

# 1 SUMMARY OF SAFETY AND EFFECTIVENESS

## 1.1 GENERAL INFORMATION

Device Generic Name:	Cardiac Resynchronization Therapy – Defibrillator (CRT-D)
Device Trade Name:	CONTAK CD Model 1823; CONTAK CD 2 Models H115 and H119; RENEWAL Model H135; and RENEWAL 3 Models H170, H175, H177 and H179
Applicant’s Name and Address:	GUIDANT Corporation, Cardiac Rhythm Management 4100 Hamline Avenue North St. Paul, Minnesota 55112-5798
Date of Panel Recommendation:	TBD
PMA Number:	P010012/S026
Date of Notice of Approval to Applicant:	TBD

## 1.2 INDICATIONS FOR USE

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction (EF  $\leq$  35%) and QRS duration  $\geq$  120 ms.

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) have demonstrated the following outcomes in the indicated population specified above:

- Reduction in risk of all-cause mortality or first all-cause hospitalization  
*Note: Hospitalization is defined as administration of IV inotropes or vasoactive drugs > 4 hours (outpatient or inpatient), or admission to a hospital that includes or extends beyond a calendar date change.*
- Reduction in risk of all-cause mortality
- Reduction of heart failure symptoms

## 1.3 CONTRAINDICATIONS

GUIDANT CRT-Ds are contraindicated for use in the following:

- Patients whose ventricular tachyarrhythmias may have reversible cause, such as 1) digitalis intoxication, 2) electrolyte imbalance, 3) hypoxia, 4) sepsis, or
- Patients whose ventricular tachyarrhythmias may have a transient cause, such as 1) acute myocardial infarction, 2) electrocution, or 3) drowning.

## **1.4 WARNINGS AND PRECAUTIONS**

Reference the Physician's System Guide specific to the device that is being implanted for the complete list of warnings and precautions.

## **1.5 DEVICE DESCRIPTION**

Reference the Physician's System Guide specific to the pulse generator being implanted. Also reference the Model 2920 ZOOM programming manual for use of the programmer.

## **1.6 ALTERNATE PRACTICES AND PROCEDURES**

Patients who have heart failure are routinely treated with medications. Cardiac resynchronization therapy pacemaker (CRT-P) devices, and CRT devices with defibrillation back-up are also available to treat heart failure. Additional medical treatments for heart failure include, but are not limited to, exercise and nutrition programs.

## **1.7 MARKETING HISTORY**

Guidant CRT-Ds are currently available for commercial distribution in the U.S. and other countries including: Australia, Austria, Belgium, Canada, Chile, Czech Republic, Denmark, Dominican Republic, Finland, France, Germany, Greece, Guadeloupe, Guyana, Hong Kong, Iceland, India, Indonesia, Ireland, Israel, Italy, Jordan, Kuwait, Lebanon, Liechtenstein, Luxembourg, Malaysia, Martinique, Netherlands, New Caledonia, New Zealand, Norway, Portugal, San Marino, Saudi Arabia, Singapore, Slovenia, South Africa, Spain, Sweden, Switzerland, Thailand, Turkey, United Kingdom, and Venezuela. As of March 25, 2004, no Guidant CRT-Ds have been withdrawn from the market in any country for any reason related to safety or effectiveness.

## **1.8 POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

### **1.8.1 OBSERVED ADVERSE EVENTS**

The CONTAK RENEWAL 3, CONTAK RENEWAL, and CONTAK CD devices provide the same cardiac resynchronization therapy (biventricular pacing) and have the same Indications for Use. Therefore, the Comparison of Medical, Pacing, and Defibrillation Therapies in Heart Failure (COMPANION) clinical trial data, (based on CONTAK CD devices) used to support expanding Guidant CRT-D indications to the COMPANION patient population, are also applicable to CONTAK RENEWAL and CONTAK RENEWAL 3.

The primary difference between CONTAK CD devices and CONTAK RENEWAL/RENEWAL 3 devices is that CONTAK CD utilizes an electrically common RV

and LV sensing/pacing circuit whereas CONTAK RENEWAL and CONTAK RENEWAL 3 incorporate an independent RV and LV sensing/pacing circuit. Additional clinical analysis was conducted with CONTAK RENEWAL, in a European study, to provide confirmation that the independent sensing and pacing capability did not adversely affect the ability of the device to detect ventricular tachyarrhythmias or provide continuous biventricular pacing therapy.

