SORIN | FREEDOM SOLO

Stentless heart valve

Instructions for use

CAUTION: Federal Law (USA) restricts the device to sale by or on the order of a physician.

SYMBOLS

CAUTION: SEE MANUAL FOR INSTRUCTIONS / WARNINGS

CONTENTS STERILIZED USING ASEPTIC PROCESSING TECHNIQUE

EXPIRY DATE

STORE BETWEEN 5°C AND 25°C

SINGLE USE ONLY

DO NOT RESTERILIZE

MR SAFE

CATALOGUE NUMBER

SERIAL NUMBER

SIZE

MANUFACTURER

QUANTITY INCLUDED IN PACKAGE

DO NOT USE IF PACKAGE IS DAMAGED

1. DESCRIPTION

The Freedom SOLO valve is a stentless bioprosthetic heart valve made of bovine pericardium stabilized in buffered glutaraldehyde solutions and indicated for the replacement of damaged or malfunctioning aortic heart valves or prostheses in humans.

The prosthesis is designed for implantation in a supraannular position, with a single suture line.

The Freedom SOLO valve consists of two pericardial sheets shaped according to a patented process. The pericardial tissue is selected and fixed in a glutaraldehyde based process in which the stabilizing agent reacts under dynamic conditions. The first sheet has the form of three valvular cusps arranged to allow the blood to flow in only one direction. The second sheet has an outflow edge that allows suturing to the aortic wall.

The two pericardium sheets are connected with a suture made of a thread coated with Carbofilm™, a thin film of turbostratic carbon with a high density.

The prosthesis is treated for the elimination of aldehyde residues and stored in a buffered solution without aldehydes.

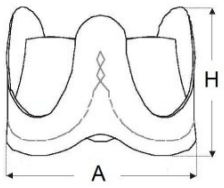
2. AVAILABLE MODELS

The Freedom SOLO valve is available in four sizes: 21, 23, 25, and 27 mm (Table 1).

The serial number identifying each prosthesis can be used to retrieve information about valve manufacturing and quality control processes from the archives of the Quality Assurance Service of Sorin Group Canada.

Table 1. Freedom SOLO Heart Valve dimensions

REF	SIZE (mm)	Supraannular Implant Diameter (mm) [A]	Height (mm) [H]
ART21SG	21	23	20
ART23SG	23	25	21
ART25SG	25	27	22
ART27SG	27	29	23



3. PACKAGING

Freedom SOLO prostheses are preserved in a buffered sterile solution without aldehydes. Each valve is packaged individually in its own container. A plastic identification tag is attached with a suture to the holder of the prosthesis. The valve is mounted on a holder. The container is externally sealed with a transparent film, which should be opened just at the time of preparing the prosthesis for implantation.

WARNING: The external surface of the container is not sterile and must not come into contact with sterile instruments.

The container holding the prosthesis is packaged in a cube of insulating material that protects the device against temperature variations. Temperature indicators are also included in the package to monitor temperature exposure during transit.

WARNING: Indicators are for transit only. They are not intended for monitoring temperatures during the shelf life of the product.

Remove the cube of insulating material and inspect each indicator immediately upon receipt.

Do not use the valve if either indicator has been activated.

Immediately contact the local representative or manufacturer to make arrangements for return and replacement.

Products found to have activated indicators later than 48 hours following receipt, will be considered to have resulted from environmental conditions within the control of the customer and subject to replacement at customer's expense.

The temperature indicators should be discarded after opening and inspecting, except in the case of an activated sensor.

Any valve to be returned to the company following authorization, as outlined above, should be shipped in the same cube of insulating material in which it was received.

4. STORAGE

The Freedom SOLO bioprosthesis must be stored at a temperature between +5°C and +25°C (41°F and 77°F). The lower limit is especially important because at temperatures near 0°C (32°F) the preserving solution will start to freeze, thus causing irreversible damage to the biological tissue.

Nevertheless, the device should be stored at a low temperature range, while remaining within the limits stated. If storeroom conditions do not allow for appropriate control of the temperature upper limit, the device must be kept refrigerated but never below 5°C (41 °F). Avoid extreme changes in temperature.

Avoid exposure to heating or air-conditioning units.

5. EXPIRATION DATE

The expiration date of the prosthesis is four years from the date of manufacture as stated on the package label (the expiration date is indicated on the product labels).

6. STERILITY

The Freedom SOLO prosthesis is sterile if its packaging is sealed and undamaged. The external surface of the container is not sterile and therefore must not come into contact with sterile instruments.

WARNING: Valves removed from their container but not implanted should be considered no longer sterile and must not be used.

Precaution: The prosthesis cannot be resterilized. Do not attempt to clean, re-sterilize, or reuse any prosthesis that has been in contact with organic blood or tissue. As with any implantable medical device supplied for single use, in sterile state, loss of sterility and/or reuse may result in serious injury to the patient, or death.

DO NOT USE THE VALVE IF CONTAINER HAS BEEN OPENED OR DAMAGED.

7. ACCESSORIES

The accessories for implanting the Freedom SOLO prosthesis are:

- set of sizers (ICV1237, Fig 1a) or, alternatively, (ICV0677, Fig. 1b)
- UNI handle (ICV0664, Fig. 1c))

Accessories are supplied in a **non-sterile** condition and must be washed and sterilized before use. Instructions on the proper process to be used are enclosed in the packaging of the accessories.

Use only the supplied sizers to select the appropriate size of prosthesis.

WARNING: Repeated washing and sterilization may damage the accessories. Check the integrity of the accessories before use.

8. INDICATIONS FOR USE

The Freedom SOLO prosthesis is indicated for the replacement of diseased, damaged, or malfunctioning native or prosthetic aortic valves.

9. CONTRAINDICATIONS

None known.

10. WARNINGS

- **Extensive calcification of the root of the aorta may prevent correct suturing. In native bicuspid valve replacement, it may be difficult to align the prosthesis cusps correctly in the implant site. In both of these cases, the use of another type of prosthesis is recommended.**
- **It is recommended that the Freedom SOLO valve not be used in children, adolescents or young adults, in patients with chronic renal impairment or calcium metabolism disorders, or in patients receiving chronic drug treatment with preparations containing calcium due to the increased risk of premature valve tissue calcification.**
- **Cases of thrombocytopenia have been observed in patients implanted with the Freedom SOLO valve. Hence, it is recommended that the use of this device in patients with lower than normal preoperative platelet levels be carefully considered.**

11. PRECAUTIONS

- The Freedom SOLO prosthesis is designed for single use only.
- Valves from containers found to be damaged or opened must not be used for implantation.
- Valves removed from their container and not implanted should be considered no longer sterile and must not be used for implantation.
- Use only the supplied sizers (ICV1237; ICV0677) to select the appropriate size of prosthesis. Use of other manufacturer's sizers may result in an inappropriate sizing.
- The prosthesis cannot be resterilized. Do not attempt to clean, re-sterilize, or reuse any prosthesis that has been in contact with organic blood or tissue. As with any implantable medical device supplied for single use, in sterile state, loss of sterility and/or reuse may result in serious injury to the patient, or death.
- The Freedom SOLO prosthesis should not come into contact with linen, gauze or any material that may give off lint or fibers that could adhere to the valve and cause embolism or adverse reactions with the blood.
- When handling the valve, pay particular attention not to touch the tissue leaflets or to deform the prosthesis.
- Avoid using sharp needles or sharp or cutting surgical instruments that could damage the valve tissue.
- Insertion of catheters across the valve is not recommended as this procedure could damage the valve.
- Do not add drugs, chemical substances, antibiotics or anything else to the storage or rinsing solutions. Foreign substances may cause damage to the tissue.
- Keep the prosthesis moist. If allowed to dry, even partially or briefly, the tissue will be irreversibly damaged. For this reason, both sides of the prosthesis must be irrigated with physiological solution every two minutes during implantation.
- Use only sterile procedures to handle the Freedom SOLO prosthesis. The storage solution is not adequate for resterilizing a contaminated valve.
- The Freedom SOLO bioprosthesis must be stored at a temperature between +5°C and +25°C (41°F and 77°F). The lower limit is especially important because at temperatures near 0°C (32°F) the preserving solution will start to freeze, thus causing irreversible damage to the biological tissue.
- The Freedom SOLO bioprosthesis should be stored at a low temperature range, while remaining within the limits stated. If storeroom conditions do not allow for appropriate control of the temperature upper limit, the device must be kept refrigerated but never below 5°C (41 °F). Avoid extreme changes in temperature. Avoid exposure to heating or air-conditioning units.

