

**CardioSEAL<sup>®</sup> Septal Occlusion System with Qwik Load<sup>®</sup>**  
**Summary of Safety and Effectiveness Data**

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**CardioSEAL® Septal Occlusion System with Qwik Load®**  
**SUMMARY OF SAFETY AND EFFECTIVENESS**

**1. GENERAL INFORMATION**

Device Generic Name: Transcatheter Cardiac Occlusion Device

Device Trade Name: CardioSEAL® Septal Occlusion System with Qwik Load

Applicant's Name and Address: NMT Medical, Inc.  
27 Wormwood Street  
Boston, Mass. 02210

PMA Application Number: P000049

Date of Panel Recommendation: September 10, 2001

Date of Good Manufacturing Practices Inspection: March 27, 2001

Date of Notice to the applicant: December 5, 2001

**2. INDICATIONS FOR USE**

The CardioSEAL Septal Occlusion System with QwikLoad™ is indicated for use in patients with complex ventricular septal defects (VSD) of significant size to warrant closure who are considered to be at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or based on overall medical condition.

High risk anatomical factors for transatrial or transarterial surgical closure include patients:

- requiring a left ventriculotomy or an extensive right ventriculotomy;
- with a failed previous VSD closure;
- with multiple apical and/or anterior muscular VSDs (“Swiss Cheese Septum”); or
- with posterior apical VSDs covered by trabeculae.

**3. DEVICE DESCRIPTION**

The CardioSEAL Septal Occlusion System with Qwik Load consists of two primary components:

- the CardioSEAL, a permanent implant, which is constructed of a metal (MP35N) framework to which polyester fabric is attached, and
- the Delivery Catheter, a coaxial polyurethane catheter designed specifically to facilitate attachment, loading, delivery and deployment of the Occluder to the defect.

The CardioSEAL implant is available in sizes 17mm, 23mm, 28mm and 33mm.

#### 4. **CONTRAINDICATIONS**

Patients with thrombus at or near the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained unless the patient is protected with other embolic protection devices such as a vena cava filter.

Active endocarditis, or other infections producing a bacteremia.

Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate a 10F delivery sheath.

Patients whose defect is too small to allow the 10 F sheath to cross the defect.

Anatomy in which the CardioSEAL size or position required would interfere with other intracardiac or intravascular structures, such as valves or pulmonary veins.

Patients who are unable to take Aspirin, Heparin, Coumadin, or other anticoagulants.

Patients with VSDs acquired post myocardial infarction.

#### 5. **WARNINGS AND PRECAUTIONS:**

*See Warnings and Precautions in the final labeling (Information for Use).*

#### 6. **ADVERSE EFFECTS OF DEVICE ON HEALTH**

##### 6.1 Observed Adverse Events

Observed adverse events are summarized in Table 1. Adverse events categorized as serious or moderately serious are reported in the table as major adverse events. All other adverse events are classified as minor. The most commonly reported major adverse events include:

- Device embolization
- Hemolysis
- Ventricular tachycardia
- Blood loss requiring transfusion
- Hypotension requiring intervention
- Mitral valve regurgitation
- Vessel perforation

