

I. General Information

Device Generic Name: Percutaneous Catheter
Radionuclide Brachytherapy Source
Radionuclide Applicator System

Device Trade Name: GALILEO™ Intravascular Radiotherapy System

Applicant's Name / Address: Guidant Corporation
Guidant Vascular Intervention
8934 Kirby Drive
Houston, TX 77054

PMA Number: P000052

Date of Notice of Approval to Applicant: November 2, 2001

II. Indications for Use

The GALILEO™ Intravascular Radiotherapy System is intended to deliver beta radiation to the site of successful Percutaneous Coronary Intervention (PCI) for the treatment of in-stent restenosis in native coronary arteries with discrete lesions ≤ 47 mm in a reference vessel diameter 2.4 mm to 3.7 mm.

III. Device Description

The GALILEO™ Intravascular Radiotherapy System is intended to deliver a controlled dose of radiation from a beta-emitting source to a target vessel segment within a previously implanted stent. The GALILEO™ Intravascular Radiotherapy System comprises three major components: the 27 mm GALILEO™ Centering Catheter, the 27 mm GALILEO™ ³²P Source Wire, and the GALILEO™ Source Delivery Unit.

The GALILEO™ Centering Catheter is a dual-lumen, closed-end catheter with a spiral-shaped balloon near its distal tip. It is a blood-contact, sterile, single-use device designed to facilitate proper positioning of the radioactive ³²P Source Wire when used with the GALILEO™ Source Delivery Unit. The primary catheter lumen is a closed-end lumen that extends longitudinally through the length of the catheter to allow for advancement and positioning of the Source Wire. The proximal end of the source wire lumen has a single lumen extension tube that is attached to a coded connector key via adaption tubing. The connector key contains a pattern of punched holes that are read by the GALILEO™ Source Delivery Unit to determine characteristics of the catheter such as balloon treatment length and balloon outer diameter. The distal end of the source wire lumen is closed to prevent blood contact. The second catheter lumen, the inflation lumen, allows for inflation and deflation of the centering balloon with saline. The inflation lumen terminates proximally in a luer-lock adapter, allowing the attachment of standard inflation devices. The distal tip of the catheter has a single guide wire lumen that allows the catheter to be placed over a 0.014" coronary guide wire using the rapid exchange (RX) technique. The guide wire lumen runs from the distal tip of the catheter to an exit notch located distal to the balloon. The length of the guide wire lumen is approximately 5 mm. The outer balloon diameter is available in a range of sizes from 2.5 mm to 3.5 mm (in 0.5 mm increments) and is sized based on the minimum lumen diameter (MLD) in the artery segment to be treated. The catheter has Microglide or Hydrophilic coating for lubricity. A radiopaque marker is located near each end of the balloon to aid in positioning the centering catheter. The markers indicate the location where the ends of the radioactive Source Wire will be placed (i.e., Treatment Zone).

Proximal shaft markers are located at 95 cm and 105 cm to aid in gauging catheter position relative to the tip of a brachial or femoral guiding catheter, respectively.

The GALILEO™ ³²P Source Wire is a thin, flexible nickel-titanium (NiTi) alloy wire that has the Phosphorus-32 (³²P) source material and a single tungsten radioopaque marker encapsulated in the distal tip. The radioopaque marker allows the physician to verify the position of the source within the Centering Catheter during treatment. The Source Wire has an active length of 27 mm. In use, the Source Wire is entirely contained in either the GALILEO™ Source Delivery Unit or the GALILEO™ Centering Catheter and does not contact human tissue. The radionuclide selected for the GALILEO™ Intravascular Radiotherapy System is the beta particle emitter Phosphorus-32 (³²P).

The GALILEO™ Source Delivery Unit (SDU) is a computer-controlled afterloader similar to commercial oncology afterloaders, but designed specifically for use in intravascular radiotherapy using a beta emitting isotope. It allows the GALILEO™ ³²P Source Wire to be positioned within the GALILEO™ Centering Catheter for treatment delivery. The SDU consists of three parts: the Head, which contains the touch screen and the insertion point for the Cartridge; the Base, which provides support for the unit and houses emergency tools; and the Cartridge, which houses the ³²P Source Wire, the InActive wire, the software, and the drive mechanism.