12. POTENTIAL ADVERSE EVENTS

The risks or potential adverse events (in alphabetical order) associated with cardiac valve replacement with a bioprosthesis include, but may not be limited to:

- angina
- cardiac arrhythmia
- cardiac tamponade
- endocarditis
- heart failure (acute cardiac failure)
- hemolysis
- hemolytic anemia
- hemorrhage (bleeding)
- infection other than endocarditis
- myocardial infarction
- nonstructural valve dysfunction (e.g., entrapment by pannus or suture, inappropriate sizing or positioning, etc.)
- pericardial effusion
- paravalvular (perivalvular) leak
- prosthesis regurgitation
- prosthesis stenosis
- prosthesis thrombosis
- stroke or any related neurologic disorders
- structural valve deterioration (SVD) (e.g. calcification, leaflet tear or perforation, etc.)
- thromboembolism
- tissue dehiscence
- stenosis

It is possible that these adverse events could lead to:

- reoperation
- explantation
- permanent disability
- death

13. DIRECTIONS FOR USE

Practical knowledge of the applicable standard implant techniques and their surgical variants is essential in order to ensure appropriate use of the prosthesis. Only surgeons having received appropriate training in stentless valve implantation should use the device.

The performance of a stentless valve is sensitive to surgical implantation technique.

Selecting the prosthesis (sizing)

Use the sizers (ICV1237; ICV0677) to select the best prosthesis size. Use only the supplied sizers to select the appropriate size of prosthesis. Use of other manufacturer's sizers may result in an inappropriate sizing.

Insert the sizer into the annulus. If it passes through easily select the corresponding prosthesis size.

WARNING: Do not oversize the prosthesis by one size. Each valve size (as marked on the label) corresponds to a prosthesis dimension suitable for supraanular implantation.

WARNING: Do not undersize the prosthesis. If the annulus size falls between two consecutive prosthesis sizes, choose the larger prosthesis. WARNING: Do not use the prosthesis if there is an excessive mismatch between the valve annulus and the sino-tubular junction diameters (dilated aorta), unless surgically corrected, as this may give rise to central regurgitation due to defective leaflet coaptation; do not undersize the prosthesis.

Preparing the prosthesis

The valve and its storage solution are sterile and do not require further treatment. Examine the valve container for integrity. Check that the transparent seal is intact and that the container has not been opened, this would result in a loss of sterility. If there is any evidence of leakage of the solution, either as visible liquid or dried residual salts, **do not implant the valve.**

WARNING: Check the "Use by" data on the labels. Do not use the valve after the date printed on the packaging.

After having examined the package, tear off the transparent film and open the container by unscrewing the cover.

Simplified procedure before implant

The Freedom SOLO storage solution does not contain glutaraldehyde, so it is not necessary to rinse the valve before implantation.

We suggest the following procedure to keep the valve moist and assist the aseptic handling:

- prepare a bowl containing sterile saline solution and place the valve into the bowl during the preparation.
- insert the handle into the holder on which the prosthesis is mounted (Fig. 2a)
- remove the valve from the container and remove the holding collar (Fig. 2b)
- **To free the prosthesis from the holder simply cut the threads at the three points marked in Fig. 3.**
- **To retrieve the identification label, cut the thread that connects it to the holder. Care should be taken during holder and identification label removal to ensure that no damage occurs to the valve.**

The device is now ready for implantation.

Before implanting the valve, check that the data on all the labels and tags are identical. Do not implant the valve in case of any mismatch.

Implantation technique

The Freedom SOLO prosthesis is designed for implantation in a supraannular subcoronary position, with a single suture line. This is begun by applying three equidistant sutures at the aortic sinus mid-point, slightly above the annulus and on prosthesis outflow side at the leaflets mid-point. After lowering the prosthesis in situ and checking the alignment of the commissures, proceed with the suturing by applying continuous suture stitches along the native aortic wall and the prosthesis outflow edge.

The appropriate suture techniques are reported in the literature and these should be referred to when applying the prosthesis.

The main points to be observed are listed below:

- The prosthesis is indicated for implantation in a supraannular position.
- The correct alignment of the prosthesis is vitally important to ensure proper functioning.

  Distortions could lead to defective valve leaflet coaptation with consequent central regurgitation. Be particularly sure to position the first three sutures so that they are aligned symmetrically. As reported in the literature, the spatiel orientation of the commissures is simplified by surgical access for transverse aortotomy.
- While suturing the prosthesis, be very careful not to scratch or damage the valve leaflets. A cutting needle should not be used. It is recommended but not required to use RB-1 Needle 4-0 Polypropylene Suture.
- Proper bioprosthesis size selection is very important to ensure proper short/ long term functioning. Dimensional indications of the annulus and sinotubular junction may be made preoperatively using angiographic and/or echocardiographic techniques.
- The use of the supplied sizers and the instructions given in "selecting the prosthesis" are required to select the appropriate prosthesis size for each individual case.
- **WARNING: Do not use the prosthesis if there is an excessive mismatch between the valve annulus and the sino-tubular junction diameters (dilated aorta), unless surgically corrected, as this may give rise to central regurgitation due to defective leaflet coaptation.**

- Do not undersize the prosthesis. Unlike a homograft, bioprosthetic stabilized tissue may not stretch to adequately compensate for underestimation of the supracommissural diameter during diastole. If the annulus size falls between two consecutive prosthesis sizes, choose the larger prosthesis.
- The use of another type of prosthesis is preferable if there is extensive calcification of the root of the aorta, as this may prevent correct suturing.
- The use of another type of prosthesis is preferable in native bicuspid valve replacement, as it may be difficult to align the prosthesis cusps correctly.
- Use only atraumatic forceps while handling the valve during implantation.
- The prosthesis must be kept moist during suturing. Both sides should be irrigated with sterile physiological solution at least every two minutes.
- Check that, after device implantation, there is no gap between the prosthesis and the native aortic wall.

Post-operation management

Some medical professional societies recommend anticoagulant therapy during the first 3 months after bioprosthetic aortic valve implantation. Such postoperative anticoagulant therapy should be determined on an individual basis.

Long-term low dose aspirin, unless contraindicated, is recommended for all patients with bioprosthetic valves. Long-term anticoagulant therapy, unless contraindicated, is recommended for all patients with bioprosthetic valves who have risk factors for thromboembolism.

It is recommended that prophylactic antibiotic therapy be given to patients undergoing dental or other procedures which are potentially bacteremic in order to minimize the risk of endocarditis.

14. SPECIFIC PATIENT POPULATIONS

The safety and effectiveness of the Freedom SOLO valve has not been established for the following specific populations because it has not been studied in these populations:

- Patients who are pregnant
- Nursing mothers
- Patients with chronic renal impairment or calcium metabolism disorders
- Patients with active endocarditis
- Children, adolescents, or young adults

15. CLINICAL STUDY

STUDY DESIGN

The clinical study for the Freedom SOLO valve was a prospective, multi-center, non-randomized, observational study without concurrent or matched controls. The study was conducted at 18 centers in Europe, 9 centers in the United States, and 6 centers in Canada. A total of 804 patients were implanted in the study, all of whom underwent isolated implantation of the Freedom SOLO valve in the aortic position. The implant period for the study was from March 17, 2009 to January 8, 2013. All sites in the study followed a common protocol including inclusion/exclusion criteria (listed below) and obtained an informed consent. Any difference in the inclusion/exclusion criteria between the European and North America sites is indicated in the sections below in italic fonts (the italic font applies to the NA sites).

The evaluation of safety involved a comparison of postoperative linearized late adverse event rates to the FDA Objective Performance Criteria (OPCs) and a comparison of postoperative early, linearized late, and Kaplan-Meier adverse event rates to literature-based control data. The evaluation of effectiveness involved a comparison of postoperative New York Heart Association (NYHA) functional classification data to baseline and literature-based control data and a comparison of postoperative echocardiographic hemodynamic data to literature-based control data.

STUDY INCLUSION CRITERIA

Candidates for enrollment were those patients who met the following inclusion criteria:

a. The patient is male or female 18 years old or older.
b. The patient is willing to sign the informed consent. *(The subject or the subject's legal representative is willing to sign the informed consent.)*
c. The patient had a preoperative evaluation which indicated the need for native or prosthetic aortic valve replacement.
d. Any patient amenable to aortic valve replacement with biological prosthesis should be enrolled in the study, even in conjunction with valve repair, coronary artery bypass grafting, and other procedures.
e. The patient is located in a geographic location that will enable the subject to return to the study site for all follow-up examinations (i.e., geographically stable).
f. Patient will be available to the investigator(s) for postoperative follow-up beyond one year.