The COMPANION study was a prospective, randomized, controlled, multi-center, blinded study conducted at 128 sites and enrolled a total of 1638 patients, of which 1520 were randomized. Patients were randomly assigned 1:2:2 to receive optimal pharmacological therapy (OPT, 308 patients) or a cardiac resynchronization therapy pacemaker (CRT-P, 617 patients) or a cardiac resynchronization therapy pacemaker with defibrillator (CRT-D, 595 patients). Of the 1520 patients randomized, 903 were randomized to OPT and CRT-D. ***This summary focuses on data and analyses for the CRT-D and OPT groups, only, with the exception of the Exercise Performance results, which are based on pooled CRT-D and CRT-P data.***

A total of 498 device or procedure-related adverse events were reported in 290 out of 595 (48.7%) patients randomized to CRT-D for an average of 0.84 events per patient. Device-related adverse events that were observed in more than 1% of patients in the following categories:

- Phrenic/diaphragmatic stimulation (58 patients, 10.7%)
- Loss of LV capture (36 patients, 6.7%)
- Pocket hematoma 31 patients, 5.7%)
- Inappropriate shock above rate cutoff due to SVT (23 patients, 4.3%)
- Multiple counting of ventricular events (17 patients, 3.1%)
- Pocket infection (14 patients, 2.6%)
- Loss of atrial capture (14 patients, 2.2%)
- Inappropriate shock due to oversensing (11 patients, 2.0%)
- Loss of RV capture (8 patients, 1.5%)
- Pacemaker-mediated tachycardia (6 patients, 1.1%)

The following types of procedure-related adverse events with a prevalence greater than 1% were reported:

- Post surgical wound discomfort (63 patients, 10.6%)
- Coronary sinus dissection (14 patients, 2.4%)
- Pneumothorax (10 patients, 1.7%)

- Hypotension (9 patients, 1.5%)
- AV block (7 patients, 1.2%)
- Physical trauma (7 patients, 1.2%)
- Physiological reaction (6 patients, 1.0%)

### **1.8.2 DEATHS**

There were a total of 182 deaths (77 OPT, 105 CRT-D) that occurred during the trial and recorded through November 30, 2002. Of the 182 deaths, 134 were classified as cardiac in nature (58 OPT, 76 CRT-D). The remaining 48 deaths were classified as either vascular, non-cardiac or were unknown/unclassified.

Procedure related mortality was defined as any death that occurred within 30 days of the implant procedure and/or including events during, or as a result of, events from pre-operative anesthesia through discharge from the operating room, electrophysiology lab, or an office visit. Three (3) (0.5%) deaths in the CRT-D arm were considered to be procedure related. Since OPT patients did not undergo an implant procedure, 30 day mortality from the time of randomization was 1.0% and 1.2% for OPT and CRT-D respectively. These rates were not statistically significant between OPT and CRT-D groups ( $p=0.779$ ).

### **1.8.3 POSSIBLE ADVERSE EVENTS**

Based on the literature and pulse generator implant experience, the following alphabetical list includes possible adverse events associated with implantation of a cardiac resynchronization therapy system:

- Acceleration of arrhythmias
- Air embolism
- Allergic reaction
- Bleeding
- Cardiac tamponade
- Chronic nerve damage
- Conductor coil fracture
- Death
- Dehydration
- Elevated thresholds
- Erosion/extrusion
- Extracardiac stimulation (eg, phrenic, diaphragm, chest wall)

- Fibrotic tissue formation (eg, keloid formation)
- Fluid accumulation
- Formation of hematomas or cysts
- Heart block
- Inability to defibrillate or pace
- Inappropriate therapy (eg, shocks, ATP, pacing)
- Incomplete lead connection with pulse generator
- Infection
- Lead displacement/dislodgment
- Lead fracture
- Lead insulation breakage or abrasion
- Lead tip deformation and/or breakage
- Local tissue reaction
- Muscle or nerve stimulation
- Myocardial trauma (eg, cardiac perforation, irritability, injury)
- Myopotential sensing
- Oversensing/undersensing
- Pacemaker mediated tachycardia
- Pericardial rub, effusion
- Pneumothorax
- Random component failures
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Thrombosis/thromboemboli
- Valve damage
- Venous occlusion
- Venous trauma (e.g., perforation, dissection, erosion)

