The stent is a low profile design with a scalloped shape permitting supra-annular placement of the sewing cuff and intra-annular placement of the inflow edge of the prosthesis. For radiopaque visualization, the valve contains a wire within the sewing cuff.

The SJM Biocor® valve is fabricated with a bovine pericardial sheath. The pericardial sheath is attached directly to the outflow edge of the valve thereby protecting the leaflets as they open and close. The pericardial sheath and the porcine valve cusps are preserved

and crosslinked in a glutaraldehyde solution. Glutaraldehyde, formaldehyde, and ethanol are used in the valve sterilization process. The SJM Biocor® valve is supplied sterile and non-pyrogenic.

The SJM Biocor® valve is available for aortic tissue annulus sizes 21mm, 23mm, 25mm, and 27mm; and mitral tissue annulus sizes 27mm, 29mm, 31mm and 33mm.

3.2 SJM Biocor® Supra Valve

The SJM Biocor® Supra valve is identical to the SJM Biocor® valve with the exception of the valve sewing cuff.

The SJM Biocor® Supra valve is a triple composite bioprosthetic heart valve manufactured from selected porcine aortic valve cusps. The cusps are matched for optimum leaflet coaptation and hemodynamics. Only cusps devoid of the septal muscle bar are utilized in the fabrication of the valve. The SJM Biocor® Supra valve is designed for supra annular placement in the aortic position. Following tissue fixation, the tissue is mounted on a polyester covered flexible acetal copolymer stent. The valve sewing cuff contains a silicone elastomer insert. For radiopaque visualization, the SJM Biocor® Supra valve contains a wire within the sewing cuff.

The SJM Biocor® Supra valve is fabricated with a bovine pericardial sheath. The pericardial sheath is attached directly to the outflow edge of the valve thereby protecting the leaflets as they open and close. The pericardial sheath and the porcine valve cusps are preserved and crosslinked in a glutaraldehyde solution. Glutaraldehyde, formaldehyde, and ethanol are used in the valve sterilization process. The SJM Biocor® Supra valve is supplied sterile and non-pyrogenic.

The SJM Biocor® Supra valve is designed for supra annular placement in the aortic position and is available for tissue annulus sizes 19mm, 21mm and 23mm.

4. Contraindications

None known.

5. Warnings and Precautions

The warnings and precautions are provided in the device labeling for the SJM Biocor® valve and the SJM Biocor® Supra valve.

6. Alternative Practices and Procedures

The alternative treatments to the SJM Biocor® valve and the SJM Biocor® Supra valve include drug therapy or surgical treatments such as annuloplasty or valvuloplasty (with or without the use of implantable materials). If a patient requires replacement of their native or

previously implanted prosthetic valve, the alternatives include other commercially available mechanical valves, homografts, or bioprosthetic valves. The choice of replacement valve depends on an assessment of patient factors which include age, preoperative condition, anatomy, and the patient' s ability to tolerate long-term anticoagulant therapy.

7. Marketing History

Commercial distribution of the SJM Biocor® valve outside the U.S. began in 1981, and the valve is currently available in the following countries: Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Columbia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Korea, Luxembourg, Netherlands, Portugal, Spain, Sweden, Switzerland, Taiwan, Thailand, and the United Kingdom.

The SJM Biocor® Supra valve has recently been approved for commercial distribution in Canada and Europe.

The SJM Biocor® valve and SJM Biocor® Supra valve have never been withdrawn from commercial distribution for any reason relating to safety and effectiveness of the device.

8. Adverse Events

8.1 Sahlgrenska University Hospital, Gothenburg, Sweden

Between January 1983 and December 1999, 1492 patients requiring aortic and/or mitral valve replacement (AVR = 1263, MVR = 172, DVR = 57) were consecutively enrolled at the Sahlgrenska University Hospital in Gothenburg, Sweden. Demographic and baseline data were collected preoperatively. Adverse event data was collected at time of occurrence or upon site notification. The cumulative follow-up for the 1492 patients in Sweden was 7718.1 patient-years with a mean follow-up of 5.2 years (SD = 4.3 years, range 0 - 16.9 years).

Data Presentation

The observed adverse event rates for AVR and MVR are presented in Tables 1 and 2, respectively. The data is presented as early events (those events that occurred on or before 30 days post-implant), late events (those events that occurred 31 days or more post-implant) and "freedom from event" survival analyses.

Early Events

For each event category, the number of patients experiencing early events is reported as an adjusted percentage. In Tables 1 and 2:

n_1 = number of patients experiencing the adverse event on or before 30 days post-implant

% = adjusted early adverse event rate based on a Bayesian "missing data approach" with rates distributed a priori as Beta (1,1)

Late Events

For each event category, the number of patients experiencing late events is reported as an adjusted linearized incidence rate. In Tables 1 and 2:

n_l = number of events that occurred 31 days or more post-implant
%/pt-yr = adjusted late rate based on a Bayesian "missing data approach" rates distributed a priori as Gamma (0.01,0.01)

Survival Analyses

Survival analyses (i.e., "freedom from event") have been performed using an adjusted Kaplan-Meier product limit method for the adverse events occurring in one or more patients. The percent free from event and 95% confidence interval is provided at 1 year, 5 year and 8 year intervals. The Kaplan-Meier (product-limit) adjusted estimates of the cumulative percentage of patients event-free at the start of the interval, based on the Bonferroni inequality, are presented. The 95% confidence limits are also provided by determining the estimate ± 1.96* standard error. Adverse events occurring in both the early and late postoperative period are included in the analysis. In Tables 1 and 2:

% = adjusted estimate of the cumulative percentage of patients event-free at the start of the interval, is based on the Bonferroni inequality.
95% CI = estimate ± 1.96* standard error. The standard error is calculated from the Greenwood standard error for each rate and conservatively assuming the highest possible covariance between the two estimates.

8.1.1 Observed Adverse Events for Aortic Valve Replacements (Sweden)

Table 1 presents the adverse events for aortic valve replacements based on 1263 isolated aortic valve patients enrolled at the Sahlgrenska University Hospital in Sweden. The cumulative follow-up for aortic valve replacements in Sweden was 6368.6 patient-years.