STUDY EXCLUSION CRITERIA

Patients were not enrolled in the study if any of the exclusion criteria listed below was met:

a. The patient has preexisting valve prosthesis in the mitral, pulmonary or tricuspid position.
b. The patient requires a double or triple valve replacement (a valve repair is not considered an exclusion criterion).
c. The patient has a previously implanted SOLO valve, within the clinical study, that requires replacement.
d. The patient has active endocarditis. *(The patient has active endocarditis or myocarditis.)*
e. The patient is or will be participating in a concomitant research study of an investigational product.

f. The patient is a minor, intravenous drug user, alcohol abuser, prisoner, institutionalized, or is unable to give informed consent.

g. The patient has a major or progressive non-cardiac disease that, in the investigator's experience, results in a life expectancy of less than 1 year, or the implant of the device produces an unacceptable increased risk to the patient.

h. The patient is pregnant or lactating. *(The patient is pregnant, planning to become pregnant, or lactating.)*

i. Patients with congenital bicuspid aortic valve.

j. Patients are known to be noncompliant or are unlikely to complete the study.

k. (The subject is undergoing renal dialysis for chronic renal failure or has been diagnosed with hyperparathyroidism.)

l. (The subject has had an acute preoperative neurological deficit, myocardial infarction, or cardiac event that has not returned to baseline or stabilized ≥ 30 days prior to the planned valve implant surgery.)

m. (The subject has an extensive calcification of the aortic root where removal of the calcified tissue cannot be achieved.)

n. (The subject has a significantly dilated aortic root that is not surgically corrected.)

o. (The subject requires replacement of the aortic root / full root procedure.)

FOLLOW-UP SCHEDULE

Patients were evaluated at each of the following time intervals:

- preoperatively,
- at implant,
- in the early postoperative period (at hospital discharge or within 30 days postoperatively),
- in the late postoperative period (between 3 and 6 months postoperatively),
- at 1 year (between 11 and 13 months postoperatively), and
- annually until study completion.

Preoperative demographic and baseline data including NHYA functional classification were collected before surgery.

Postoperative data, including blood value, NYHA functional class, and echocardiography data were collected at each follow-up. All echos were sent to the Echocardiography Core Laboratory for interpretation. Adverse event data were collected at the time of occurrence or site notification using the definitions from Edmunds *et al.* (Guidelines for reporting morbidity and mortality after cardiac valvular operations. J Thorac Cardiovasc Surg 1996;112:708-711)

CLINICAL ENDPOINT

The objectives of the clinical investigation were:

1) to demonstrate that the complication and survival rates for the Freedom SOLO valve are comparable to appropriate historical controls manifested as Objective Performance Criteria (OPCs), and to that reported in the literature for other stentless bioprostheses and stented pericardial valves;
2) to demonstrate that the hemodynamic performance of the Freedom SOLO valve is comparable to that reported in the literature for other stentless bioprostheses and stented pericardial valves; and
3) to demonstrate clinically significant improvement in overall patient condition by comparison of preoperative and postoperative NYHA functional classifications, and to demonstrate that the postoperative NYHA functional classification is comparable to that reported in the literature for other stentless bioprostheses and stented pericardial valves.

ACCOUNTABILITY OF PMA COHORT

As noted above, the Freedom SOLO valve cohort consisted of 804 patients who underwent isolated aortic valve replacement from March 17, 2009 to January 8, 2013. The cut-off date for data included in the PMA application was February 19, 2013. Total follow-up through last protocol evaluation for all 804 patients was 1101.5 patient-years with a mean follow-up of 16.5 ± 10.8 months (1.4 ± 0.9 years) and a range of follow-up of 0 to 40.5 months (0 to 3.4 years).

The following Table 2 summarizes patient compliance in the study.

Table 2 – Patient Compliance

Visit interval	Eligible patients (n)	Completed n_1 (%[1])
Preoperative	804	804 (100%)
Early Post-op	787	787 (100%)
3-6 Months	697	661 (94.8%)
1 Year	584	572 (97.9%)
2 Years	366	363 (99.2%)
3 Years	70	70 (100%)

[1] Percent calculated as = n_1 /n

STUDY POPULATION: PREOPERATIVE PATIENT DEMOGRAPHICS AND CHARACTERISTICS

The study cohort consisted of 804 patients who received an isolated aortic valve implant with the Freedom SOLO valve at sites in Europe (EU), Canada, and the United States (NA). The following Table 3 presents the patients' preoperative characteristics including the demographic profile of the study cohort. The mean age at implant was 74.9 years old (range 42.4 - 90.3 years). There were 45.1% females and 54.9% males. The majority of the patients were in NYHA Classes II and III.

Table 3 – Freedom SOLO Study Preoperative Patient Characteristics

Total patients in study cohort	804
Mean age ± SD (range)	74.9 ± 6.3 (42-90)
Age	
40-49	2 (0.2%)
50-59	10 (1.2%)
60-69	159 (19.8%)
70-79	484 (60.2%)
80-89	146 (18.2%)
90-99	3 (0.4%)
Sex	
F	363 (45.1%)
M	441 (54.9%)
Race	
White	796 (99.0%)
Black	2 (0.2%)
Asian	3 (0.4%)
Other[1]	3 (0.4%)

[1] One Native American, one Persian, one Filipino

SAFETY AND EFFECTIVENESS RESULTS

A. Safety Results

The analysis of safety was based on the treated cohort of 804 patients over the course of 1101.5 patient-years. The key safety outcomes and adverse event rates for aortic valve replacement for the study are presented in the following Table 4. The data are presented as percentages for early events, linearized rates (%/patient-year) for the late events, and "freedom from event" as actuarial analyses at years 1, 2, and 3 post-implant.

Table 4 – Observed Adverse Event Rates

(Total patients N= 804, Cumulative follow-up = 1101.5 patient-years and 1099.6 late patient-years)

Adverse event	Early events [1]		Late events [2]		Freedom From Event (%) [95% CI] [4]		
	n	%	n	%/pt-yr [3]	1 year	2 years	3 years
All mortality	14	1.7	50	4.55	94.0 [91.9 – 95.5]	90.5 [87.7 – 92.7]	82.6 [75.7 – 89.6]
Valve-related death	1	0.1	11	1.00	98.8 [97.6 – 99.4]	98.3 [96.8 – 99.1]	95.5 [89.2 – 98.2]
Explant	4	0.5	19	1.73	97.4 [95.8 – 98.3]	96.5 [94.6 – 97.8]	95.2 [91.3 – 97.4]
All bleeding	36	4.5	35	3.18	86.2 [83.6 – 88.5]	85.7 [83.0 – 88.1]	84.7 [81.3 – 87.6]
Major bleeding	23	2.9	25	2.27	88.4 [85.9 – 90.5]	87.9 [85.3 – 90.1]	87.9 [85.3 – 90.1]
Anticoagulation-related bleeding	3	0.4	9	0.82	98.6 [97.4 – 99.2]	98.1 [96.5 – 98.9]	97.0 [93.4 – 98.6]
Thromboembolic events	17	2.1	40	3.64	93.3 [91.1 – 94.9]	89.9 [87.1 – 92.2]	87.4 [82.7 – 91.1]
Major thromboembolic events	12	1.5	14	1.27	96.9 [95.3 – 97.9]	95.6 [93.6 - 97.0]	94.3 [90.5 – 96.7]
Endocarditis	2	0.2	17	1.55	97.6 [96.1 – 98.5]	97.0 [95.3 - 98.2]	97.0 [95.3 - 98.2]
Valve thrombosis	0	0	0	0.00	100 [100 - 100]	100 [100 - 100]	100 [100 - 100]
Structural valve deterioration	0	0	6	0.55	99.8 [98.6 - 100]	99.2 [97.4 – 99.7]	97.1 [91.8 – 99.0]
Nonstructural valve dysfunction[5]	13	1.6	9	0.82	97.2 [95.7 – 98.2]	97.2 [95.7 – 98.2]	94.6 [89.3 – 97.3]
Major Paravalvular leak	4	0.5	2	0.18	99.3 [98.4 – 99.7]	99.3 [98.4 – 99.7]	98.0 [92.6 – 99.5]
Hemolysis secondary to PVL	0	0	0	0.00	100 [100 - 100]	100 [100 - 100]	100 [100 - 100]

1- Early valve related events include postoperative events occurring 1-30 days post-implant. Early events rates calculated as the number of events divided by the total number of patients, times 100.
2-Late postoperative events (>30 days).
3-Late adverse event rate(%/pt-yr) is calculated as the number of late events divided by the total late patient-years, times 100.
4-Freedom from first event (early or late) rates were calculated using the Kaplan-Meier method.
5-Including paravalvular leak.