IV. Contraindications

- Unprotected left main disease (>50% narrowing)
- Patients in whom antiplatelet and/or anticoagulant therapy are contraindicated.

V. Warnings

- **Every attempt should be made to avoid restenting of the target lesion to minimize the risk of thrombosis.**
- The GALILEO™ Intravascular Radiotherapy System (GALILEO™ System), including the Centering Catheter, should be used by physicians trained in the practice of intravascular radiotherapy. A thorough understanding of the technical principles, clinical applications and risks associated with intravascular radiotherapy is necessary before performing the procedure.
- Misuse or malfunction of the GALILEO™ System can expose the patient, operator and others in the procedure room to unintended radiation exposure.
- Coronary intravascular radiotherapy should be performed only at hospitals where emergency coronary artery bypass surgery can be performed quickly in the event of a potentially injurious or life-threatening complication.
- To minimize the risk of thrombosis when new stents are implanted in conjunction with radiation therapy, a minimum of six (6) months antiplatelet therapy is recommended. If a new stent is not implanted in conjunction with the radiation therapy, antiplatelet therapy should be administered at the physician's discretion.
- Treatment should be interrupted and any extended wire must be retracted into the SDU if a patient requires defibrillation or cardioversion while either the InActive or Active wire is extended. The GALILEO™ System is not certified as defibrillation-proof.
- Coronary intravascular radiotherapy using the GALILEO™ System should be carried out only after achieving sufficiently successful intervention of stenotic atherosclerotic lesions in the native coronary arteries.

- Always perform Patient, Centering Catheter, and SDU radiation surveys before and after every treatment. There is no guarantee that the SDU will detect a condition of the source not being in the storage safe under all fault conditions.
- Guide wire prolapse can occur as the Centering Catheter is withdrawn. Do not advance or retract the Centering Catheter over the floppy portion of the guide wire. Do not advance or retract the Centering Catheter unless the balloon is fully deflated and under vacuum. If resistance is met during manipulation, determine the cause of the resistance before proceeding.
- The Centering Catheter is intended for single-procedure use only. Do not resterilize and/or reuse it, as this can compromise device performance and increase the risk of cross-contamination due to inappropriate reprocessing.
- This centering catheter should not be used for percutaneous transluminal coronary angioplasty (PTCA) and should not be used for vessel dilatation. The centering catheter is used solely for the centering of the radiation source.
- The balloon pressure of the Centering Catheter should not exceed the operating pressure of 4 atm. The operating pressure is based on results of *in vitro* testing. At least 90% of the balloons (with a 95% confidence) will hold pressure when inflated to the operating pressure (4 atm) for 15 minutes. Use of a pressure-monitoring device is recommended to prevent over-pressurization.
- Use the Centering Catheter prior to the “Use By” date specified on the package.

VI. Precautions

- Only Guidant-manufactured Cartridges, Source Wires, and Catheters should be used with the GALILEO™ Source Delivery Unit.
- The GALILEO™ Centering Catheter is designed to be used by a team of appropriately trained personnel. At a minimum, this team should include an interventional cardiologist, radiation oncologist and medical physicist.
- Prior to each use, ensure that all daily quality assurance checks have been performed.
- Before inserting the GALILEO™ Centering Catheter in the SDU, check the catheter shaft to ensure that there are no kinks or severe bends in order to avoid obstruction errors during treatment.
- In general, balloon diameter should be no more than 0.25 mm larger or smaller than the minimum lumen diameter (MLD) of the lumen in the area to be treated.
- The total artery length that has undergone interventional treatment and injury (including post-stent dilatation) must not exceed 47 mm. Total injured arterial lengths exceeding 22 mm must be treated with tandem balloon positioning.
- During tandem balloon positioning procedures (that is, repositioning the balloon), ideal balloon positioning is achieved when there is no gap or overlap between the distal and proximal segments. At no time should an overlap exceeding 2 mm or a gap exceeding 1 mm be allowed. An overlap will increase the dose delivered to the overlap region, while a gap will decrease the dose delivered to the treated area.
- Do not use a Centering Catheter balloon size larger than the interventional device size used.
- Difficulty with advancement of the InActive or Active wires may be encountered if the catheter is used in patients with:
 - abnormal or severe vessel tortuosity
 - lesions located in extremely angulated vessel segments