Table 1. Observed Adverse Event Rates for AVR (Sweden)

All isolated aortic valve replacements: N=1263, cumulative follow-up=6268.7 late patient-years

Adverse Event	Early Events[1] n=1263		Late Events[2] n=1189		Freedom From Event		
					1 Year	5 Year	8 Year
	n_l	%	n_l	%/pt-yr	% [95% CI]	% [95% CI]	% [95% CI]
Mortality (All)	50	4.11	363	5.79	91.7 [90.1, 93.2]	75.4 [72.7, 78.2]	61.4 [57.9, 65.0]
- Valve-related (includes unknowns)	9	0.87	41	0.66	98.2 [97.5, 99.0]	96.5 [95.3, 97.7]	94.1 [92.2, 96.0]
Reoperation (including explant)	4	0.48	104	1.86	97.8 [96.4, 99.2]	94.2 [92.1, 96.4]	89.0 [84.5, 93.6]
Explant	4	0.48	104	1.86	97.8 [96.4, 99.2]	94.2 [92.1, 96.4]	89.0 [84.5, 93.6]
Endocarditis	0	0.16	32	0.56	98.9 [97.7, 100.0]	97.3 [95.6, 99.1]	96.0 [93.8, 98.3]
Anticoagulant-related hemorrhage	7	0.71	47	0.80	97.3 [95.7, 98.9]	95.8 [93.9, 97.8]	94.1 [91.6, 96.5]
Nonstructural dysfunction[3]	4	0.48	16	0.26	98.9 [97.7, 100.0]	98.3 [96.9, 99.7]	98.0 [96.5, 99.6]
- Paravalvular leak[4]	4	0.48	16	0.26	98.9 [97.7, 100.0]	98.3 [96.9, 99.7]	98.0 [96.5, 99.6]
Structural deterioration	0	0.16	67	1.12	99.4 [98.9, 99.8]	97.3 [96.2, 98.4]	92.4 [88.2, 96.7]
Embolism (All)	7	0.71	117	1.96	97.0 [95.3, 98.8]	89.6 [85.7, 93.6]	85.1 [80.3, 89.8]
- Permanent	6	0.63	45	0.77	98.7 [97.5, 99.9]	95.5 [92.8, 98.2]	93.4 [90.2, 96.7]
Valve Thrombosis	0	0.16	0	0.00	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]

1 Early events are those occurring on or before 30 days post-implant. Adjusted early adverse event rate based on a Bayesian "missing data approach" with rates distributed a priori as Beta(1,1) for the events in the 2000 database and events in data reconstruction.
2 Late events are those occurring 31 days post-implant or thereafter. Adjusted late rate based on a Bayesian "missing data approach" rates distributed a priori as Gamma (0.01,.0.01) for the events in the 2000 database and events in data reconstruction.
3 Including paravalvular leak
4 No events related to endocarditis

8.1.2 Observed Adverse Events for Mitral Valve Replacements (Sweden)

Table 2 presents the adverse events for mitral valve replacements based on 172 isolated mitral valve patients enrolled at the Sahlgrenska University Hospital in Sweden. The cumulative follow-up for mitral valve replacements in Sweden was 968.3 patient-years.

Table 2. Observed Adverse Event Rates for MVR (Sweden)

All isolated mitral valve replacements: N=172, cumulative follow-up=955.2 late patient-years

Adverse Event	Early Events[1] n=172		Late Events[2] n=152		Freedom From Event		
					1 Year	5 Year	8 Year
	n_1	%	n_1	%/pt-yr	% [95% CI]	% [95% CI]	% [95% CI]
Mortality (All)	19	12.07	66	7.31	80.5 [74.5, 86.5]	63.6 [55.9, 71.3]	47.4 [28.5, 66.3]
- Valve-related (includes unknowns)	2	2.30	10	1.42	96.8 [93.9, 99.6]	94.9 [91.1, 98.7]	88.0 [72.8, 100.0]
Reoperation (including explant)	0	1.15	21	2.55	97.3 [94.6, 99.9]	92.7 [88.0, 97.4]	86.9 [79.9, 93.9]
Explant	0	1.15	21	2.55	97.3 [94.6, 99.9]	92.7 [88.0, 97.4]	86.9 [79.9, 93.9]
Endocarditis	0	1.15	10	1.06	96.5 [93.5, 99.5]	93.7 [89.3, 98.0]	93.7 [89.3, 98.0]
Anticoagulant-related hemorrhage	0	1.15	10	1.44	94.8 [86.6, 100.0]	92.5 [82.7, 100.0]	90.9 [80.1, 100.0]
Nonstructural dysfunction[3]	0	1.15	3	0.32	99.3 [98.0, 100.0]	97.3 [94.3, 100.0]	97.3 [94.3, 100.0]
- Paravalvular leak[4]	0	1.15	3	0.32	99.3 [98.0, 100.0]	97.3 [94.3, 100.0]	97.3 [94.3, 100.0]
Structural deterioration	0	1.15	10	1.05	100.0 [100.0, 100.0]	99.1 [97.3, 100.0]	94.5 [89.2, 99.9]
Embolism (All)	2	2.30	24	2.52	92.7 [88.5, 96.9]	87.1 [81.2, 93.0]	82.6 [75.2, 90.1]
- Permanent	2	2.30	9	0.95	97.5 [95.0, 99.9]	94.7 [90.7, 98.6]	93.3 [88.5, 98.0]
Valve Thrombosis	0	1.15	0	0.01	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]

1 Early events are those occurring on or before 30 days post-implant. Adjusted early adverse event rate based on a Bayesian "missing data approach" with rates distributed a priori as Beta(1,1) for the events in the 2000 database and events in data reconstruction.

2 Late events are those occurring 31 days post-implant or thereafter. Adjusted late rate based on a Bayesian "missing data approach" rates distributed a priori as Gamma (0.01,.0.01) for the events in the 2000 database and events in data reconstruction.

3 Including paravalvular leak

4 No events related to endocarditis

8.2 University of Padua Medical Center, Padua, Italy

Between May 1992 and December 2000, 442 patients requiring aortic and/or mitral valve replacement (AVR = 262, MVR = 129, DVR = 51) were consecutively enrolled at the University of Padua Medical Center in Padua, Italy. Demographic and baseline data were collected preoperatively. Adverse event data was collected at time of occurrence or site notification. The cumulative follow-up for the 442 patients in Italy was 2080.9 patient-years with the mean follow-up of 4.7 years (SD = 2.8 years, range 0 - 11.4 years).

Data Presentation

The observed adverse event rates for AVR and MVR are presented in Tables 3 and 4, respectively. The data is presented as early events (those events that occurred on or before 30 days post-implant), late events (those events that occurred 31 days or more post-implant) and "freedom from event" survival analyses.