B. Effectiveness Results

The analysis of effectiveness was based on the evaluable patients at the annual endpoints. Key effectiveness outcomes are presented in Table 5 and Table 6.

Reduction in mean gradients and increase in EOA were observed at one year follow up. An improvement at one year follow up was reported in NYHA class. This improvement remained stable over time.

Table 5 – Effectiveness Outcome: NYHA Functional Classification

	Preoperative (n=804)	1 year follow-up (n=572)	2 years follow-up (n= 354)	3 years follow-up (n=70)
Class I	46 (5.7%)	374 (65.4%)	225 (63.6%)	43 (61.4%)
Class II	352 (43.8%)	176 (30.8%)	113 (31.9%)	21 (30.0%)
Class III	383 (47.6%)	15 (2.6%)	16 (4.5%)	6 (8.6%)
Class IV	22 (2.7%)	2 (0.3%)	0 (0.0%)	0 (0.0%)
Unable to assess	1 (0.1%)	5 (0.9%)	-	-

Table 6 – Effectiveness Outcomes at 1 Year Follow-up Visit: Hemodynamic Results

Hemodynamic parameter	**19 mm**	**21 mm**	**23 mm**	**25 mm**	**27 mm**
1 Year Postoperative	N[1]=6	N=83	N=177	N=192	N=79
Mean Gradient [mmHg]	N[2]=4	n=74	n=153	n=176	n=69
Mean ±SD	10.6 ± 2.9	9.6 ± 4.4	7.7 ± 4.3	6.0 ± 2.9	5.6 ± 2.9
EOA [cm^2]	n=4	n=65	n=131	n=160	n=65
Mean ±SD	0.9 ± 0.2	1.2 ± 0.3	1.5 ± 0.4	1.7 ± 0.5	1.8 ± 0.5
Regurgitation	n=5	n=83	n=176	n=192	n=78
None	2 (40.0%)	32 (38.6%)	78 (44.3%)	93 (48.4%)	39 (50.0%)
Trace	1 (20.0%)	42 (50.6%)	76 (43.2%)	77 (40.1%)	24 (30.8%)
Mild	2 (40.0%)	7 (8.4%)	13 (7.4%)	20 (10.4%)	14 (17.9%)
Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown[3]	0 (0%)	2 (2.4%)	9 (5.1%)	2 (1.0%)	1 (1.3%)

1 N=number of patients with a complete echo per valve size.
2 n=number of patients per valve size with available hemodynamic parameter.
3 Unknown included echos that did not contain appropriate images to evaluate aortic regurgitation.

16. PATIENT INFORMATION

Registration Form and Identification card

A Patient Registration Form is enclosed in each valve carton. The registration form must be completed and returned to the manufacturer by the implanting surgeon/ hospital. Upon receipt of the form, the manufacturer will prepare and forward an identification card with patient and valve information to the patient.

Patient's card

Every artificial heart valve is supplied with a patient's card that identifies the bearer. This system enables the surgeon to give the patient a document containing concise but comprehensive data about the operation and the implanted valve, which can be used whenever this information needs to be produced immediately.

Magnetic Resonance Imaging (MRI) Safety Information

MR Safe: This device contains no metals, and therefore, poses no known hazards in all MR environments.

17. RETURN OF EXPLANTED DEVICES

For information regarding the return of any product, contact your local Customer Service or Sales Representative. The required Return Material Authorization number and packaging instructions will be provided. Explanted valves should be placed into a suitable histological fixative solution, such as 10% formalin, before being returned.

18. WARRANTIES

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PRODUCT AVAILABILITY

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FIGURES

Figure 1a

Figure 1b

Figure 1c

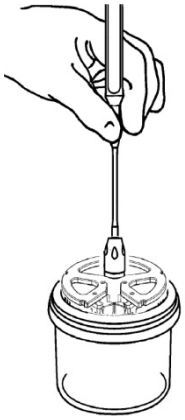

Figure 2a

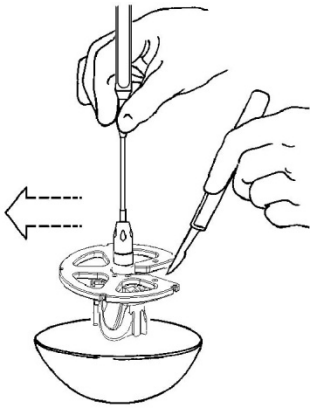

Figure 2b

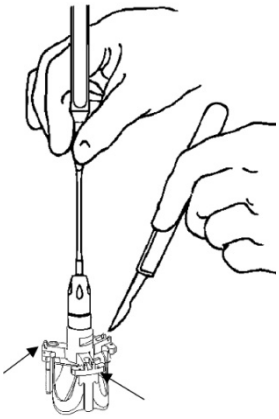

Figure 3

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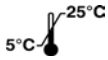
SOLO SMART
Stentless heart valve – Instructions for use

CAUTION: Federal Law (USA) restricts the device to sale by or on the order of a physician.

SYMBOLS

	CAUTION: SEE MANUAL FOR INSTRUCTIONS/WARNINGS
	CONTENTS STERILIZED USING ASEPTIC PROCESSING TECHNIQUE
	USE BY
	STORE BETWEEN 5°C AND 25°C
	SINGLE USE ONLY
	DO NOT RESTERILIZE
	CATALOGUE NUMBER
	SERIAL NUMBER
	SIZE
	MANUFACTURER
	QUANTITY INCLUDED IN PACKAGE
	DO NOT USE IF PACKAGE IS DAMAGED
	MR SAFE

1. DESCRIPTION

The SOLO Smart valve is a stentless bioprosthetic aortic heart valve made of bovine pericardium stabilized in buffered glutaraldehyde solutions and indicated for the replacement of damaged or malfunctioning aortic heart valves or prostheses in humans. The valve is attached to a flexible holder that acts as a temporary stent. The flexible holder is made of shape-memory alloy (Nitinol) and is designed to provide support to the valve while suturing and enhance the ergonomics of implantation. Once the valve is sutured to the aortic root, the holder is removed leaving the stentless valve in place.

The prosthesis is designed for implantation in a supraannular position, with a single suture line. The SOLO Smart valve consists of two pericardial sheets shaped according to a patented process. The pericardium tissue is selected and fixed in a glutaraldehyde-based process in which the stabilizing agent reacts under dynamic conditions. The first sheet has the form of three valvular cusps arranged to allow the blood to flow in only one direction. The second sheet has an outflow edge that allows suturing to the aortic wall. The two pericardium sheets are connected with a suture made of a thread coated with Carbofilm™, a thin film of turbostratic carbon with a high density.

The prosthesis is treated for the elimination of aldehyde residues and stored in a buffered solution without aldehydes.

2. AVAILABLE MODELS

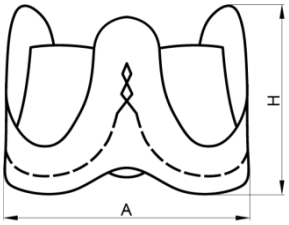
The SOLO Smart valve is available in four sizes: 21, 23, 25, and 27 mm (Table 1).

Each prosthesis is identified by a catalog number and a serial number. The catalog number consists of the letters ART, two numbers indicating the valve size and three letters (SMT) identifying the SOLO Smart prosthesis.

The serial number identifying each prosthesis can be used to retrieve information about valve manufacturing and quality control processes from the archives of the Quality Assurance Service of Sorin Group Canada.

Table 1. SOLO Smart Heart Valve dimensions

REF	SIZE (mm)	Supraannular Implant Diameter (mm) [A]	Height (mm) [H]
ART21SMT	21	23	20
ART23SMT	23	25	21
ART25SMT	25	27	22
ART27SMT	27	29	23



3. PACKAGING

SOLO Smart prostheses are preserved in a buffered sterile solution without aldehydes. Each valve is packaged individually in its own container (Fig. 1).