- Saline should be used to inflate the balloon. Never use air or any other gaseous medium to inflate the balloon. Use of contrast medium to inflate the balloon will make it difficult to visualize Source Wire position and may attenuate radiation dose.
- Do not excessively tighten the hemostatic valve. This can prevent the proper advancement of the Source Wire.
- Do not hold the GALILEO™ Centering Catheter while the Source Wire is in transit.
- The SDU is non-sterile. When attaching the GALILEO™ Centering Catheter to the SDU, do not contaminate the sterile field or the sterile Centering Catheter. Avoid contact with the more distal portion of the catheter.
- The SDU will accept only the GALILEO™ Centering Catheter. Do not attempt to insert any other catheter.
- Prepare the GALILEO™ SDU and GALILEO™ Centering Catheter as described in their respective Instructions for Use.

VII. Special Considerations

The GALILEO™ Radiotherapy System has not been evaluated in the following patient or lesion subsets:

- patients with history of previous external radiotherapy to the heart or target vessel area
- coronary artery sites previously treated with radiotherapy
- bifurcation lesions
- saphenous vein grafts or internal mammary bypass grafts
- thrombotic lesions
- patients who experienced a myocardial infarction less than or equal to 72 hours prior to the procedure
- unprotected left main stenosis >50%
- aorto-ostial lesions
- patients with previously diagnosed autoimmune diseases such as rheumatoid arthritis, scleroderma, SLE
- fractionated dose administration other than interruption within index procedure
- patients presenting with multiple vessel lesions
- patients who have received a heart transplant
- patients unable to tolerate the recommended dwell time required by the system

VIII. Alternative Practices and Procedures

Treatment of patients with coronary artery disease including in-stent restenosis may include exercise, diet, drug therapy, percutaneous coronary interventions and coronary artery bypass surgery. Some of the patients who could be treated with the GALILEO™ Intravascular Radiotherapy System may also be able to be treated with the Novoste Beta-Cath™ System, which uses beta radiation, or the Johnson & Johnson / Cordis Checkmate™ System, which uses gamma radiation, both of which are commercially available.

IX. Marketing History

The GALILEO™ Intravascular Radiotherapy System has been distributed commercially in Austria, Belgium, Denmark, Germany, Italy, Lebanon, Netherlands, Poland, Portugal, Spain, Sweden, Switzerland, United Kingdom, Singapore, Hong Kong, Australia, New Zealand, and Canada.

The device has not been withdrawn from the market for any reason related to the safety and effectiveness of the device.

X. Potential Adverse Effects of the Device on Health

Adverse Events

The Guidant Intravascular Radiotherapy System was evaluated in the INTimal Hyperplasia Inhibition with Beta In-stent Trial (INHIBIT), a multi-center, randomized, placebo-controlled trial involving 332 patients. The major adverse events are summarized in Table 1. Major Adverse Cardiac Events (MACE) are presented as “MACE with TLR” defined as Death, MI, and Target Lesion Revascularization through the nine-month follow-up. “MACE with TVR” is defined as Death, MI, and Target Vessel Revascularization (which is inclusive of target lesion revascularization) through the nine-month follow-up. Table 1 also lists bleeding and vascular complications as well as occurrence of thrombosis. The table shows Acute (within 30 days), Late (31 days to 290 days), and Total complications. The MACE category is a hierarchical tally, where only the most significant event is counted per patient with a hierarchy of Death > MI > CABG > PTCA. All events were adjudicated by a blinded Clinical Events Committee.