Early Events

For each event category, the number of patients experiencing early events is reported as a simple percentage. In Tables 3 and 4:

n_1 = number of patients experiencing the adverse event on or before 30 days post-implant
% = number of patients experiencing early events (n_1)/total patients implanted (n)*100

Late Events

For each event category, the number of patients experiencing late events is reported as a linearized incidence rate. In Tables 3 and 4:

n_1 = number of events that occurred 31 days or more post-implant
%/pt-yr = (number of late events (n_1)/total patient-years at risk for the event)*100

Survival Analyses

Survival analyses (i.e., "freedom from event") have been performed using the Kaplan-Meier product limit method for the adverse events occurring in one or more patients. The percent free from event and 95% confidence interval is provided at 1 year, 5 year and 8 year intervals. The 95% confidence limits are determined by the estimate ± 1.96* standard error. Adverse events occurring in both the early and late postoperative period are included in the analysis. In Tables 3 and 4:

% = estimate of the cumulative percent of patients event-free at the start of the interval, calculated using the KM (product-limit) method
95% CI = calculated by: estimate ± 1.96* standard error (Greenwood formula)

8.2.1 Observed Adverse Events for Aortic Valve Replacements (Italy)

Table 3 presents the adverse events for aortic valve replacements based on 262 isolated aortic valve patients enrolled at the University of Padua Medical Center in Italy. The cumulative follow-up for aortic valve replacements in Italy was 1330.0 patient-years.

Table 3. Observed Adverse Event Rates for AVR (Italy)

All aortic valve replacements: N=262, cumulative follow-up=1309.2 late patient-years

Adverse Event	Early Events[1] n=262		Late Events[2] n=251		Freedom From Event		
					1 Year	5 Year	8 Year
	n_1	% (n_1/n)	n_1	%/pt-yr	% [95% CI]	% [95% CI]	% [95% CI]
Mortality (All)	11	4.20	90	6.87	91.5 [88.2, 94.9]	72.0 [66.5, 77.6]	50.8 [42.6, 59.0]
- Valve-related (includes unknowns)	1	0.38	29	2.22	98.4 [96.8, 100.0]	91.2 [87.4, 95.0]	80.8 [73.7, 87.9]
Reoperation (including explant)	1	0.38	5	0.38	98.4 [96.8, 100.0]	98.4 [96.8, 100.0]	96.8 [94.2, 99.5]
Explant	1	0.38	5	0.38	98.4 [96.8, 100.0]	98.4 [96.8, 100.0]	96.8 [94.2, 99.5]
Endocarditis	0	0.00	3	0.23	99.6 [98.8, 100.0]	98.5 [96.8, 100.0]	98.5 [96.8, 100.0]
Hemolysis	0	0.00	0	0.00	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]
Anticoagulant-related hemorrhage	6	2.29	6	0.46	97.2 [95.2, 99.3]	96.3 [93.9, 98.7]	94.1 [90.3, 97.9]
Nonstructural dysfunction[3]	0	0.00	6	0.46	98.8 [97.4, 100.0]	98.3 [96.7, 100.0]	97.6 [95.5, 99.7]
- Paravalvular leak[4]	0	0.00	6	0.46	98.8 [97.4, 100.0]	98.3 [96.7, 100.0]	97.6 [95.5, 99.7]
Structural deterioration	0	0.00	2	0.15	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	96.8 [91.9, 100.0]
Embolism (All)	2	0.76	17	1.30	96.7 [94.5, 99.0]	92.6 [89.0, 96.1]	91.5 [87.4, 95.6]
- Permanent	0	0.00	9	0.69	98.7 [97.3, 100.0]	96.7 [94.3, 99.1]	95.6 [92.5, 98.8]
Valve Thrombosis	1	0.38	2	0.15	99.2 [98.1, 100.0]	98.7 [97.3, 100.0]	98.7 [97.3, 100.0]

1 Early events are those occurring on or before 30 days post-implant
2 Late events are those occurring 31 days post-implant or thereafter
3 Including paravalvular leak
4 No events related to endocarditis

8.2.2 Observed Adverse Events for Mitral Valve Replacements (Italy)

Table 4 presents the adverse events for mitral valve replacements based on 129 isolated mitral valve patients enrolled at the University of Padua Medical Center in Italy. The cumulative follow-up for mitral valve replacements in Italy was 509.1 patient-years.

Table 4. Observed Adverse Event Rates for MVR (Italy)

All isolated mitral valve replacements: N=129, cumulative follow-up=499.4 late patient-years

Adverse Event	Early Events[1] n=129		Late Events[2] n=114		Freedom From Event		
					1 Year	5 Year	8 Year
	n_i	% (n_i/n)	n_i	%/pt-yr	% [95% CI]	% [95% CI]	% [95% CI]
Mortality (All)	15	11.63	39	7.81	78.2 [71.0, 85.3]	62.5 [53.5, 71.4]	48.1 [35.9, 60.4]
- Valve-related (includes unknowns)	1	0.78	15	3.00	94.4 [90.1, 98.8]	86.5 [79.1, 93.9]	80.9 [71.7, 90.2]
Reoperation (including explant)	0	0.00	6	1.20	98.2 [95.7, 100.0]	94.1 [89.5, 98.7]	94.1 [89.5, 98.7]
Explant	0	0.00	6	1.20	98.2 [95.7, 100.0]	94.1 [89.5, 98.7]	94.1 [89.5, 98.7]
Endocarditis	1	0.78	5	1.00	96.4 [92.9, 99.9]	95.3 [91.3, 99.4]	91.9 [84.3, 99.5]
Hemolysis	0	0.00	0	0.00	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]
Anticoagulant-related hemorrhage	8	6.20	5	1.00	92.4 [87.6, 97.2]	91.2 [85.9, 96.5]	84.9 [75.0, 94.8]
Nonstructural dysfunction[3]	0	0.00	9	1.80	98.1 [95.5, 100.0]	93.1 [88.1, 98.0]	86.5 [76.1, 96.8]
- Paravalvular leak[4]	0	0.00	9	1.80	98.1 [95.5, 100.0]	93.1 [88.1, 98.0]	86.5 [76.1, 96.8]
Structural deterioration	0	0.00	0	0.00	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]
Embolism (All)	2	1.55	7	1.40	96.5 [93.2, 99.9]	91.1 [85.0, 97.3]	88.6 [80.9, 96.3]
- Permanent	1	0.78	4	0.80	98.3 [95.9, 100.0]	94.3 [89.1, 99.4]	94.3 [89.1, 99.4]
Valve Thrombosis	0	0.00	0	0.00	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]	100.0 [100.0, 100.0]