**Table 1 - Observed Adverse Events**

	<i>Percent</i> [95% Confidence Interval]	<i>Number of Patients</i>
Device-Related		
Major Adverse Events		
48-hours	13.8% (6.1, 25.4)	8
30-days	17.2% (8.6, 29.4)	10
6-month	17.2% (8.6, 29.4)	10
Most recent follow -up	17.2% (8.6, 29.4)	10
Procedure-Related		
Major Adverse Events		
48-hours	55.2% (41.5, 68.3)	32
30-days	56.9% (43.2, 69.8)	33
6-month	58.6% (44.9, 71.4)	34
Most recent follow-up	58.6% (44.9, 71.4)	34
Minor Adverse Events		
48-hours	27.6% (16.7, 40.9)	16
30-days	37.9% (25.5, 51.6)	22
6-month	41.4% (28.6, 55.1)	24
Most recent follow -up	60.3% (46.6, 73.0)	35
Device-embolization		
Percutaneous retrieval	1.7% (0.0, 9.2)	1
Surgical retrieval	0.0% (0.0, 6.2)	0
Device Malposition		
No intervention	8.6% (2.9, 19.0)	5
Intervention required	0.0% (0.0, 6.2)	0
Device Fracture		
48-hours	1.7% (0.0, 9.2)	1
30-days	3.4% (0.4, 11.9)	2
6-month	5.2% (1.1, 14.4)	3
Most Recent follow -up	20.7% (11.2, 33.4)	12
Device Fracture		
Associated with adverse event	20.7% (11.2, 33.4)	12
No adverse events	0.0% (0.0, 6.2)	0
		1
Cardiac Perforation	1.7% (0.0, 9.2)	
		36
Blood Loss Requiring Transfusion	62.1% (48.4, 74.5)	

6.2 Potential Adverse Events:

Placement of the CardioSEAL involves using standard interventional cardiac catheterization techniques. Complications commonly associated with these procedures include, but are not limited to:

- Air Embolus
- Allergic dye reaction
- Anesthesia reactions
- Apnea
- Arrhythmia
- Death
- Fever
- Headache / Migraines
- Hematoma and/or Pseudoaneurysm including blood loss requiring transfusion
- Hypertension; Hypotension
- Infection including Endocarditis
- Perforation of Vessel or Myocardium
- Stroke / Transient Ischemic Attack
- Thromboembolic events
- Valvular regurgitation

Fractures of the CardioSEAL framework have been reported in some implanted patients. The risk of fracture appears to be related to the size of the Occluder selected relative to the size of the heart chamber it was implanted in. In the independent, multi-center clinical trial sponsored by Children's Hospital, Boston, Massachusetts, the arm fracture rate was 15% in the Ventricular Septal Defect population. No adverse events were attributed to the occurrence of a device arm fracture in this population.

### 6.3 Observed Device Malfunctions:

There were five reports of a kink in the delivery system occurring during 107 device implantation procedures (4.7%). Four were identified during device placement, and one was identified during device loading. There were no clinical sequelae associated with any of these device malfunctions.

## 7. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative treatments for VSDs that cannot be closed through the standard transatrial or transarterial surgical approaches include medical management and/or pulmonary artery banding. In select patients, defects located in the apical portion of the heart may be surgically closed.

## 8. MARKETING HISTORY

The CardioSEAL Septal Occlusion System has received the CE Mark for marketing in Europe, Humanitarian Device Exemption approval, and Canadian approval. The CardioSEAL has not been withdrawn from marketing for any reason related to the safety or effectiveness of the device.

## 9. SUMMARY OF PRECLINICAL STUDIES

### 9.1 Biocompatibility

Biocompatibility testing of the implant and delivery system was conducted in accordance to Good Laboratory Practice regulations and ISO 10993-1. Test results indicate that the CardioSEAL Septal Occlusion System with Qwik Load is biocompatible and non-toxic.

The tests conducted on the delivery system include: cytotoxicity, sensitization, systemic toxicity, intracutaneous reactivity, pyrogenicity, hemolysis, hemocompatibility, thromboresistance, mutagenicity, primary skin irritation, muscle implantation and USP Physicochemical studies.

The tests conducted on the implant include: cytotoxicity, sensitization, systemic toxicity, intracutaneous reactivity, pyrogenicity, hemolysis, hemocompatibility, mutagenicity, muscle implantation and toxicity analysis. Carcinogenicity testing was not conducted due to the historical *in-vivo* use of the materials comprising the implant.

## 9.2 Animal Testing

Following successful initial acute studies, three chronic animal studies were conducted to evaluate the CardioSEAL Septal Occlusion System using both sheep and canine models. Explants occurred at 2 weeks, and at 1, 3, 6, 12 and 24 months. Atrial septal defects were created either via blade septostomy or Brockenbrough needle puncture followed by balloon dilation. In the first study, oversized devices were placed in freshly created defects in canines, which resulted in thrombosis and a device arm fracture. Subsequent animal studies confirmed that devices implanted in freshly created defects had higher levels of protein deposition and thrombosis.