Table 1. Major Adverse Events – Acute and Late Term to 290 days
 All Patients Treated (N=332)

Combined (Acute & Late) Complications to 290 days	³² P Radiation Patients N=166		Control Patients N=166		All Randomized Patients N=332	
	Number	%	Number	%	Number	%
Hierarchical MACE (Death, MI, TLR)	24	14.5%	51	30.7%	75	22.6%
Hierarchical MACE (Death, MI, TVR)	39	23.5%	56	33.7%	95	28.6%
Death	5	3.0%	5	3.0%	10	3.0%
Myocardial Infarction	13	7.8%	8	4.8%	21	6.3%
Q wave Myocardial Infarction	3	1.8%	3	1.8%	6	1.8%
Non-Q wave Myocardial Infarction	10	6.0%	5	3.0%	15	4.5%
Target Lesion Revascularization	17	10.2%	46	27.7%	63	19.0%
CABG	5	3.0%	20	12.0%	25	7.5%
PTCA	12	7.2%	26	15.7%	38	11.4%
Target Vessel Revascularization	34	20.5%	52	31.3%	86	25.9%
CABG	9	5.4%	23	13.9%	32	9.6%
PTCA	25	15.1%	29	17.5%	54	16.3%
Acute Thrombosis (to 30 days)	3	1.8%	1	0.6%	4	1.2%
Late Thrombosis (31-290 days)	5	3.0%	1	0.6%	6	1.8%
Bleeding complication	4	2.4%	4	2.4%	8	2.4%
Vascular complications	4	2.4%	2	1.2%	6	1.8%

Five (5) patients who received radiation died during the INHIBIT Trial. The deaths occurred between 70 and 281 days. Three deaths were determined to be cardiac deaths. The other two patients experienced sudden death which could not be explicitly adjudicated but acute closure of the target lesion could not be excluded.

The following adverse events were NOT observed during the clinical investigation, but are recognized as potential adverse events associated with interventional cardiology and vascular brachytherapy procedures. The list is not limited to the following:

- arteriovenous fistula
- coronary artery aneurysm
- coronary artery spasm
- coronary vessel dissection, perforation, rupture or injury
- delayed endothelialization
- drug reactions, allergic reaction to contrast media
- embolism
- endocarditis
- hemorrhage or hematoma
- hypo/hypertension
- infection
- loss of vaso-reactivity immediately following treatment
- short-term hemodynamic deterioration

Device Performance

There were 332 patients randomized in the INHIBIT Trial. In the INHIBIT Trial, a modified oncology afterloader was used to deliver the treatment. The GALILEO™ SDU provides the same function as the modified oncology afterloader, but was designed specifically for use in intravascular radiotherapy. The GALILEO™ SDU automates many of the functions performed by the user in the INHIBIT trial. Table 2 outlines the details of the malfunctions reported as part of the treatment of the 332 patients.

Table 2. Device Performance – INHIBIT Trial

Number of patients enrolled in INHIBIT Trial	332	
Number of cases with unsuccessful delivery of randomized treatment	18	5.4%
Number of cases with Device Related Malfunctions	10	3.0%
Number of cases with Patient Related Malfunctions	6	1.8%
Number of cases with User Related Malfunctions	2	0.6%
Number of cases reporting initial device malfunction with subsequent treatment success	6	1.8%
Number of cases with Device Related Malfunctions	6	1.8%
Number of cases with Patient Related Malfunctions	0	0.0%
Number of cases with User Related Malfunctions	0	0.0%

Table 3 outlines the details of the malfunctions based on the reported device complaints for the first 850 patients (approximation based on GALILEO Centering Catheter International Sales) treated with the commercially available 27 mm GALILEO™ Intravascular Radiotherapy System.

Table 3. Device Performance – GALILEO

Number of patients treated with the 27mm GALILEO™ System	850	
Number of cases with unsuccessful delivery of treatment	1	0.1%
Number of cases with Device Related Malfunctions	1	0.1%
Number of cases with Patient Related Malfunctions	0	0.0%
Number of cases with User Related Malfunctions	0	0.0%
Number of cases reporting initial device malfunction with subsequent treatment success	7	0.8%
Number of cases with Device Related Malfunctions	3	0.4%
Number of cases with Patient Related Malfunctions	2	0.2%
Number of cases with User Related Malfunctions	2	0.2%

XI. Summary of Non-Clinical Studies

Non-clinical laboratory studies were conducted on the GALILEO™ Intravascular Radiotherapy System, including hardware testing on each component, animal studies, biocompatibility testing, shelf life testing, packaging validation, and software testing.

GALILEO™ Centering Catheter

The GALILEO™ Centering Catheter, available with Microglide and Hydrophilic coatings, were subjected to bench testing as listed in Table 4 to verify the integrity and acceptability of the Centering Catheter for *in vivo* use. A summary of this testing is described in the following.