Patients susceptible to frequent shocks despite antiarrhythmic medical management may develop psychologic intolerance to an implantable system that may include the following:

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of shocking while conscious
- Fear that shocking capability may be lost
- Imagined shocking

In addition to the implantation of a cardiac resynchronization therapy system, potential adverse events associated with implantation of a coronary venous lead system are listed below in alphabetical order:

- Allergic reaction to contrast media
- Breakage/failure of implant tools
- Coronary venous occlusion
- Coronary venous trauma (e.g., perforation, dissection, erosion)
- Prolonged exposure to fluoroscopic radiation
- Renal failure from contrast media used to visualize coronary veins

## **1.9 SUMMARY OF PRE-CLINICAL STUDIES**

Guidant's commercially available CONTAK CD system was implanted for the CRT-D device arm of the COMPANION study. The CONTAK CD system was previously tested via non-clinical laboratory testing including bench testing, biocompatibility evaluation and animal studies. Device design and system compatibility involved verification and validation of the system. The test results were previously found acceptable.

The COMPANION data gathered with CONTAK CD is also applicable to all Guidant commercially available CRT-Ds. Design differences between CONTAK CD and subsequent generation devices were supported by bench and/or clinical data in the following submissions: CONTAK CD Model 1823 (P010012 / approved 5/2/2002); CONTAK CD2 Models H115 and H119 (P010012/S004 approved 10/07/2002); and in particular RENEWAL Model H135 where we first introduced independent RV and LV pacing outputs, and where we justified the applicability of existing CONTAK CD clinical data to RENEWAL and provided additional Holter data to verify the independent outputs (P010012/S002, approved 12/20/2002); and RENEWAL 3 Models H170, H175, H177 and H179 (P010012/S008, approved 6/13/03).

## **1.10 SUMMARY OF COMPANION CLINICAL STUDY**

The COMPANION clinical study was designed to determine whether combined all-cause mortality or all-cause hospitalization in heart failure patients receiving optimal pharmacologic therapy (OPT) can be reduced by combining OPT and 1) biventricular pacing therapy alone (CRT-P) or 2) biventricular pacing with defibrillation (CRT-D). All cause mortality or all cause hospitalization (time to first event) analyzed from the time of randomization, was the primary endpoint of the study.

Guidant conducted the COMPANION trial to demonstrate the safety and effectiveness of Guidant CRT-D devices in the COMPANION patient population. Trial objectives included establishing that OPT combined with biventricular pacing with defibrillation [CONTAK CD] is superior to OPT alone in improving exercise performance, (Sub-study), reducing combined all-cause mortality or all-cause hospitalization (Primary endpoint), reducing cardiac morbidity (Secondary endpoint) and reducing all-cause mortality (Secondary endpoint).

The clinical study began January 20, 2000 and was conducted at 128 centers within the United States.

### **1.10.1 STUDY DESIGN**

COMPANION was a prospective, randomized [1:2:2 to OPT, CRT-P (delivered by the CONTAK TR device), or CRT-D (delivered by the CONTAK CD device)], controlled, multi-center study. Randomization was stratified by centers and by beta-blocker use to assure proper balance between the treatment groups within each center. Each randomized patient remained counted as a member of the original randomization assignment (intention-to-treat) regardless of subsequent crossover or protocol adherence.

#### **1.10.1.1 ENDPOINTS**

This summary focuses on the CRT-D vs. OPT contrast, providing evidence of safety and effectiveness for Guidant CRT-Ds in the COMPANION patient population. The clinical data and analyses herein address the following study endpoints for CRT-D vs. OPT only:

##### ***Primary Endpoint***

The primary endpoint, a composite endpoint of all-cause mortality or all-cause hospitalization (time to first event) analyzed from the time of randomization, was designed to show a 25% reduction in the CRT-D group from an OPT annual rate of 40%. All-cause mortality was defined as death from any cause, while all-cause hospitalization was defined as admission to hospital involving a calendar date change. Also, administration of IV inotropes or vasoactive drugs for more than 4 hours was considered a hospitalization.