The next two studies were conducted in both sheep and canine models with defects created a minimum of two weeks prior to implant. Both studies resulted in an acceptable histological response. There was one arm fracture noted at one month in a device, which did not appear to be appropriately placed with the defect. Friction lesions were noted acutely near the suture coil location of arms not yet healed to the septal wall surface; these healed over time. The 3, 6, 12 and 24 month explants showed good fibrous tissue overgrowth and endothelialization with no recent thrombosis or arm fractures.

An acute study was conducted to evaluate the front load delivery system modifications. The study was conducted in the sheep model in freshly created defects via blade septostomy followed by balloon dilation. Study results confirmed the modified delivery system conformed to product performance requirements.

## 9.3 Sterility Testing

The CardioSEAL Septal Occlusion System with Qwik Load is sterilized using a 100% ETO cycle that has been validated to achieve an SAL of  $10^{-6}$  in accordance with ANSI/AAMI/ISO 11135-1994. Sterilization residual limits meet the requirements of ANSI/AAMI/ISO 10993-9:1995.

## 9.4 Package Integrity

Shipping tests of packaged implants and delivery systems were conducted in accordance with ASTM D4169 ISTA 1A. All packages were intact with no physical damage to the product. Pouch ARO burst testing was conducted on implant and delivery system pouches. All pouches passed test requirements.

## 9.5 Bench Testing - Implant

### *Spring Arm Fatigue*

Spring Arm Accelerated Lifetime Fatigue Testing was performed to confirm that the spring arms could withstand 10 years equivalent pediatric heart rate (630 million cycles) without fracturing. Spring arms from the largest device size were tested (n=48). The tested units met performance requirements.

### *Engineering Analysis*

An engineering analysis, including finite element analysis was conducted. It concludes that the combination of spring arm fatigue testing to 630 million cycles, computer modeling and Goodman diagram fatigue life predictions demonstrate that under a worst case loading scheme, the implant can withstand twice the cyclic

deflection of previous implant models. In addition, problems are predicted to occur if the implant is oversized to the defect or septal anatomy.

#### *Arm/Fabric Strength*

Testing was performed to confirm that the fabric is securely attached to the arm framework and that it can withstand a 1.0 lb minimum tensile load. All tested units (n=20) met performance requirements.

#### *Dislodgement Resistance*

Testing was performed to confirm that the implant could withstand an applied dislodgement force of 38.0 grams minimum in a simulated defect. Implant sizes 17, 23 and 40mm were tested (n=10 each). All tested units met performance requirements.

#### *Arm/Body Joint Strength*

Testing was performed to confirm that the device springarm to device body attachment joint could withstand a 10.0 lb minimum tensile load. All tested units (n=14) met performance requirements.

#### *Ball/Body Joint Strength*

Testing was performed to confirm that the device ball to device body attachment joint could withstand an 8.0 lb minimum tensile load. All tested units (n=21) met performance requirements.

#### *Qwik Loader Funnel to Shaft Tensile*

Testing was performed to confirm that the funnel to shaft joint could withstand an 8.0 lb minimum tensile load. All tested units (n=35) met performance requirements.

#### *MRI Compatibility*

MRI testing was performed to confirm that the implant is non-ferromagnetic and MRI compatible. All tested units (n=5) met performance requirements. It was determined that the implant is MRI safe up to 1.5 Tesla and artifact generated was less than the size of the implant.

#### *Chemical Analysis of Implant Materials*

A chemical analysis of each of the materials comprising the implant was conducted to verify material composition. All tested samples passed raw material specifications.

#### *MP35N Wire Mechanical Properties-Tensile and Elongation*

Testing was performed to confirm that the tensile and elongation of the MP35N wire conformed to performance requirements. All samples tested (n=64) met performance requirements.