A plastic identification tag is attached with suture to the flexible holder. The valve is mounted on the flexible holder.

The container is externally sealed with a transparent film, which should be opened just before preparing the prosthesis for implantation.

WARNING: The external surface of the container is not sterile and must not come into contact with sterile instruments.

The container holding the prosthesis is packaged in a cube of insulating material that protects the device against temperature variations. Temperature indicators are also included in the package to monitor temperature exposure during transit.

WARNING: Indicators are for transit only. They are not intended for monitoring temperatures during the shelf life of the product.

Remove the cube of insulating material and inspect each indicator immediately upon receipt.

Do not use the valve if either indicator has been activated.

Immediately contact the local representative or manufacturer to make arrangements for return and replacement.

Products found to have activated indicators later than 48 hours following receipt, will be considered to have resulted from environmental conditions within the control of the customer and subject to replacement at customer's expense.

The temperature indicators should be discarded after opening and inspecting, except in the case of an activated sensor.

Any valve to be returned to the company following authorization, as outlined above, should be shipped in the same cube of insulating material in which it was received.

4. STORAGE

The SOLO Smart bioprosthesis must be stored at a temperature between +5°C and +25°C (41°F and 77°F). The lower limit is especially important because at temperatures near 0°C (32°F) the preserving solution will start to freeze, thus causing irreversible damage to the biological tissue.

Nevertheless, the device should be stored at a low temperature range, while remaining within the limits stated. If storeroom conditions do not allow for appropriate control of the temperature upper limit, the device must be kept refrigerated but never below 5°C (41°F). Avoid extreme changes in temperature.

Avoid exposure to heating or air-conditioning units.

5. EXPIRATION DATE

The expiration date of the prosthesis is four years from the date of manufacture as stated on the package label (the expiration date is indicated on the product labels).

6. STERILITY

The SOLO Smart prosthesis is sterile if its packaging is sealed and undamaged. The external surface of the container is not sterile and therefore must not come into contact with sterile instruments.

WARNING: Valves removed from their container but not implanted are no longer sterile and must not be used.

Precaution: The prosthesis cannot be resterilized. Do not attempt to clean, re-sterilize, or reuse any prosthesis that has been in contact with organic blood or tissue. As with any implantable medical device supplied for single use, in sterile state, loss of sterility and/or reuse may result in serious injury to the patient, or death.

DO NOT USE THE VALVE IF CONTAINER HAS BEEN OPENED OR DAMAGED.

7. ACCESSORIES

The accessories for implanting the SOLO Smart prosthesis are a set of sizers (ICV1237).

The sizers (ICV1237, Fig. 2) are used to measure the valve annulus and to choose the correct size prosthesis.

The set of sizers (ICV1237) consists of a series of obturators mounted on a handle. Use only the supplied sizers to select the appropriate size of prosthesis. Use of other manufacturer's sizers may result in inappropriate sizing.

Accessories are supplied in a **non-sterile** condition and must be washed and sterilized before use. Instructions on the proper process to be used are enclosed in the packaging of the accessories.

WARNING: Repeated washing and sterilization may damage the accessories. Check the integrity of the accessories before use.

8. INDICATIONS FOR USE

The SOLO Smart prosthesis is indicated for the replacement of diseased, damaged, or malfunctioning native or prosthetic aortic valves.

9. CONTRAINDICATIONS

None known.

10. WARNINGS

- **Extensive calcification of the root of the aorta may prevent correct suturing.**
- **In native bicuspid valve replacement, it may be difficult to align the prosthesis cusps correctly in the implant site. In both these cases, the use of another type of prosthesis is recommended.**
- **It is recommended that the Smart Solo valve not be used in children, adolescents or young adults, in patients with chronic renal impairment or calcium metabolism disorders, or in patients receiving chronic drug treatment with preparations containing calcium due to the increased risk of premature valve tissue calcification.**
- **Cases of thrombocytopenia have been observed in patients implanted with the Solo valve. Hence, it is recommended that the use of this device in patients with lower than normal preoperative platelet levels be carefully considered.**

11. PRECAUTIONS

- The SOLO Smart prosthesis is designed for single use only.
- Valves from containers found to be damaged or opened must not be used for implantation.
- Valves removed from their container and not implanted are no longer sterile and must not be used for implantation.
- Use only the supplied sizers (ICV1237) to select the appropriate size of prosthesis. Use of other manufacturer's sizers may result in an appropriate sizing.
- The prosthesis cannot be resterilized. Do not attempt to clean, re-sterilize, or reuse any prosthesis that has been in contact with organic blood or tissue. As with any implantable medical device supplied for single use, in sterile state, loss of sterility and/or reuse may result in serious injury to the patient, or death.
- The SOLO Smart prosthesis should not come into contact with linen, gauze or any material that may give off lint or fibers that could adhere to the valve and cause embolism or adverse reactions with the blood.
- When handling the valve, pay particular attention not to touch the tissue leaflets or to deform the prosthesis.
- Avoid using sharp needles or sharp or cutting surgical instruments that could damage the valve tissue.
- Insertion of catheters across the valve is not recommended as this procedure could damage the valve.
- Do not add drugs, chemical substances, antibiotics or anything else to the storage or rinsing solutions. Foreign substances may cause damage to the tissue.
- Keep the prosthesis moist. If allowed to dry, even partially or briefly, the tissue will be irreversibly damaged. For this reason, both sides of the prosthesis must be irrigated with physiological solution every two minutes during implantation.
- Use only sterile procedures to handle the SOLO Smart prosthesis. The storage solution is not adequate for resterilizing a contaminated valve.
- The SOLO Smart bioprosthesis must be stored at a temperature between +5°C and +25°C (41^{o}F and 77^{o}F). The lower limit is especially important because at temperatures near 0°C (32^{o}F) the preserving solution will start to freeze, thus causing irreversible damage to the biological tissue.
- The SOLO Smart bioprosthesis should be stored at a low temperature range, while remaining within the limits stated. If storeroom conditions do not allow for appropriate control of the temperature upper limit, the device must be kept refrigerated but never below 5°C (41^{o}F). Avoid extreme changes in temperature. Avoid exposure to heating or air-conditioning units.

12. POTENTIAL ADVERSE EVENTS

The risks or potential adverse events (in alphabetical order) associated with cardiac valve replacement with a bioprosthesis include, but may not be limited to:

- angina
- cardiac arrhythmia
- cardiac tamponade
- endocarditis
- heart failure (acute cardiac failure)
- hemolysis
- hemolytic anemia
- hemorrhage (bleeding)
- infection other than endocarditis
- myocardial infarction
- nonstructural valve dysfunction (e.g., entrapment by pannus or suture, inappropriate sizing or positioning, etc.)
- pericardial effusion
- paravalvular (perivalvular) leak
- prosthesis regurgitation
- prosthesis stenosis
- prosthesis thrombosis
- stroke or any related neurologic disorders
- structural valve deterioration (SVD) (e.g. calcification, leaflet tear or perforation, etc.)
- thromboembolism
- tissue dehiscence
- stenosis

It is possible that these adverse events could lead to:

- reoperation
- explantation
- permanent disability
- death

13. DIRECTIONS FOR USE

Practical knowledge of the applicable standard implant techniques and their surgical variants is essential in order to ensure appropriate use of the prosthesis. Only surgeons having received appropriate training in stentless valve implantation should use the device.

The performance of a stentless valve is sensitive to surgical implantation technique.

Selecting the prosthesis (sizing)

Use the sizers (ICV1237) to select the best prosthesis size. Use only the supplied sizers to select the appropriate size of prosthesis. Use of other manufacturer's sizers may result in an inappropriate sizing.

Insert the sizer into the annulus. If it passes through easily select the corresponding prosthesis size.

WARNING: Do not oversize the prosthesis by one size. Each valve size (as marked on the label) corresponds to a prosthesis dimension suitable for supraanular implantation.

WARNING: Do not undersize the prosthesis. If the annulus size falls between two consecutive prosthesis sizes, choose the larger prosthesis.

WARNING: Do not use the prosthesis if there is an excessive mismatch between the valve annulus and the sino-tubular junction diameters (dilated aorta), unless surgically corrected, as this may give rise to central regurgitation due to defective leaflet coaptation; do not undersize the prosthesis.

Preparing the prosthesis

The valve and its storage solution are sterile and do not require further treatment.