1 Early events are those occurring on or before 30 days post-implant
2 Late events are those occurring 31 days post-implant or thereafter
3 Including paravalvular leak
4 No events related to endocarditis

8.3 Potential Adverse Events

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

- angina
- cardiac arrhythmia
- endocarditis
- heart failure
- hemolysis
- hemolytic anemia
- hemorrhage
- leak, transvalvular or paravalvular
- myocardial infarction
- nonstructural dysfunction (entrapment by pannus or suture, inappropriate sizing or positioning, or other)
- prosthesis regurgitation
- stroke
- structural deterioration (e.g. calcification, leaflet tear, or other)
- thromboembolism
- valve thrombosis

It is possible that these complications could lead to:

- reoperation
- explantation
- permanent disability
- death

9. Summaries of Non-Clinical Studies

9.1 In-Vitro Pre-Clinical Bench Testing

9.1.1 Biocompatibility

The results of the biocompatibility testing performed, the materials used in the SJM Biocor® valve and the SJM Biocor® Supra valve suggested that the valve is biocompatible, non-mutagenic, non-toxic and, therefore, safe for the device's intended use.

Non-Biological Components

The non-biological components of the SJM Biocor® valve consist of surgical sutures, polyester knitted fabric and yarn, stainless steel wire and an acetal copolymer stent, each of which have a long history of use in cardiovascular implantation devices. The Biocor® Supra configuration contains the same materials as described above and also contains a silicone ring within the polyester sewing cuff.

Biocompatibility testing of stent sub-assemblies, containing all non-biological components of the valve, was performed in accordance with the requirements detailed in International Standards Organization 10993-1 and United States Food and Drug Administration General Program Memorandum G95-1. For the non-biological components of the SJM Biocor® valve and the SJM Biocor® Supra valve, the tests performed, the test objective and results are provided in Table 5. Carcinogenicity, chronic and reproductive toxicity testing were not conducted since the chemical residual profile of the valve did not indicate that these long-term chronic studies were necessary.

Table 5. Biocompatibility Tests and Results - Non-Biological Components

Test Performed	Objective and Method	Controls	Test Article	Results
Cytotoxicity (Medium Eluate Method)	Evaluation of the biocompatibility of test article extract using an *in-vitro* mammalian cell culture test (MEM method).	Negative control: low density polyethylene Positive control: Tin stabilized polyvinyl chloride Reagent control: MEM fluid	Covered stent[1] Silicone ring	**Passed** Only slight (grade 1) cytotoxicity observed
Sensitization (Maximization Method)	Maximization test in guinea pigs to determine the potential for delayed dermal contact sensitization.	Vehicle controls/ control animals	Covered stent[1]	**Passed** No evidence of sensitization
Irritation / Acute Intracutaneous Reactivity (Rabbit Intracutaneous Reactivity Test)	Evaluation of local dermal irritation or toxic effects of leachables extracted from the test article following intra-cutaneous injection in rabbits.	Reagent control per animal	Covered stent[1] Silicone ring	**Passed** No evidence of significant irritation or toxicity
Acute Systemic Toxicity (USP Mouse Systemic Injection)	Evaluation of acute systemic toxicity of leachables extracted from the test article following a single intravenous or intraperitoneal injection in mice.	Control animals dosed with extract vehicles	Covered stent[1] Silicone ring	**Passed** No mortality or evidence of systemic toxicity
Sub-Chronic Toxicity	Evaluation of the toxicity of leachables extracted from the test article following intravenous injection into mice.	14 day intravenous injections (clinical observation, body weights, necropsy, organ weights, clinical hematology, histopathology); Control animals dosed with extract vehicle	Covered stent[1]	**Passed** No evidence of systemic toxicity
Genotoxicity (Ames Reverse Mutation)	Evaluation of test article to determine its ability to evoke a mutagenic response in strains of Salmonella typhimurium.	Negative control: extract vehicle; positive control: Dexon, sodium azide, and 2-aminoflourine	Covered stent[1]	**Passed** Non-mutagenic
Implantation (Rabbit Intramuscular Implantation Test)	Evaluation of a test article to local pathological effects on living tissue in rabbit.	2 week muscle implant (macro and microscopic examinations of implant muscle sites); negative control material: USP polyethylene	Uncovered stent[2]	**Passed** Classified as a non-irritant
Hemocompatibility	Determination as to whether leachables extracted from the test article will cause a significant level of hemolysis in blood.	Hemolysis- direct contact with rabbit blood, 1 hour at 37°C exposure	Covered stent[1] Cuff filler Stent wire Silicone ring	**Passed** Non-hemolytic

1 The covered stent tested is a subassembly of the SJM Biocor® valve which contains the implanted non-biological components of the tissue valve. This sub-assembly consists of an acetal copolymer stent (Celcon® M270) that is covered with polyester tubular cloth that has been fashioned around the stent and also forms the sewing cuff exterior. The sewing cuff is filled with braided polyester cloth. Also, a 316 surgical stainless steel (SST) wire is placed in the cuff for radiographic visualization. These components are secured to the stent using polyamide suture material. The stent sub-assemblies were ethylene oxide sterilized prior to testing.

2 The implantation test was not performed using the entire covered stent assembly. The implantation method required 1 mm X 10 mm test samples for loading into muscle tissues using 16 gauge needles/ stylets. This preparation separated the materials of the stent sub-assembly and consequently only the Celcon® M270 stent material was implanted during this test.

Biological Components

The use of glutaraldehyde-fixed porcine leaflets and bovine pericardium are well established for bioprosthetic heart valves and each has an acceptable biocompatibility profile for this indication. The tissues in the SJM Biocor® valve and SJM Biocor® Supra Valve are liquid chemically processed in a similar manner to other commercially available heart valves incorporating animal tissues. A thorough assessment of potential leachables from the Biocor® valves has been performed which includes a study of extractable residuals during rinsing. The results confirm that the extractable chemical residues from the Biocor® valves are similar in type and concentration as compared to a clinically approved (U.S.) control valve.

Valve Accessories and Packaging Components

The non-implantable valve accessories and packaging components (valve holders, valve sizers, jar, lid and lid liner) were subjected to appropriate biocompatibility tests as for these components. Results suggested that these components are non-toxic.

9.1.2 Hydrodynamic Performance

The SJM Biocor® Supra valve is identical to the SJM Biocor® valve with the exception of the device sewing cuff. All hydrodynamic measurements on the SJM Biocor® valve were conducted with sealed fixtures which isolates the cuff from the flow areas of the valve. Therefore, the hydrodynamic results summarized in Table 6 support the safe performance of the SJM Biocor® valve and the SJM Biocor® Supra valve.