#### *MP35N Wire Mechanical Properties-Corrosion Resistance*

To evaluate the susceptibility of the implant to stress corrosion cracking, spring arm subassemblies (n=27) were subjected to static deflections in simulated body fluids. Scanning electron microscopy was performed at 6, 9 and 12 months on nine of the test samples. There was no evidence of stress corrosion cracking. All samples tested met performance requirements.

## **9.6 Bench Testing – Delivery System**

#### *Control Clamp/Proximal Sleeve Joint Strength*

Testing was performed to confirm that the control clamp to proximal sleeve joint could withstand a 6.5 lb minimum tensile load. All samples tested (n=30) met performance requirements.

#### *Control Clamp/Handle Sleeve Joint Strength*

Testing was performed to confirm that the control clamp to handle sleeve joint could withstand a 6.5 lb minimum tensile load. All samples tested (n=30) met performance requirements.

#### *Extrusion Luer/Shaft Tensile*

Testing was performed to confirm that the extrusion luer to shaft joint could withstand a 10.0 lb minimum tensile load. All samples tested (n=18) met performance requirements.

#### *Extrusion Sub-Assembly/Marker Band Tensile*

Testing was performed to confirm that the extrusion sub-assembly to marker band joint could withstand a 5.0 lb minimum tensile load. All samples tested (n=24) met performance requirements.

#### *Handle Sleeve/Core Wire Tensile*

Testing was performed to confirm that the handle sleeve to core wire joint could withstand a 6.5 lb minimum tensile load. All samples tested (n=20) met performance requirements.

#### *Locking Collar/Y-body Torsion*

Testing was performed to confirm that the locking collar to y-body joint could withstand a 10.0 lb minimum applied torsional force. All samples tested (n=18) met performance requirements.

### **9.7 Bench Testing – Implant and Delivery System Tested Together**

#### *Ball-to-Ball Strength*

Testing was conducted to confirm that the implant to the delivery system attachment mechanism could withstand a 6.5 lb minimum tensile load. All samples tested (n=30) met performance requirements.

#### *QL Locking Cap to QL Funnel Pod Leak Test*

Testing was performed to confirm that the delivery system locking cap to Qwik Loader funnel pod attachment complied with ISO 10555-1, Annex C. All samples tested (n=31) met performance requirements.

#### *Pivotability*

Testing was conducted to confirm that the implant, once attached to the delivery system, could freely pivot. All samples tested (n=20) met performance requirements.

#### *Simulated Use Load and Deployment*

Testing was conducted under conditions that simulate the use of the system in the clinical environment. Implant minimum side lengths, forces into and out of the loader and springback gap measurements were collected. All samples tested met performance requirements.

#### *Shelf Life*

Testing was conducted on implants and delivery systems that were subjected to an accelerated aging protocol, simulating a shelf life of 4 years for the implant and 2 years for the delivery system. Tensile testing was conducted on critical joints and load and deployment forces were collected. All samples tested met performance requirements.



## 10. CLINICAL STUDIES:

**Study Design/Objective:** The multi-center clinical trial conducted by Children's Hospital, Boston, Massachusetts, is a prospective, non-randomized trial studying the use of the CardioSEAL ® Septal Occlusion system to close a variety of hemodynamically significant defects. The risks of surgical closure for the patients enrolled in this trial were considered sufficient to justify the known and potentially unknown risks of transcatheter closure with the CardioSEAL device. The study (referred to as the High-risk study) is ongoing and is summarized below. Data from patients undergoing VSD closure were extracted from this study.

**Patient Entry:** Patients were eligible for enrollment in the High risk study if they had a defect(s) of sufficient size to require closure, but were considered to be at high risk for surgical closure, due to either complex medical or cardiac disease. An independent peer review group determined whether a patient should be enrolled into the trial based on the following criteria:

- the patient had a type of defect that was technically difficult or impossible to close surgically, such that the surgical risks were sufficient to justify the known and potential unknown risks of the device, or
- the patient's overall medical condition was such that the surgical risks were sufficient to justify the known and potential unknown risks of the device.