Examine the valve container for integrity. Check that the transparent seal is intact and that the container has not been opened, this would result in a loss of sterility. If there is any evidence of leakage of the solution, either as visible liquid or dried residual salts, **do not implant the valve.**

WARNING: Check the "Use by" data on the labels. Do not use the valve after the date printed on the packaging.

After having examined the package, tear off the transparent film and open the container by unscrewing the lid.

Simplified procedure before implant

The SOLO Smart storage solution does not contain free glutaraldehyde, so it is not necessary to rinse the valve before implantation.

We suggest the following procedure to keep the valve moist and assist the aseptic handling:

- prepare a bowl containing sterile saline solution and place the valve into the bowl during the preparation;
- prepare a commonly used needle holder with fine tip (less than 2 mm);
- remove the valve from the container by inserting the needle holder into the end of the flexible holder shaft (Fig. 3);
- **To free the prosthesis from the holding collar, simply cut the green thread of the holding collar (Fig.4).**
- **To retrieve the identification label, cut the thread that connects it to the flexible holder.**

The device is now ready for implantation.

The flexible holder is specifically designed as a temporary stent to provide support to the valve while suturing and enhance the ergonomics of implantation. Should you prefer to implant the prosthesis without the aid of the flexible holder, cut the three blue threads connecting it to the valve and gently remove the flexible holder.

Before implanting the valve check that the data on all the labels and tags are identical. Do not implant the valve if the data are not identical.

Implantation technique

The SOLO Smart prosthesis is designed for implantation in a supraannular subcoronary position, with a single suture line. The flexible holder acts as a temporary stent and provides support to the valve while suturing, enhancing the ergonomics of implantation. Start the valve implantation by applying three equidistant sutures at the aortic sinus mid-point, slightly above the annulus and on the prosthesis outflow side at the leaflets mid-point. After lowering the prosthesis in situ and checking the alignment of the commissures, proceed with the suturing by applying continuous suture stitches along the native aortic wall and the prosthesis outflow edge. The appropriate suture techniques are reported in the literature and these should be referred to when applying the prosthesis.

The main points to be observed are listed below:

- The prosthesis is indicated for implantation in a supraannular position.
- The correct alignment of the prosthesis is fundamental to ensure proper functioning. Distortions could lead to defective valve leaflet coaptation with consequent central regurgitation. Be particularly sure to position the first three sutures so that they are aligned symmetrically. As reported in the literature, the spatial orientation of the commissures is simplified by surgical access for transverse aortotomy.
- While suturing the prosthesis, be very careful not to scratch or damage the valve leaflets. A cutting needle should not be used. It is recommended but not required to use RB-1 Needle 4-0 Polypropylene Suture.
- Proper bioprosthesis size selection is very important to ensure proper short/long term functioning. Dimensional indications of the annulus and sino-tubular junction may be made preoperatively using angiographic and/or echocardiographic techniques.
- The use of the supplied sizers and the instructions given in "selecting the prosthesis" are required to select the appropriate prosthesis size for each individual case.

- **WARNING: Do not use the prosthesis if there is an excessive mismatch between the valve annulus and the sino-tubular junction diameters (dilated aorta), unless surgically corrected, as this may give rise to central regurgitation due to defective leaflet coaptation**.
- Do not undersize the prosthesis. Unlike a homograft, bioprosthetic stabilized tissue may not stretch to adequately compensate for underestimation of the supracommissural diameter during diastole. If the annulus size falls between two consecutive prosthesis sizes, choose the larger prosthesis.
- The use of another type of prosthesis is recommended if there is extensive calcification of the root of the aorta, as this may prevent correct suturing.
- The use of another type of prosthesis is recommended in native bicuspid valve replacement, as it may be difficult to align the prosthesis cusps correctly.
- The valve is assembled to a flexible holder; the flexible holder can be handled by means of a needle holder inserted into the end of the flexible holder shaft. By changing needle holder position, the shaft can be bent away from the suturing field.
- Keep the needle holder attached to the flexible holder shaft to avoid any interference with suturing threads, which might appear similar to the blue monofilament threads used for assembling the valve to the flexible holder.
- The prosthesis must be kept moist during suturing. Both sides should be irrigated with sterile physiological solution at least every two minutes.
- Check that, after device implantation, there is no gap between the prosthesis and the native aortic wall.
- Remove the flexible holder by cutting the upper portion of the three blue threads connecting it to the valve (Fig.5) and gently pulling the flexible holder shaft. Incorrect cutting position might cause incomplete removal of threads from the valve; check and remove any piece of thread.

  Dispose of flexible holder as medical/biohazard waste.

Post-operation management

Some medical professional societies recommend anticoagulant therapy during the first 3 months after bioprosthetic aortic valve implantation. Such postoperative anticoagulant therapy should be determined on an individual basis.

Long-term low dose aspirin, unless contraindicated, is recommended for all patients with bioprosthetic valves. Long-term anticoagulant therapy, unless contraindicated, is recommended for all patients with bioprosthetic valves who have risk factors for thromboembolism.

It is recommended that prophylactic antibiotic therapy be given to patients undergoing dental or other procedures which are potentially bacteremic in order to minimize the risk of endocarditis.

14. SPECIFIC PATIENT POPULATIONS

The safety and effectiveness of the SOLO Smart valve has not been established for the following specific populations because it has not been studied in these populations:

- Patients who are pregnant
- Nursing mothers
- Patients with chronic renal impairment or calcium metabolism disorders
- Patients with active endocarditis
- Children, adolescents, or young adults

15. CLINICAL STUDY

STUDY DESIGN

The clinical study for the SOLO Smart valve was a prospective, multi-center, non-randomized, observational study on the Freedom SOLO valve without concurrent or matched controls. The SOLO Smart valve is identical to the Freedom SOLO valve except that it has a flexible holder intended to facilitate the implant procedure. The study was conducted at 18 centers in Europe, 9 centers in the United States, and 6 centers in Canada. A total of 804 patients were implanted in the study, all of whom underwent isolated implantation of the Freedom SOLO valve in the aortic position. The implant period for the study was from March 17, 2009 to January 8, 2013. All sites in the study followed a common protocol including inclusion/exclusion criteria (listed below) and obtained an informed consent. Any difference in the inclusion/exclusion criteria between the European and North America sites is indicated in the sections below in italic fonts (the italic font applies to the NA sites).

The evaluation of safety involved a comparison of postoperative linearized late adverse event rates to the FDA Objective Performance Criteria (OPCs) and a comparison of postoperative early, linearized late, and Kaplan-Meier adverse event rates to literature-based control data. The evaluation of effectiveness involved a comparison of postoperative New York Heart Association (NYHA) functional classification data to baseline and literature-based control data and a comparison of postoperative echocardiographic hemodynamic data to literature-based control data.

STUDY INCLUSION CRITERIA

Candidates for enrollment were those patients who met the following inclusion criteria:

a. The patient is male or female 18 years old or older.
b. The patient is willing to sign the informed consent. *(The subject or the subject's legal representative is willing to sign the informed consent.)*
c. The patient had a preoperative evaluation which indicated the need for native or prosthetic aortic valve replacement.
d. Any patient amenable to aortic valve replacement with biological prosthesis should be enrolled in the study, even in conjunction with valve repair, coronary artery bypass grafting, and other procedures.
e. The patient is located in a geographic location that will enable the subject to return to the study site for all follow-up examinations (i.e., geographically stable).
f. Patient will be available to the investigator(s) for postoperative follow-up beyond one year.