##### ***Secondary Endpoints***

**All-cause mortality:** The all-cause mortality (death from any cause) endpoint was designed to show a 25% reduction in mortality in the CRT-D arm from an OPT annual mortality rate of 24%. Difference in mortality was determined by contrasting patients randomized to CRT-D in addition to OPT versus patients randomized to OPT alone using a two-tailed test for treatment versus control.

**Cardiac morbidity:** To determine whether the occurrence of cardiac morbid events is reduced in patients randomized to CRT-D compared to OPT.

##### ***Sub-study Primary Endpoint and Tertiary Endpoints***

**Exercise performance:** This co-primary endpoint for the sub-study, which consists of Peak VO<sub>2</sub> and Six-Minute Walk, is designed to demonstrate improvement in exercise performance

with CRT (CONTAK TR and CONTAK CD data pooled) compared to OPT at six months post-baseline.

Quality of Life as measured by the Minnesota Living with Heart Failure Questionnaire© and NYHA Class.

### ***Safety***

CRT-D system-related complication-free rate is determined by measuring complications related to any of the implanted components or their associated implant procedure in those patients *who were successfully implanted* with the CRT-D system.

#### **1.10.1.2 PATIENTS STUDIED**

##### **Demographics for Patients Randomized to CRT-D and OPT**

The mean age of randomized patients was 66.7 and 65.6 years in the OPT and CRT-D arms, respectively. The patient population consisted of 68.5% and 67.3% male for OPT and CRT-D respectively. A majority of the OPT and CRT-D patients were NYHA class III, 82.1% and 86.1% respectively. Disease etiology was ischemic in 58.7% and 54.6% for OPT and CRTD. There were no statistical differences between OPT and CRT-D at baseline.

##### **Demographics for Sub-Study Patients**

The mean age of patients randomized in the Exercise Performance sub-study was 63.1 and 62.1 years in OPT and CRT arms respectively. The Exercise Performance sub-study population consisted of 63 (72.4%) and 209 (65.7%) males and 24 (27.6%) and 109 (34.3%) females in the OPT and CRT arm respectively. The characteristics of the patient population are presented in Table 1-5.

Patients contributing to the exercise performance effectiveness endpoints were randomized to OPT, CRT-P and CRT-D. Four hundred forty eight (448) patients were enrolled in the Exercise Performance sub-study of which three hundred sixty-one (361) were randomized to CRT, and eighty-seven (87) were randomized to optimal pharmacological therapy. Of the 448 patients enrolled, 405 patients contributed to the effectiveness endpoint with a data cut off of November 15, 2002.

#### **1.10.1.3 METHODS AND STATISTICS**

The COMPANION DSMB met approximately every six months to review the trial's progress and to review the safety and efficacy data collected. An "O'Brien-Fleming" type boundary as implemented by Lan and DeMets was used in monitoring the trial. The Group sequential procedure ensured that the total alpha spent across repeated analyses did not exceed the total type I error, in this case  $\alpha = 0.03$ .

On November 18, 2002 the DSMB reviewed the study progress for the final time. The CRT-D arm of the Study had reached the significance for both the combined mortality and hospitalization endpoint as well as the all-cause mortality endpoint prompting the DSMB to recommend to the Steering Committee that enrollment be stopped. All efficacy follow-ups ended on December 1, 2002.

## **1.10.2 OVERALL STUDY RESULTS**

### **PRIMARY ENDPOINT**

The 12-month event rate was 68.0% for OPT and 55.9% for CRT-D. This demonstrates an absolute reduction of 12.1% for the composite endpoint of all-cause mortality or all-cause hospitalization at one year in patients implanted with CRT-D. The log-rank test for difference in time to first event for combined all-cause mortality or all-cause hospitalization resulted in a p-value of 0.010. This demonstrates that CRT-D significantly reduces the risk of the combined endpoint of all-cause mortality or all-cause hospitalization compared to OPT alone. Additionally, the results of the proportional hazards analysis displayed a 20% relative reduction in the risk of the combined endpoint event in CRT-D compared to OPT [Hazard Ratio (HR) 0.80 (95% Confidence Interval (CI): 0.68, 0.95),  $p=0.010$ , adjusted  $p=0.011$ ].