Hydrodynamic performance studies were completed on the SJM Biocor® valve in accordance with the *FDA Draft Replacement Heart Valve Guidance* (1994) or *ISO 5840, Cardiovascular Implants-Cardiac Valve Prosthesis* (1989). Testing included steady flow pressure drop, pulsatile flow pressure drop, dynamic regurgitation, static leakage, flow visualization and verification of the Bernoulli relationship. Commercially available bioprosthetic heart valves were used as controls.

Table 6. Hydrodynamic Performance Summary

Test Type	Sample Size	Control Size	Results
Steady Flow Pressure Drop	3 each size and type	Aortic: 1 each 21mm and 25mm Mitral: 1 each 29mm and 33mm	Steady flow pressure drop is directly correlated to and consistent with pulsatile flow pressure drop results.
Pulsatile Flow Pressure Drop/EOA	Biocor: 3 each size and type Biocor Supra: 3 each size	Aortic: 1 each 21mm and 25mm Mitral: 1 each 29mm and 33mm	Meets requirements in ISO/FDIS: 5840 2004 (E), Cardiovascular implants-Cardiac valve prostheses.
Dynamic Regurgitation	3 each size and type	Aortic: 1 each 21mm and 25mm Mitral: 1 each 29mm and 33mm	Valve maintains complete coaptation and meets requirements in ISO/FDIS: 5840 2004 (E), Cardiovascular implants-Cardiac valve prostheses.
Static Leakage	3 each size and type	Aortic: 1 each 21mm and 25mm Mitral: 1 each 29mm and 33mm	Valve closes completely and maintains complete coaptation under a back pressure of 200mmHg.
Flow Visualization	Aortic: 1 each 21mm and 25mm	N/A	The flow field produced by the Biocor® valve produces a flow field typical of stented tissue valves. Results indicate that the valve opens efficiently and symmetrically.
Verification of the Bernoulli Relationship	Aortic: 1 each 21mm, 25mm, and 29mm Mitral: 1 each 25, and 29mm	N/A	The Bernoulli equation accurately projects true pressure gradient for the valve.

9.1.3 Structural Performance

Since the SJM Biocor® Supra valve is identical to the SJM Biocor® valve, except for the construction of the sewing cuff, all structural performance testing conducted on the SJM Biocor® valve is applicable to the SJM Biocor® Supra valve. The one exception is the sewing cuff integrity test which was conducted on both valve models. The structural performance results presented in Table 7 show acceptable performance of the Biocor® and the Biocor® Supra.

Structural performance studies were completed on the SJM Biocor® valve in accordance with the *FDA Draft Replacement Heart Valve Guidance* (1994). Testing included accelerated wear, dynamic failure mode, fatigue, stent creep, and sewing cuff integrity. The structural performance testing summary is provided in Table 7.

Table 7. Structural Performance Summary

Test Type	Sample Size	Control Size	Results
Accelerated Wear	Aortic: 3 each 21mm, 25mm, and 29mm Mitral: 3 each 25mm, 29mm and 33mm	Aortic: 1 each 21mm and 29mm Mitral: 1 each 25mm and 33mm	All valves functioned normally exhibiting proper opening and closing while maintaining back pressure throughout the test. No failures were observed at 200 million cycles.
Dynamic Failure Mode	Aortic: 1 each 21mm, 25mm, and 29mm Mitral: 1 each 25mm, 29mm and 33mm	Aortic: 1 each 21mm and 29mm Mitral: 1 each 25mm and 33mm	The failure mode observed was excessive regurgitation due to leaflet holes and tears. This is consistent with typical failure modes for tissue valves in this in-vitro test. Failures occurred between 340 and 770 million cycles; similar to the control valve.
Fatigue: Finite Element Analysis	Ten 29mm, 31mm and 33mm stents	N/A	The largest stress observed was 25.9 MPa (3750 psi) for the 29 mm stent.
Fatigue Lifetime Analysis	Ten 29mm, 31mm and 33mm stents	N/A	No failures through 600 million cycles at 5,000psi load.
Stent Creep	Ten 29mm stents	N/A	All stents recovered within minutes with no signs of creep
Sewing Cuff Integrity SJM Biocor® valve	Ten of each size	N/A	All test samples exhibited cuff retention in excess of the minimum device specification.
Sewing Cuff Integrity SJM Biocor® Supra valve	Three of each size	N/A	All test samples exhibited cuff retention in excess of the minimum device specification

9.2 Pre-Clinical Animal Studies

Long-term (20 week) animal studies with the SJM Biocor® valve were performed using the juvenile sheep model to evaluate the safety and effectiveness of the valve design. The animal model consisted of juvenile sheep either male or female that were between three and five months old at the time of implant. The implant position was the mitral valve and the valve size implanted was 25 mm for the test and control valves. Baxter Carpentier-Edwards valves (model 2625) were implanted as control valves.

The study included an evaluation of handling and implant characteristics, animal survival, hemodynamic performance, valve pathology, hematology and mineralization. The results of this study are described in more detail below.

9.2.1 Handling and Implant Characteristics

Handling and implantation characteristics of the SJM Biocor® valve were evaluated by the implanting surgeon and were considered comparable to the control valve.

9.2.2 Animal Survival

There was one early death at 4 days post-operative in the test group; however, it was not attributed to valve performance.

9.2.3 Hemodynamic Performance

At the time of explant, all animals were subjected to standard heart (direct) catheterization to obtain hemodynamic measurements. Hemodynamic parameters obtained on all animals were typically within the normal physiologic range.

9.2.4 Valve Pathology

Valve pathology included photographic analysis of the explanted valves. The fibrous tissue on the SJM Biocor® valve at the time of sampling was mature characterized by minimally activated fibroblasts and well-organized extracellular matrix, primarily collagen. Immature fibrous reaction was seen only infrequently. The pathology results suggest that the SJM Biocor® valve and the SJM Biocor® Supra valve are safe.

9.2.5 Hematology

The blood chemistries for the SJM Biocor® valve were not different from the control valves and all of the animals tested in this study fell within the reference range for juvenile ovine provided by Marshfield Laboratories (Marshfield, WI) and Nemi C. Jain *Veterinary Hematology* (Fourth Edition). There were no remarkable anomalies or any indication of excessive blood trauma in the blood chemistries in any of the test groups that could be attributed to the prosthetic device.