STUDY EXCLUSION CRITERIA

Patients were not enrolled in the study if any of the exclusion criteria listed below was met:

a. The patient has preexisting valve prosthesis in the mitral, pulmonary or tricuspid position.
b. The patient requires a double or triple valve replacement (a valve repair is not considered an exclusion criterion).
c. The patient has a previously implanted SOLO valve, within the clinical study, that requires replacement.
d. The patient has active endocarditis. *(The patient has active endocarditis or myocarditis.)*
e. The patient is or will be participating in a concomitant research study of an investigational product.
f. The patient is a minor, intravenous drug user, alcohol abuser, prisoner, institutionalized, or is unable to give informed consent.
g. The patient has a major or progressive non-cardiac disease that, in the investigator's experience, results in a life expectancy of less than 1 year, or the implant of the device produces an unacceptable increased risk to the patient.
h. The patient is pregnant or lactating. *(The patient is pregnant, planning to become pregnant, or lactating.)*
i. Patients with congenital bicuspid aortic valve.
j. Patients are known to be noncompliant or are unlikely to complete the study.
k. (The subject is undergoing renal dialysis for chronic renal failure or has been diagnosed with hyperparathyroidism.)

l. *(The subject has had an acute preoperative neurological deficit, myocardial infarction, or cardiac event that has not returned to baseline or stabilized ≥ 30 days prior to the planned valve implant surgery.)*

m. *(The subject has an extensive calcification of the aortic root where removal of the calcified tissue cannot be achieved.)*

n. *(The subject has a significantly dilated aortic root that is not surgically corrected.)*

o. *(The subject requires replacement of the aortic root / full root procedure.)*

FOLLOW-UP SCHEDULE

Patients were evaluated at each of the following time intervals:

- preoperatively,
- at implant,
- in the early postoperative period (at hospital discharge or within 30 days postoperatively),
- in the late postoperative period (between 3 and 6 months postoperatively),
- at 1 year (between 11 and 13 months postoperatively), and
- annually until study completion.

Preoperative demographic and baseline data including NHYA functional classification were collected before surgery.

Postoperative data, including blood value, NYHA functional class, and echocardiography data were collected at each follow-up. All echos were sent to the Echocardiography Core Laboratory for interpretation. Adverse event data were collected at the time of occurrence or site notification using the definitions from Edmunds *et al.* (Guidelines for reporting morbidity and mortality after cardiac valvular operations. J Thorac Cardiovasc Surg 1996;112:708-711)

CLINICAL ENDPOINT

The objectives of the clinical investigation were:

1) to demonstrate that the complication and survival rates for the Freedom SOLO valve are comparable to appropriate historical controls manifested as Objective Performance Criteria (OPCs), and to that reported in the literature for other stentless bioprostheses and stented pericardial valves;
2) to demonstrate that the hemodynamic performance of the Freedom SOLO valve is comparable to that reported in the literature for other stentless bioprostheses and stented pericardial valves; and
3) to demonstrate clinically significant improvement in overall patient condition by comparison of preoperative and postoperative NYHA functional classifications, and to demonstrate that the postoperative NYHA functional classification is comparable to that reported in the literature for other stentless bioprostheses and stented pericardial valves.

ACCOUNTABILITY OF PMA COHORT

As noted above, the Freedom SOLO valve cohort consisted of 804 patients who underwent isolated aortic valve replacement from March 17, 2009 to January 8, 2013. The cut-off date for data included in the PMA application was February 19, 2013. Total follow-up through last protocol evaluation for all 804 patients was 1101.5 patient-years with a mean follow-up of 16.5 ± 10.8 months (1.4 ± 0.9 years) and a range of follow-up of 0 to 40.5 months (0 to 3.4 years).

The following Table 2 summarizes patient compliance in the study.

Table 2 – Patient Compliance

Visit interval	Eligible patients (n)	Completed n_1 (%[1])
Preoperative	804	804 (100%)
Early Post-op	787	787 (100%)
3-6 Months	697	661 (94.8%)
1 Year	584	572 (97.9%)
2 Years	366	363 (99.2%)
3 Years	70	70 (100%)

[1] Percent calculated as = n_1 /n

STUDY POPULATION: PREOPERATIVE PATIENT DEMOGRAPHICS AND CHARACTERISTICS

The study cohort consisted of 804 patients who received an isolated aortic valve implant with the Freedom SOLO valve at sites in Europe (EU), Canada, and the United States (NA). The following Table 3 presents the patients' preoperative characteristics including the demographic profile of the study cohort. The mean age at implant was 74.9 years old (range 42.4 - 90.3 years). There were 45.1% females and 54.9% males. The majority of the patients were in NYHA Classes II and III.

Table 3 – Freedom SOLO Study Preoperative Patient Characteristics

Total patients in study cohort	804
Mean age ± SD (range)	74.9 ± 6.3 (42-90)
Age	
40-49	2 (0.2%)
50-59	10 (1.2%)
60-69	159 (19.8%)
70-79	484 (60.2%)
80-89	146 (18.2%)
90-99	3 (0.4%)
Sex	
F	363 (45.1%)
M	441 (54.9%)
Race	
White	796 (99.0%)
Black	2 (0.2%)
Asian	3 (0.4%)
Other[1]	3 (0.4%)

[1] One Native American, one Persian, one Filipino

SAFETY AND EFFECTIVENESS RESULTS

A. Safety Results

The analysis of safety was based on the treated cohort of 804 patients over the course of 1101.5 patient-years. The key safety outcomes and adverse event rates for aortic valve replacement for the study are presented in the following Table 4. The data are presented as percentages for early events, linearized rates (%/patient-year) for the late events, and "freedom from event" as actuarial analyses at years 1, 2, and 3 post-implant.

Table 4 – Observed Adverse Event Rates
(Total patients N= 804, Cumulative follow-up = 1101.5 patient-years and 1099.6 late patient-years)

Adverse event	Early events [1]		Late events [2]		Freedom From Event (%) [95% CI] [4]		
	n	%	n	%/pt-yr [3]	1 year	2 years	3 years
All mortality	14	1.7	50	4.55	94.0 [91.9 – 95.5]	90.5 [87.7 – 92.7]	82.6 [75.7 – 89.6]
Valve-related death	1	0.1	11	1.00	98.8 [97.6 – 99.4]	98.3 [96.8 – 99.1]	95.5 [89.2 – 98.2]
Explant	4	0.5	19	1.73	97.4 [95.8 – 98.3]	96.5 [94.6 – 97.8]	95.2 [91.3 – 97.4]
All bleeding	36	4.5	35	3.18	86.2 [83.6 – 88.5]	85.7 [83.0 – 88.1]	84.7 [81.3 – 87.6]
Major bleeding	23	2.9	25	2.27	88.4 [85.9 – 90.5]	87.9 [85.3 – 90.1]	87.9 [85.3 – 90.1]
Anticoagulation-related bleeding	3	0.4	9	0.82	98.6 [97.4 – 99.2]	98.1 [96.5 – 98.9]	97.0 [93.4 – 98.6]
Thromboembolic events	17	2.1	40	3.64	93.3 [91.1 – 94.9]	89.9 [87.1 – 92.2]	87.4 [82.7 – 91.1]
Major thromboembolic events	12	1.5	14	1.27	96.9 [95.3 – 97.9]	95.6 [93.6 – 97.0]	94.3 [90.5 – 96.7]
Endocarditis	2	0.2	17	1.55	97.6 [96.1 – 98.5]	97.0 [95.3 - 98.2]	97.0 [95.3 - 98.2]
Valve thrombosis	0	0	0	0.00	100 [100 - 100]	100 [100 - 100]	100 [100 - 100]
Structural valve deterioration	0	0	6	0.55	99.8 [98.6 - 100]	99.2 [97.4 – 99.7]	97.1 [91.8 – 99.0]
Nonstructural valve dysfunction[5]	13	1.6	9	0.82	97.2 [95.7 – 98.2]	97.2 [95.7 – 98.2]	94.6 [89.3 – 97.3]
Major Paravalvular leak	4	0.5	2	0.18	99.3 [98.4 – 99.7]	99.3 [98.4 – 99.7]	98.0 [92.6 – 99.5]
Hemolysis secondary to PVL	0	0	0	0.00	100 [100 - 100]	100 [100 - 100]	100 [100 - 100]

1- Early valve related events include postoperative events occurring 1-30 days post-implant. Early events rates calculated as the number of events divided by the total number of patients, times 100.
2-Late postoperative events (>30 days).
3-Late adverse event rate(%/pt-yr) is calculated as the number of late events divided by the total late patient-years, times 100.
4-Freedom from first event (early or late) rates were calculated using the Kaplan-Meier method.
5-Including paravalvular leak.

B. Effectiveness Results

The analysis of effectiveness was based on the evaluable patients at the annual endpoints. Key effectiveness outcomes are presented in Table 5 and Table 6.

Reduction in mean gradients and increase in EOA were observed at one year follow up. An improvement at one year follow up was reported in NYHA class. This improvement remained stable over time.