### **SECONDARY ENDPOINT FOR ALL-CAUSE MORTALITY**

The log-rank test for difference in survival resulted in a p-value of 0.003. This demonstrates that CRT-D when combined with OPT reduces the risk of all-cause mortality compared to OPT alone. Additionally, the results of the proportional hazards analysis displayed a 36% relative reduction in the risk of a mortality event in the CRT-D arm compared to OPT [Hazard Ratio (HR) 0.64, (95% Confidence Interval (CI): 0.48, 0.86),  $p = 0.003$ , adjusted  $p = 0.004$ ].

### **SECONDARY ENDPOINT FOR CARDIAC MORBIDITY**

During the trial, 49% of the OPT patients experienced cardiac morbid events compared to 32% of CRT-D patients. This demonstrates a 35% reduction in the risk of having cardiac morbid events in patients treated with CRT-D. Adjusting for the greater average follow-up time per patient in the CRT-D group, CRT-D patients experienced 51% fewer cardiac morbid events per year of patient follow-up than OPT patients (0.49 events/year for CRT-D compared to 1.01 events/year for OPT). Additionally, CRT-D patients spent 43% fewer days in the hospital for cardiac morbid events per year compared to OPT patients. OPT patients spent 7.5 days in the hospital associated with cardiac morbid events per patient year and CRT-D patients were in hospital for 4.3 days associated with cardiac morbid events per patient year.

## **CRT-D SYSTEM SAFETY**

Device safety was determined by a system complication-free rate. The system-related complication-free rate was defined as the number of patients who do not experience a system-related complication divided by the total number of patients who were successfully implanted with the investigational system. A total of 81 system-related complications were reported in 68 of the 541 (12.6%) patients implanted with a CONTAK CD system yielding a 87.4% with a lower 95% confidence boundary of 85.1% system-related complication-free rate. Three system-related complications resulting in invasive intervention were reported in more than 1% of the patient population. These complications were as follows;

- Loss of left ventricular capture (25 patients, 4.6%)
- Loss of atrial capture (9 patients, 1.7%)
- Phrenic/diaphragmatic stimulation (8 patients, 1.5%)

### **1.10.3 SUB-STUDY RESULTS**

#### **MAXIMAL OXYGEN CONSUMPTION (PEAK VO<sub>2</sub>)**

Peak VO<sub>2</sub> was determined from a standardized protocol for exercise testing as a means of measuring a patient's capacity for performing physical activity. Peak VO<sub>2</sub> was improved by 1.2 ml/kg/min in CRT-D patients compared to 0.6 ml/kg/min in OPT patients at six-months. This demonstrates a between group difference of 0.6 ml/kg/min (p=0.074).

#### **EFFECTIVENESS ENDPOINT: SIX-MINUTE WALK DISTANCE**

The Six-Minute Walk test is a measure of a patient's ability to sustain exercise during an activity similar to that which a patient may typically perform on a daily basis. For this test, patients are instructed to walk as far as possible in 6 minutes in a level corridor. Six-minute walk distance was improved by 41 meters in CRT-D patients compared to 17 meters in OPT patients at six-months. This demonstrates a between group difference of 24 meters (p=0.017).

#### **ANCILLARY EFFECTIVENESS: NEW YORK HEART ASSOCIATION CLASS (NYHA)**

The determination for New York Heart Association (NYHA) Class is based on mutual assessment, by the patient and physician, of the patient's heart failure symptoms both at rest and while performing ordinary physical activity. NYHA class improved by one or more classes in 58% of the CRT-D patients compared to 46.2% of the OPT patients at six-months (p=0.03)

### **ANCILLARY EFFECTIVENESS: QUALITY OF LIFE (QOL)**

Quality of Life (QOL) was assessed using the 21-question Minnesota Living with Heart Failure questionnaire. Each question, answered by the patient, is ranked on a scale ranging from 0 to 5. A lower total score indicates an improved quality of life. QOL was improved by -23 points in CRT-D patients compared to -10 points OPT patients at six-months. This demonstrates a -13 point between group difference ( $p < 0.0001$ ).