**Methods:** After enrollment, patients underwent cardiac catheterization. Position and size of the defect were confirmed by angiography. A hemodynamic assessment was performed pre-implant, and after test occlusion of the defect with a balloon. When these data suggested that the defect contributed to unfavorable hemodynamics and was feasible for transcatheter closure, device placement proceeded. Patients received aspirin, 1mg/kg/day, rounded to the nearest half tablet of 80 mg size, for at least six months following the procedure. Patients were seen for follow up assessments at 1, 6, 12 and 24 months.

**Primary Endpoints:** A 6-category ordinal scale (clinical status scale) was used to measure clinical status. The Clinical Status Scale grouped patients into eight different categories (right to left shunt, left to right shunt, anatomic, systemic embolic, hemodynamic compromise not due to shunt, arrhythmia, elevated PVR, and medical illness). The left to right shunt category was the category most closely related to the patient's indication for device closure of the VSD. This scale is shown in Table 2 below. The scale took values from 0 to 5, and was constructed so that an improvement by one category (e.g., from category 1 to category 2, or from 2 to 3) would be considered clinically meaningful. Deceased patients and those who have had their device explanted receive a value of -1. Data used in the construction of the scale were measured objectively by diagnostic laboratory tests, documented clinical status, or echocardiography.

The data were collected prospectively before device implantation, at discharge from the hospital, and at each follow-up visit, so that patient classification at each time point could be implemented using a computer algorithm.

Table 2 Clinical Status Scale						
Category	0	1	2	3	4	5
L to R shunt	ventilator dependent and/or intractable CHF	heart failure, symptomatic	Left ventricular volume overload, significant/large shunt	moderate shunt	small shunt	trivial or no shunt

1. Deceased patients and those who have had their device explanted are rated as -1 on the Clinical Status Scale.

Patients with prior placement of a pulmonary artery band to limit the degree of left to right shunting are categorized, where possible, according to the estimated anatomic size of the defect.

Additionally, an assessment of the echocardiographic closure status was made at each time point both at the evaluating facility, and by an unaffiliated core laboratory. Residual flow was assessed using Doppler color flow mapping, and graded using the following guidelines:

**"Trivial" to "Absent":** barely detectable or no detectable residual color flow through the defect. If flow present, it is a single color flow jet, well-circumscribed, with a proximal jet width measuring less than 1 mm in diameter in all views.

**"Small":** single color flow jet, well-circumscribed, and measuring 1-2mm (maximal proximal width) in all views in infants and children weighing less than 20 kg, or between 1 and 3 mm in diameter in larger children and adults.

**"More than small":** single color flow jet, well-circumscribed, measuring greater than 2 mm in diameter in all views in infants and children weighing less than 20 kg, or greater than 3 mm in diameter in all views in larger children and adults.

**Results:** At the time the VSD data was analyzed, 74 patients with no additional anatomic lesions were enrolled in the study for closure of a VSD. Enrollment occurred at two investigational sites. Thirteen of these patients did not have a device implant attempted, in most cases because the defect was smaller than anticipated.

Device placement was successful in 57 of 58 patients (98%) in whom an implant was attempted. Multiple procedures were performed in 6 patients, and multiple devices were implanted in 25 patients for a total of 107 implanted devices. There were 4 device embolizations which all occurred in the same patient while attempting to close a large post operative residual defect. All 4 were retrieved at catheterization. No other embolizations occurred.

The types of VSD defects closed with a CardioSEAL device were: congenital muscular (26); and post-operative (31). Seventeen patients (23%) had previously undergone placement of a pulmonary artery band.

Among the 57 patients implanted with a CardioSEAL device, there were 24 (42%) males and 33 (58%) females. The age of the patients ranged from 0.3 years to 70.1 years, with a median age of 3.7 years.

Four patients had devices that were explanted, 2 at the time of a heart transplant, 1 at a Fontan surgery performed after a failed septation, and 1 at a catheterization during which an unsuccessful attempt was made to close a large residual defect.