Table 4. Non-Clinical Tests on GALILEO™ Centering Catheter

<i>Test Performed</i>	<i>Catheter Coating</i>		<i>Test Performed</i>	<i>Catheter Coating</i>	
	<i>Microglide</i>	<i>Hydrophilic</i>		<i>Microglide</i>	<i>Hydrophilic</i>
Source Wire Access Test	✓		Distal & Proximal Lap Joint Test	✓	
Tip Puncture Test	✓		Connector Joint Test	✓	
Catheter Shaft Puncture Resistance Test	✓		Dimensional Tests	✓	✓ (subset)
Catheter Extension Tubing Puncture Resistance Test	✓		Source Lumen Collapse Test	✓	
Catheter Preparation Test	✓	✓	Balloon Centering Capability Test	✓	
Balloon Size Test	✓	✓	Catheter Coating Particulate Test		✓
Balloon Inflation / Deflation Times Test	✓	✓	Catheter Coating Friction Test		✓
Catheter Fatigue Test	✓		Catheter Coating Dry Adhesion Test		✓
Soft Tip Pull Test	✓				

Source Wire Access Test:

Testing was conducted to verify the ability of the SDU to deploy the source to the target location at the distal end of the catheter and to ensure that the InActive Source Wire can be fully inserted into the source wire lumen. With balloons inflated to the operating pressure, the Source Wire was extended and retracted within a heart model. The GALILEO™ Centering Catheters passed the source wire access test in that at least 95% of the deployment attempts were successful and did not result in an obstruction error (with 95% confidence).

Tip Puncture Test:

Testing was conducted to verify the integrity, safety and reliability of the distal seal of the source wire lumen and to ensure that the end of the closed lumen is strong enough to prevent contamination of the sterile field. With the balloon inflated to the operating pressure, catheters were subjected to multiple extensions of the Source Wire and inspected for puncture after each wire extension. The GALILEO™ Centering Catheters passed the Tip Puncture Test in that the closed tip seal did not leak, separate or puncture with 95% confidence and 99% reliability.

Catheter Shaft Puncture Resistance Test:

Testing was conducted to verify the integrity, safety and reliability of the catheter shaft when impacted by the Source Wire. Four sections of the shaft (balloon section, distal section, mid-section, and proximal section) were each subjected to extensions of the InActive Source Wire and inspected for puncture after each extension. The GALILEO™ Centering Catheters passed the Catheter Shaft Puncture Resistance Test in that all locations of the catheter shafts were able to withstand all puncture attempts with at least 95% confidence and 99% reliability.

Catheter Extension Tubing Puncture Resistance Test:

Testing was conducted to verify the integrity, safety and reliability of the catheter extension tubing when impacted by the Source Wire. The GALILEO™ Centering Catheters passed the Catheter Extension Tubing Puncture Resistance Test in that all locations of the extension tubing shafts were able to withstand multiple cycles without puncture, leak, or separation with at least 90% confidence and 90% reliability.

Catheter Preparation Test:

Testing was conducted to evaluate the ease of preparing the GALILEO™ Centering Catheter using the aspiration method. The GALILEO™ Centering Catheters passed the Catheter Preparation Test in that all catheters were able to be successfully prepared in three or fewer cycles with the aspiration method.

Balloon Size Test:

Testing was conducted to verify the capability of the balloon to maintain the specified diameter and length for the duration of the radiation procedure and to verify the capability of the source wire lumen to withstand the operating pressure without collapse. The GALILEO™ Centering Catheters passed the Balloon Size Test in that each balloon maintained the specified dimensions after holding pressure for 2 minutes and 15 minutes.

Balloon Inflation / Deflation Times Test:

Testing was conducted to determine the balloon inflation and deflation times of the GALILEO™ Centering Catheter. The balloons were inflated to the operating pressure and the inflation and deflation times were recorded. The GALILEO™ Centering Catheters passed the Balloon Inflation / Deflation Times Test in that all balloons were able to be inflated in less than 6 seconds and deflated in less than 30 seconds.