#### **1.10.4 ADDITIONAL FUNCTIONAL CAPACITY DATA FOR ALL CRT-D AND OPT PATIENTS**

In addition to the Exercise Performance sub-study, functional capacity was evaluated by means of NYHA Class, six-minute walk distance, and Minnesota Living with Heart Failure Questionnaire© QOL for the **all** patients randomized to OPT and CRT-D through 6-months of follow up.

The NYHA Class, six-minute walk distance, and QOL scores were significantly improved in the CRT-D group compared to the OPT group at 3 and 6 months. These findings are similar to those presented in the exercise performance sub-study and previous cardiac resynchronization therapy trials.

In conclusion, the ability of the CRT-D system to effectively deliver CRT therapy has been demonstrated. The result of this success was improved exercise performance, as measured by Peak  $VO_2$  and Six-Minute Walk distance, for those patients receiving optimal pharmacological therapy (OPT) with CRT as compared to patients receiving optimal pharmacological therapy alone. Additionally, New York Heart Association (NYHA) Class and Quality of Life test scores improved for those patients receiving OPT + CRT compared to the control.

### **1.11 RISK/BENEFIT CONCLUSION**

The observed all-cause mortality risk reduction (36%,  $p = 0.003$ ) and improvement in exercise performance provided by the CRT-D, outweigh the risks associated with implanting the system (complication-free rate 85.1%).

#### **1.10.6 EFFECTIVENESS CONCLUSIONS**

The results of the combined primary endpoint of all-cause mortality or all-cause hospitalization demonstrate that heart failure patients implanted with CRT-D in addition to OPT have a significant and substantial reduction in all-cause mortality or all-cause hospitalization compared to heart failure patients treated with OPT alone

- The addition of CRT-D to OPT reduced the risk of the composite endpoint of all-cause mortality or all-cause hospitalization by 20%  $p=0.010$

- The significant reduction in the composite endpoint demonstrates that patients with moderate to severe heart failure benefit from CRT-D
- This observed CRT-D risk reduction in the composite endpoint confirms that patients with moderate to severe heart failure are at high risk of all-cause mortality or all-cause hospitalization

The results of the all-cause mortality endpoint demonstrate that heart failure patients implanted with CRT-D in addition to OPT have a significant and substantial reduction in mortality compared to heart failure patients treated with OPT alone

- The addition of CRT-D to OPT reduced the risk of an all-cause mortality event by 36%  $p = 0.003$   
The significant risk reduction in all-cause mortality demonstrates that patients with moderate to severe heart failure benefit from CRT-D  
This observed CRT-D risk reduction in all-cause mortality confirms that patients with moderate to severe heart failure are at high risk of a mortality event
- The results of CRT (CRT-P and CRT-D) demonstrated a significant improvement in exercise performance as measured by peak VO<sub>2</sub> and six-minute walk distance

During the trial, 49% of the OPT patients experienced cardiac morbid events compared to 32% of CRT-D patients. This demonstrates a 35% reduction in the risk of having cardiac morbid events in patients treated with CRT-D. Adjusting for the greater average follow-up time per patient in the CRT-D group, CRT-D patients experienced 51% fewer cardiac morbid events per year of patient follow-up than OPT patients (0.49 events/year for CRT-D compared to 1.01 events/year for OPT).

The ability of the CRT-D therapy to effectively deliver CRT therapy has been demonstrated. The result of this success was improved exercise performance, as measured by Peak VO<sub>2</sub> and Six-Minute Walk distance, for those patients receiving optimal pharmacological therapy (OPT) with CRT as compared to patients receiving optimal pharmacological therapy alone. Additionally, New York Heart Association (NYHA) Class and Quality of Life test scores improved for those patients receiving OPT + CRT compared to the control.

### **1.10.7 SAFETY CONCLUSIONS**

The system-related complication free rate was 85.1% for all patients implanted with a CRT-D device and is within the limits established by commercially available CRT-D devices i.e. greater than 70%.

### **1.12 PANEL RECOMMENDATION (TBD)**

### **1.13 CDRH DECISION (TBD)**

### **1.14 APPROVAL SPECIFICATIONS (TBD)**

Directions for use: See the labeling.

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

Postapproval Requirements and Restrictions: See approval order.