Table 5 – Effectiveness Outcome: NYHA Functional Classification

	Preoperative (n=804)	1 year follow-up (n=572)	2 years follow-up (n= 354)	3 years follow-up (n=70)
Class I	46 (5.7%)	374 (65.4%)	225 (63.6%)	43 (61.4%)
Class II	352 (43.8%)	176 (30.8%)	113 (31.9%)	21 (30.0%)
Class III	383 (47.6%)	15 (2.6%)	16 (4.5%)	6 (8.6%)
Class IV	22 (2.7%)	2 (0.3%)	0 (0.0%)	0 (0.0%)
Unable to assess	1 (0.1%)	5 (0.9%)	-	-

Table 6– Effectiveness Outcome at 1 Year Follow-up Visit: Hemodynamic Results

Hemodynamic parameter	**19 mm**	**21 mm**	**23 mm**	**25 mm**	**27 mm**
1 Year Postoperative	N[1]=6	N=83	N=177	N=192	N=79
Mean Gradient [mmHg]	N[2]=4	n=74	n=153	n=176	n=69
Mean ±SD	10.6 ± 2.9	9.6 ± 4.4	7.7 ± 4.3	6.0 ± 2.9	5.6 ± 2.9
EOA [cm^2]	n=4	n=65	n=131	n=160	n=65
Mean ±SD	0.9 ± 0.2	1.2 ± 0.3	1.5 ± 0.4	1.7 ± 0.5	1.8 ± 0.5
Regurgitation	n=5	n=83	n=176	n=192	n=78
None	2 (40.0%)	32 (38.6%)	78 (44.3%)	93 (48.4%)	39 (50.0%)
Trace	1 (20.0%)	42 (50.6%)	76 (43.2%)	77 (40.1%)	24 (30.8%)
Mild	2 (40.0%)	7 (8.4%)	13 (7.4%)	20 (10.4%)	14 (17.9%)
Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown[3]	0 (0%)	2 (2.4%)	9 (5.1%)	2 (1.0%)	1 (1.3%)

1 N=number of patients with a complete echo per valve size.
2 n=number of patients per valve size with available hemodynamic parameter.
3 Unknown included echos that did not contain appropriate images to evaluate aortic regurgitation.

16. PATIENT INFORMATION

Registration Form and Identification card

A Patient Registration Form is enclosed in each valve carton. The registration form must be completed and returned to the manufacturer by the implanting surgeon/ hospital. Upon receipt of the form, the manufacturer will prepare and forward an identification card with patient and valve information to the patient.

Patient's Card

Every artificial heart valve is supplied with a patient's card that identifies the bearer. This system enables the surgeon to give the patient a document containing concise but comprehensive data about the operation and the implanted valve, which can be used whenever this information needs to be produced immediately.

Magnetic Resonance Imaging (MRI) Safety information

MR Safe: This device contains no metals and, therefore, poses no known hazards in all MR environments.

17. RETURN OF EXPLANTED DEVICES

For information regarding the return of any product, contact your local Customer Service or Sales Representative. The required Return Material Authorization number and packaging instructions will be provided. Explanted valves should be placed into a suitable histological fixative solution, such as 10% formalin, before being returned.

18. WARRANTY

SORIN GROUP CANADA INC. WARRANTS THAT REASONABLE CARE WAS USED IN THE MANUFACTURE OF THIS DEVICE. SORIN GROUP CANADA INC. WARRANTS THAT THIS DEVICE WAS MANUFACTURED ACCORDING TO STRICT SPECIFICATIONS. NO OTHER WARRANTY, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR PURPOSE, IS EITHER EXPRESSED OR IMPLIED SINCE HANDLING, STORAGE, AND CLEANING OF THIS DEVICE AS WELL AS FACTORS RELATING TO THE PATIENT, DIAGNOSIS, TREATMENT, SURGICAL PROCEDURES AND OTHER MATTERS BEYOND SORIN GROUP CANADA INC. CONTROL DIRECTLY AFFECT THIS DEVICE AND THE RESULTS OBTAINED FROM ITS USE. SPECIFICALLY DISCLAIMED ARE ANY AND ALL WARRANTIES OR CONDITIONS TO THE EXTENT THAT SUCH MAY BE IMPLIED UNDER THE PROVISIONS OF THE SALE OF GOODS ACT OF BRITISH COLUMBIA. NO REPRESENTATIVE OF THE COMPANY MAY MODIFY ANY OF THE FOREGOING AND THE PURCHASER AND/OR USER ACCEPTS THE PRODUCT SUBJECT TO ALL TERMS HEREIN STATED.

PRODUCT AVAILABILITY

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FIGURES

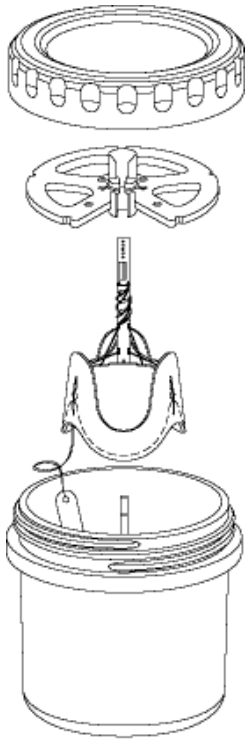


Figure 1

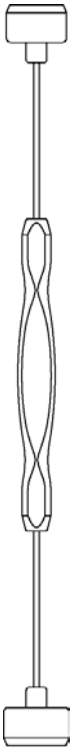
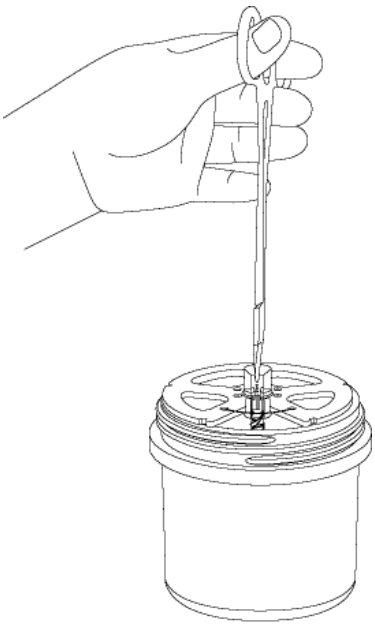


Figure 2



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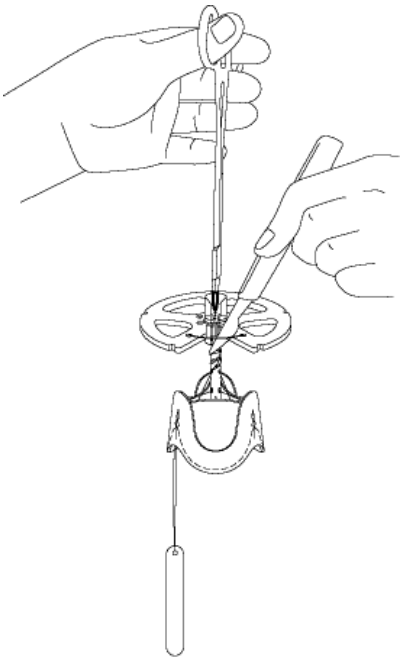

Figure 4

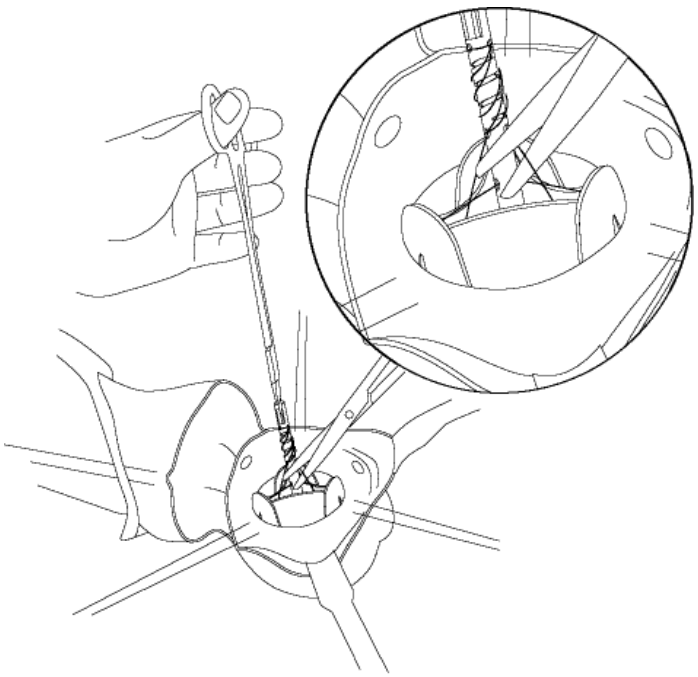

Figure 5