The primary efficacy outcome was defined as a change in Clinical Status Scale by Lesion from baseline to the 6-month follow up visit. Secondary efficacy measures included change in Clinical Status by Patient from baseline to the 6-month follow up visit and echocardiographic assessment of residual flow at 6 months.

Among the 57 implanted patients, 44 (77%) could be assessed according to the Clinical Status Scale by Lesion at both pre-implantation and at the 6-month follow-up time point. In this group, the median change in scale value was an increase of 2 categories ( $p < 0.0001$  compared to no improvement); 84.1% of the procedures were successful at 6 months (95%CI [69.9, 93.4]). Six patients were in a lower clinical status category than prior to implantation; this includes 3 patients who died and 2 who had their devices explanted. Success rates at 6 months did not differ for patients with congenital defects (85.7%, [63.7, 97.0]) and those with postoperative defects (82.6% [61.2, 95.0]). Patients under 10 years of age had a higher rate of success than those between 10 and 30 ( $p = 0.008$ ).

Fifty-three of the 57 implanted patients (93%) could be evaluated according to the Clinical Status Scale by Patient at both pre-implantation and at the 6 month follow-up visit. The median change in scale value was an increase of 2 categories ( $p < 0.0001$ ); 71.7% [57.7, 83.2] of the procedures were successful at 6 months.

Echocardiographic closure status changed from a median of 3 (more than small residual flow) prior to implantation to a median of 2 (small residual flow) at the 6-month time point ( $p < 0.0001$ ).

Baseline demographics and principal safety and effectiveness results are summarized in Table 3.

**Table 3 - Baseline Demographics, Principal Effectiveness Measures, & Principal Safety Measures**

<b>Patient Enrollment (number of patients)</b>				
Enrolled				74
Occluder Implant not Attempted <sup>1</sup>				13
Occluder Implant Attempted <sup>2</sup>				58
Occluder(s) Implanted				57
Single Procedure				52
Multiple Procedures <sup>3</sup>				6
More than One Occluder Placed <sup>4</sup>				25
<b>Principal Effectiveness Measures (n=57, patients with CardioSEAL Device)</b>				
	Percent [95% C.I.]	Median Scale Value	p-value	Number of Patients
Procedural Success-by lesion <sup>5</sup>	84.1% [69.9, 93.4]			44
Pre-implant Clinical Status Score <sup>6,7</sup>		1.5	-	50
Post-implant clinical Status Score 6-month		4	<.0001	44
Most recent follow -up		4	<.0001	48
Procedural Success-by patient <sup>8</sup>	71.7% [57.7, 83.2]			53
Pre-implant Echo Closure Score <sup>9,10</sup>		3	-	34
Post-implant Echo Closure Score 6-month		2	<.0001	22
Most recent follow -up		2	<.0001	28
<b>Principal Safety Measures (n=58, patients with implant attempted)</b>				
	Percent [95% C.I.]	Number of Patients		
Major Adverse Events <sup>11</sup>				
48-hours	63.8% (50.1, 76.0)	37		
30-days	70.7% (57.3, 81.9)	41		
6-month	74.1% (61.0, 84.7)	43		
Minor Adverse Events				
48-hours	27.6% (16.7, 40.9)	16		
30-days	37.9% (25.5, 51.6)	22		
6-month	41.4% (28.6, 55.1)	24		
Device-related Adverse Events				
Embolization	1.7% (0.0, 9.2)	1		
Delivery System	8.6% (2.9, 19.0)	5		
Fractures	20.7% (11.2, 33.4)	12		
Procedure-related Adverse Events <sup>12</sup>	84.5% (72.6, 92.7)	49		
Blood loss requiring transfusion	62.1% (48.4, 74.5)	36		
Vascular	15.5% (7.3, 27.4)	9		
ANY Adverse Event	98.3% (90.8, 100.0)	57		