9.2.6 Mineralization

Mineralization was evaluated by X-ray radiographs of whole valves and quantitative analysis using inductively coupled plasma atomic emission spectroscopy (ICP). Only minimal calcium content was measured in the SJM Biocor® valve cusps and there was a statistical difference found in cuspal tissue calcification between the SJM Biocor® valves and the control valves. There was no statistically significant difference found between any of the aortic wall samples.

9.3 Sterilization

The SJM Biocor® valve and the SJM Biocor® Supra valve are sterilized with a multi-component liquid chemical sterilant. Microbial screening studies were conducted with a variety of organisms exposed to the sterilant in a simulated manufacturing sterilization process. The D-values derived from the screening studies showed *Bacillus subtilis* var. *niger* is the most resistant microbial organism to this sterilization process.

Microbial survival studies were conducted in triplicate with tissue utilizing *B. subtilis* as the challenge organism. The D-value obtained from the *B. subtilis* microbial survival study was used to calculate the minimum sterilization time required to meet a minimum Sterility Assurance Level (SAL) of 10^{-6}.

9.4 Magnetic Resonance Imaging (MRI) Compatibility

The SJM Biocor® valve and the SJM Biocor® Supra valve have been shown to be MR safe when tested using an MR system with a static magnetic field of 3-Tesla or less. Testing has demonstrated that the MRI procedure will present no substantial or increased risk to the patient relative to magnetic field interactions (e.g. migration and/or heating). The MRI procedure should not cause significant image artifacts or distortion.

9.5 Shelf Life

The shelf life for the SJM Biocor® valve and the SJM Biocor® Supra valve was validated to ensure that both the package integrity and the product integrity were maintained for 4 years.

9.5.1 Package Integrity

The packaging used for the SJM Biocor® valve and the SJM Biocor® Supra valve has been shown to maintain sterility for 4 years. Structural integrity of the package was evaluated after exposure to thermal shock cycling, vibration, drop conditioning and accelerated aging to 4 years. Performance evaluation of the package included vacuum leakage testing, temperature indicator testing and microbial challenge after real-time aging to four years. The results demonstrate that the package integrity is acceptable for a 4 year shelf life.

9.5.2 Product Integrity

Integrity of the finished devices was evaluated after real-time aging to 4 years. The evaluation included shrinkage temperature, moisture content, collagen content (i.e. collagenase resistance and hydroxyproline content), solution volume, solution concentration, solution pH, sewing cuff integrity, and hydrodynamic testing. The results demonstrate that the product integrity of the SJM Biocor® valve and the SJM Biocor® Supra valve is acceptable for a 4 year shelf life.

10. Summary of Clinical Studies

10.1 Objectives

The objective of these studies was to evaluate the valve-related adverse events and mortality of patients receiving the SJM Biocor® valve in the aortic and/or mitral position. In addition, New York Heart Association (NYHA) functional classification and hemodynamic performance were evaluated for effectiveness endpoints.

10.2 Description of Patients

The clinical investigations of the SJM Biocor® valve were conducted as single-center, non-randomized, observational studies, without concurrent or matched controls at two centers; Sahlgrenska University Hospital (Gothenburg, Sweden) and University of Padua Medical Center (Padua, Italy).

A total of 1492 patients (AVR = 1263, MVR = 172, DVR = 57) were enrolled at Sahlgrenska University Hospital between January 1983 and December 1999. At the University of Padua Medical Center, 442 patients (AVR = 262, MVR = 129, DVR = 51) were enrolled between May 1992 and December 2000. Demographic and baseline data were collected preoperatively. Adverse event data was collected at time of occurrence or upon site notification.

Tables 8-9 present the number of patients implanted, cumulative follow-up, and mean follow-up for each patient implant group in Sweden and Italy. Tables 10-11 present the number of patients implanted and cumulative follow-up by valve size and patient implant group in Sweden and Italy.

Table 8. Follow-up (Sahlgrenska University Hospital, Gothenburg, Sweden)
All patients entered into study, N=1492
Mean, SD, Min, and Max are represented in "Years"

Patient Implant Group	Number of Patients	Number of Patient-years	Mean	SD	Min	Max
Isolated Aortic Patients	1263*	6368.6	5.0	4.1	0.0	16.9
Isolated Mitral Patients	172	968.3	5.6	4.9	0.0	16.6
Double Valve Patients	57	381.2	6.7	5.3	0.0	14.6
All Patients	1492	7718.1	5.2	4.3	0.0	16.9

* Data includes aortic valve sizes 21mm, 23mm, 25mm, 27mm, 29mm, 31mm, and 33mm.

Table 9. Follow-up (University of Padua Medical Center, Padua, Italy)
All patients entered into study, N=442
Mean, SD, Min, and Max are represented in "Years"

Patient Implant Group	Number of Patients	Number of Patient-years	Mean	SD	Min	Max
Isolated Aortic Patients	262	1330.0	5.1	2.5	0.0	11.4
Isolated Mitral Patients	129	509.1	3.9	3.0	0.0	11.2
Double Valve Patients	51	241.7	4.7	2.9	0.1	9.6
All Patients	442	2080.9	4.7	2.8	0.0	11.4

Table 10. Aortic Patient Numbers and Cumulative Follow-up by Valve Size

	Number of Implants by Valve Size					
	21mm	23mm	25mm	27mm	29mm	Total
University of Sahlgrenska, Gothenburg, Sweden						
Number of Isolated Aortic Patients	83	524	407	186	47	1247[#]
Number of Patient-Years	661.4	2189.2	2110.2	1038.3	267.0	6266.0
Padua University, Padua, Italy						
Number of Isolated Aortic Patients	48	116	76	20	2	262
Number of Patient-Years	242.3	586.6	396.8	99.4	4.9	1330.0

[#] Data excludes aortic valve sizes 31mm and 33mm.

Table 11. Mitral Patient Numbers and Cumulative Follow-up by Valve Size

	Numbers of Implants by Valve Size					
	25mm	27mm	29mm	31mm	33mm	Total
University of Sahlgrenska, Gothenburg, Sweden						
Number of Isolated Mitral Patients	3	17	45	52	55	172
Number of Patient-Years	35.9	105.2	223.5	296.0	307.8	968.3
Padua University, Padua, Italy						
Number of Isolated Mitral Patients	0	4	56	56	13	129
Number of Patient-Years	0.0	14.5	188.8	249.1	56.8	509.1

10.3 Analysis for Gender Bias

Sahlgrenska University Hospital, Gothenburg, Sweden

Of the 1492 total patients implanted with the SJM Biocor® valve at Sahlgrenska University Hospital, 38.2% were female (AVR – 36.2%, MVR – 52.3%, and DVR – 40.4%). The gender is consistent with the incidence of patients presenting for valve replacement in the U.S. The log-rank test was performed to compare all valve-related morbidities and mortality. For AVR patients, males had a slightly higher incidence of structural valve deterioration. For MVR patients, males had a slightly higher incidence of thromboembolism. There were no significant differences between gender for all other valve-related morbidity and mortality for each patient group. The rank-sum test was performed for NYHA functional classification improvement; there was no significant difference between gender.

University of Padua Medical Center, Padua, Italy

Of the 442 total patients implanted with SJM Biocor® valve at the University of Padua Medical Center, 57.5% were female (AVR – 51.1%, MVR – 68.2%, and DVR – 62.7%). The gender is consistent with the incidence of patients presenting for valve replacement in the U.S. The log-rank test was performed to compare all valve-related morbidities and mortality; there were no significant differences between gender. The rank-sum test was performed for NYHA functional classification improvement; there was no significant difference between gender.

10.4 Patient Demographics

Table 12 and 13 present preoperative patient demographics for Sahlgrenska University Hospital and University of Padua Medical Center, respectively.

Table 12. Preoperative Patient Demographics (Sahlgrenska University Hospital, Sweden)
All patients entered into study, N=1492; n=number per subgroup

Patient Characteristics		Isolated AVR n=1263		Isolated MVR n=172	
		n_1	% (n_1/n)	n_1	% (n_1/n)
Gender	Male	806	63.8	82	47.7
	Female	457	36.2	90	52.3
Age at Implant	≤39	49	3.9	11	6.4
	40-49	42	3.3	9	5.2
	50-59	83	6.6	27	15.7
	60-69	222	17.6	51	29.7
	70-79	724	57.3	70	40.7
	≥80	143	11.3	4	2.3
NYHA Functional Classification	I	89	7.0	1	0.6
	II	301	23.8	16	9.3
	III	732	58.0	116	67.4
	IV	123	9.7	39	22.7
	Unknown	18	1.4	0	0.0
Valve Dysfunction	Insufficiency	169	13.4	116	67.4
	Stenosis	905	71.7	30	17.4
	Mixed	189	15.0	26	15.1
	Unknown	0	0.0	0	0.0

Table 13. Preoperative Patient Demographics (University of Padua Medical Center, Italy)
All patients entered into study, N=442; n=number per subgroup

Patient Characteristics		Isolated AVR n=262		Isolated MVR n=129	
		n_1	% (n_1/n)	n_1	% (n_1/n)
Gender	Male	128	48.9	41	31.8
	Female	134	51.1	88	68.2
Age at Implant	≤39	0	0.0	0	0.0
	40-49	2	0.8	0	0.0
	50-59	5	1.9	6	4.7
	60-69	33	12.6	30	23.3
	70-79	175	66.8	89	69.0
	≥80	47	17.9	4	3.1
NYHA Functional Classification	I	26	9.9	3	2.3
	II	88	33.6	26	20.2
	III	95	36.3	66	51.2
	IV	53	20.2	32	24.8
	Unknown	0	0.0	2	1.6
Valve Dysfunction	Insufficiency	33	12.6	82	63.6
	Stenosis	178	67.9	15	11.6
	Mixed	50	19.1	32	24.8
	Unknown	1	0.4	0	0.0

10.5 Results

Table 14 presents patient NYHA functional classification at two time points: preoperative and ≥ 11 months follow-up for both Sweden and Italy. The patients included in these analyses have both the preoperative and postoperative NYHA classification reported.

Tables 15-16 present hemodynamic results at ≥ 11 months follow-up for both Sweden and Italy.

Table 14. Effectiveness Outcomes, NYHA Functional Classification: ≥ 11 months follow-up

Sahlgrenska University Hospital, Gothenburg, Sweden All patients entered into study, N=1492; n=number per subgroup								
NYHA Class	**Isolated AVR**				**Isolated MVR**			
	Preoperative Assessment n = 949		Postoperative ≥ 11 months n = 949		Preoperative Assessment n = 116		Postoperative ≥ 11 months n = 116	
	n_1	% (n_1/n)	n_1	% (n_1/n)	n_1	% (n_1/n)	n_1	% (n_1/n)
I	59	6.2	528	55.6	0	0.0	57	49.1
II	242	25.5	310	32.7	12	10.3	44	37.9
III	557	58.7	108	11.4	84	72.4	14	12.1
IV	91	9.6	3	0.3	20	17.2	1	0.9
University of Padua Medical Center, Padua, Italy All patients entered into study, N=442; n=number per subgroup								
NYHA Class	**Isolated AVR**				**Isolated MVR**			
	Preoperative Assessment n = 215		Postoperative ≥ 11 months n = 215		Preoperative Assessment n = 89		Postoperative ≥ 11 months n = 89	
	n_1	% (n_1/n)	n_1	% (n_1/n)	n_1	% (n_1/n)	n_1	% (n_1/n)
I	23	10.7	122	56.7	3	3.4	38	42.7
II	77	35.8	76	35.3	22	24.7	37	41.6
III	72	33.5	14	6.5	52	58.4	9	10.1
IV	43	20.0	3	1.4	12	13.5	5	5.6