1. Occluder implant not attempted: defect smaller than anticipated (12), unfavorable anatomy (1).
2. 3 patients received a STARFlex device (which is not the subject of this PMA); 1 attempted but not placed.
3. Multiple procedures: 2 procedures (4), 3 procedures (2).
4. More than one occluder placed: 2 occluders (11), 3 occluders (8), 4 occluders (3), 5 occluders (2), 7 occluders (1).
5. Procedural success by lesion: primary efficacy outcome defined as improvement from pre-implantation Clinical Status Scale by Lesion by at least 1 category at 6 months. Among 57 implanted patients, 44 could be assessed according to Clinical Status Scale by Lesion at both pre-implantation and 6 month follow up.
6. Clinical Status Score: A 6-category ordinal scale used to measure clinical status was developed for the High-Risk Study. The scale takes values from 0 to 5, & was constructed so that an improvement by 1 category (e.g., 1 to 2, etc.) is considered clinically meaningful. All data used in the construction of the scale are measured objectively by diagnostic lab tests, documented clinical status, and/or echocardiography. Data are collected pre-implant, at discharge and at each follow -up visit.
7. 7 patients could not be assessed according to Clinical Status by Lesion pre-implantation, one did not have baseline echo and 6 had echo characterized as uncertain.
8. Procedural success by patient: secondary efficacy outcome defined as improvement from pre-implantation Clinical Status Scale by Patient by at least 1 category at 6 months. Among 57 implanted patients, 53 could be assessed according to Clinical Status Scale by Patient at both pre-implantation and 6 month follow up.

9. Echo Closure Score: A 3-category ordinal scale used to measure residual flow, categorized as (1) trivial to absent, (2) small, (3) more than small.
10. Only patients with echocardiographic images adequate to assess flow are included.
11. Major Adverse Events: equals serious and moderately serious adverse events. Minor adverse events are all those not considered serious or moderately serious.
12. Includes all implantation and catheterization procedure related events.

## 11. **Conclusions Drawn from Studies**

The preclinical studies indicate that the CardioSEAL Septal Occlusion System with Qwik Load is biocompatible and meets performance specification requirements.

Despite a high degree of comorbid illness within the treated patient group, in suitable patients, the overall success rate was high, with 72% of the patients having an improved clinical status at 6 months after implantation, and 84% of the patients having a reduction in flow through the defect or reduction in the anatomic defect size. Peri-procedure events, including some serious events, occurred frequently, but all moderately serious or serious events had resolved by 6 months after the procedure.

In conclusion, the CardioSEAL Septal Occlusion System with Qwik Load is safe and effective in the intended patient population.

## 12. **Panel Recommendations**

At an advisory meeting held on September 10, 2001, the Circulatory System Devices Panel recommended nine to one that the CardioSEAL Septal Occluder be approved subject to the submission to, and approval by, the Center for Devices and Radiological Health (CDRH) the following:

- changes to the labeling for the CardioSEAL Septal Occluder;
- items to be incorporated into the training program; and
- collection of 5-year follow-up data for patients enrolled in the clinical trial as well as prospective evaluation of technical success and patient outcome for the initial patients to be treated.

## 13. **FDA DECISION**

CDRH concurred with the Circulatory System Devices Panel recommendation of September 10, 2001, and conveyed Conditions of Approval in a facsimile dated November 16, 2001. NMT indicated concurrence with those Conditions of Approval.

FDA issued and approval order on December 5, 2001. The applicant's manufacturing facility was inspected on May 27, 1999, and March 28, 2001, and the sterilization facilities were inspected on August 10, 200, and May 25, 2000. These facilities were found to be in compliance with the Good Manufacturing Practice regulations.

## 14. **APPROVAL SPECIFICATIONS**

Indications for Use: See the Instructions for Use (Attachment 1)

Hazards to Health from use of the Device: See CONTRAINDICATIONS, WARNINGS and PRECAUTIONS, and ADVERSE EVENTS in the Instructions for Use (Attachment 1).

Postapproval requirements and restrictions: See approval order.

The Approval Order, Summary of Safety and Effectiveness Data, and labeling can be found on the Internet at address  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.