Table 15. Effectiveness Outcomes, Aortic Hemodynamic Results

Sahlgrenska University Hospital, Gothenburg, Sweden All Aortic Valve Replacements, N=1320										
Hemodynamic Parameter	Results by Valve Size									
	21mm		23mm		25mm		27mm		29mm	
Data from the Follow-up interval ≥ 11 months										
Mean Gradient (mmHg)	N=63		N=170		N=205		N=104		N=28	
♦ Mean ± SD	22.4 ± 7.4		18.9 ± 9.9		17.9 ± 11.4		16.4 ± 11.5		17.2 ± 11.2	
EOA (cm^2)	N=15		N=37		N=31		N=19		N=2	
♦ Mean ± SD	1.0 ± 0.3		1.3 ± 0.5		1.4 ± 0.5		1.9 ± 0.7		1.7 ± 0.4	
Regurgitation	21mm		23mm		25mm		27mm		29mm	
	n	%	n	%	n	%	n	%	n	%
♦ None	37	58.7	111	60.0	104	48.4	60	56.6	13	40.6
♦ Trivial	18	28.6	45	24.3	56	26.1	26	24.5	10	31.3
♦ Mild	6	9.5	16	8.7	29	13.5	14	13.2	3	9.4
♦ Moderate	1	1.6	12	6.5	19	8.8	4	3.8	6	18.8
♦ Severe	1	1.6	1	0.5	7	3.3	2	1.9	0	0.0
University of Padua Medical Center, Padua, Italy All Aortic Valve Replacements, N=313										
Hemodynamic Parameter	Results by Valve Size									
	21mm		23mm		25mm		27mm		29mm	
Data from the Follow-up interval ≥ 11 months										
Mean Gradient (mmHg)	N=40		N=93		N=61		N=12		N=1	
♦ Mean ± SD	18.8 ± 6.3		17.3 ± 7.6		15.2 ± 5.2		13.9 ± 4.8		11.00 ± NA	
EOA (cm^2)	N=36		N=88		N=59		N=9		N=1	
♦ Mean ± SD	1.3 ± 0.3		1.5 ± 0.3		1.5 ± 0.3		1.5 ± 0.2		3.3 ± NA	
Regurgitation	21mm		23mm		25mm		27mm		29mm	
	n	%	n	%	n	%	n	%	n	%
♦ None	34	79.1	84	90.3	56	91.8	10	83.3	1	100
♦ Trivial	7	16.3	8	8.6	4	6.6	2	16.7	0	0.0
♦ Mild	2	4.7	1	1.1	0	0.0	0	0.0	0	0.0
♦ Moderate	0	0.0	0	0.0	1	1.6	0	0.0	0	0.0
♦ Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 16. Effectiveness Outcomes, Mitral Hemodynamic Results

Sahlgrenska University Hospital, Gothenburg, Sweden All Mitral Valve Replacements, N=229										
Hemodynamic Parameter	Results by Valve Size									
	25mm		27mm		29mm		31mm		33mm	
Data from the Follow-up interval ≥ 11 months										
Mean Gradient (mmHg)	N=2		N=6		N=23		N=29		N=26	
♦ Mean ± SD	6.5 ± 2.1		7.5 ± 2.7		6.6 ± 2.3		5.2 ± 1.9		7.2 ± 3.9	
EOA (cm^2)	N=1		N=0		N=2		N=4		N=3	
♦ Mean ± SD	0.9 ± N/A		N/A		1.5 ± 0.1		1.7 ± 0.8		1.8 ± 1.1	
Regurgitation	25mm		27mm		29mm		31mm		33mm	
	n	%	n	%	n	%	n	%	n	%
♦ None	0	0.0	4	50.0	18	58.1	23	60.5	27	64.3
♦ Trivial	2	66.7	1	12.5	9	29.0	7	18.4	6	14.3
♦ Mild	1	33.3	0	0.0	3	9.7	5	13.2	4	9.5
♦ Moderate	0	0.0	2	25.0	0	0.0	1	2.6	3	7.1
♦ Severe	0	0.0	1	12.5	1	3.2	2	5.3	2	4.8

University of Padua Medical Center, Padua, Italy All Mitral Valve Replacements, N=180										
Hemodynamic Parameter	Results by Valve Size									
	25mm		27mm		29mm		31mm		33mm	
Data from the Follow-up interval ≥ 11 months										
Mean Gradient (mmHg)	N=0		N=3		N=43		N=39		N=11	
♦ Mean ± SD	N/A		6.1 ± 1.3		6.3 ± 3.1		5.9 ± 3.1		6.5 ± 3.8	
EOA (cm^2)	N=0		N=2		N=40		N=25		N=11	
♦ Mean ± SD	N/A		1.2 ± 0.3		2.3 ± 0.6		2.2 ± 0.6		2.3 ± 0.7	
Regurgitation	25mm		27mm		29mm		31mm		33mm	
	n	%	n	%	n	%	n	%	n	%
♦ None	0	0.0	3	100	34	79.1	29	74.4	9	75.0
♦ Trivial	0	0.0	0	0.0	8	18.6	5	12.8	3	25.0
♦ Mild	0	0.0	0	0.0	1	2.3	5	12.8	0	0.0
♦ Moderate	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
♦ Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Hemodynamic data was also obtained from another foreign institution to augment the 27mm mitral data from Sweden and Italy. Hemodynamic data was collected from the Biocor Hospital de Doencas Cardiovaculares Ltda., Brazil (Biocor Hospital). The hemodynamic results at ≥ 11 months follow-up from the Biocor Hospital are presented in Table 16.

Table 17. Effectiveness Outcomes, 27mm Mitral Hemodynamic Results

Biocor Hospital de Doencas Cardiovaculares Ltda, Brazil All 27mm Mitral Valve Replacements, N=228		
Hemodynamic Parameter	27mm Mitral Valve	
Data from the Follow-up interval ≥ 11 months		
Mean Gradient (mmHg)	N=30	
Mean ± SD	7.3 ± 3.7	
EOA (cm^2)	N=13	
♦ Mean ± SD	1.5 ± 0.3	
Regurgitation	27mm Mitral Valve	
	n	%
♦ None	24	70.6
♦ Trivial	3	8.8
♦ Mild	6	17.7
♦ Moderate	0	0.0
♦ Severe	1	2.9

11.0 Conclusions Drawn from Studies

The results from the in-vitro pre-clinical studies performed for biocompatibility, hydrodynamic performance and structural performance suggest that the SJM Biocor® valve and the SJM Biocor® Supra valve are non-toxic and perform acceptably.

The in-vivo animal studies in sheep demonstrate the SJM Biocor® valve and the SJM Biocor® Supra valve perform acceptably.

The clinical results from the Salhgrenska University and the University of Padua Medical Center demonstrate that the SJM Biocor® valve and SJM Biocor® Supra valve perform acceptably.

12.0 Panel Recommendations

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 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.

13.0 FDA Decision

FDA issued an approval order on AUG - 5 2005. The applicant's manufacturing facility was inspected on June 16, 2004 and was found to be in compliance with the Quality System Regulation (21 CFR 820).

The FDA recommends approval of the SJM Biocor® Valve aortic sizes 21, 23, 25, and 27 mm and mitral sizes 27, 29, 31, and 33 mm SJM Biocor® Supra Valve aortic valve sizes 19, 21 and 23 mm for which there are adequate data. The FDA further recommends that a post approval study be conducted in order to further evaluate the long-term safety and effectiveness of the SJM Biocor™ Valve and the SJM Biocor™ Supra Valve.

14.0 Approval Specifications

Instructions 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: See approval order.