Catheter Fatigue Test:

Testing was conducted to demonstrate that with 95% confidence, at least 90% of the GALILEO™ Centering Catheters would sustain repeated inflations to the operating pressure. The balloons were inflated multiple times to the operating pressure, held for 5 seconds at each inflation, and deflated after each inflation. The GALILEO™ Centering Catheters met product specifications.

Soft Tip Pull Test:

Testing was conducted to determine the tensile strength of the distal tip segment of the GALILEO™ Centering Catheter. The distal tips of the catheters were clamped in stationary grips. The catheter shafts were clamped 1 cm distal to the balloon and pulled in a tensile tester until failure. The GALILEO™ Centering Catheters passed the Soft Tip Pull Test in that all catheters were able to withstand a minimum of 0.5 lbs. pull force in the distal tip.

Distal and Proximal Lap Joint Test:

Testing was conducted to determine the tensile strength of the proximal and distal segments of the GALILEO™ Centering Catheter and to ensure that the catheter has sufficient tensile strength to withdraw the balloon from the anatomy. The distal tips of the catheters were clamped in stationary grips. The catheter shafts were clamped proximal to the balloon and pulled in a tensile tester until failure. This procedure was repeated while clamping the distal portion of the mid-proximal lap joint. The GALILEO™ Centering Catheters passed the Distal and Proximal Lap Joint Test in that all catheters were able to withstand a tensile strength of 2 lbs. minimum.

Connector Joint Test:

Testing was conducted to determine the tensile strength of the connector segment of the GALILEO™ Centering Catheter and to ensure that the catheter has sufficient tensile strength to maintain attachment to the GALILEO™ Source Delivery Unit and contain the Source Wire while it is deployed. The connector of the catheters was clamped into stationary grips. The catheter shafts were clamped proximal to the side arm and pulled in a tensile tester until failure. The GALILEO™ Centering Catheters passed the Connector Joint Test in that the connector and extension tubing of the catheters was able to withstand the required pull force of 5 lbs. minimum.

Dimensional Tests:

A series of dimensional tests were conducted to verify the dimensional requirements of the GALILEO™ Centering Catheter. The dimensions measured are listed below:

- Overall Length
- Crossing Profile
- Treatment Length
- Source Wire Lumen Length
- Proximal Outer Diameter
- Distal Outer Diameter
- Guide Wire Riding Length
- Laser Bond Joint OD
- Adhesive Bond Joint OD
- Total Tip Length
- Free Space Length

Source Wire Lumen Collapse Test:

Testing was conducted to determine the source wire lumen collapse pressure of the GALILEO™ Centering Catheters and to ensure that the Source Wire has the ability to be fully inserted into the source wire lumen. The GALILEO™ Centering Catheters passed the Source Lumen Collapse Test in that the source lumens did not experience irreversible collapse at pressures less than or equal to 5 atm.

Balloon Centering Capability Test:

Testing was conducted to determine the capability of the balloon to maintain the centering of the Source Wire within the vessel lumen for the duration of the radiation procedure. The catheters were placed into a centering fixture. The Source Wire was inserted into the catheters and the balloons were inflated to 3, 4, and 5 atm. The centering of the wire was measured at each pressure at three locations: distal, middle, and proximal locations of the wire. The GALILEO™ Centering Catheters met product specifications.

Catheter Coating Particulate Test:

Testing was conducted to determine the number of coating particulates generated by the hydrocoat hydrophilic coated portion of the GALILEO™ Centering Catheter. With a mandrel inserted in the catheters, the balloons were inflated and the samples were soaked in sterile water. After soaking, the balloons were inserted into and retracted from a test fixture smaller in diameter than the inflated balloon diameter. The number of particles generated was counted. The GALILEO™ Centering Catheters passed the Catheter Coating Particulate Test in that the particle count did not exceed the specified maximum of 200 particulates.

Catheter Coating Friction Test:

Testing was conducted to determine the coefficient of friction (cof) of the GALILEO™ Centering Catheter with the Hydrophilic coating. The test samples were submerged in water and fixed in a test fixture. The samples were pulled and the average load was recorded. The cof was calculated by dividing the average load by the normal force. The GALILEO™ Centering Catheters passed the Catheter Coating Friction Test in that the coefficient of friction for each catheter was below the specified maximum of 0.157.

Catheter Coating Dry Adhesion Test:

Testing was conducted to demonstrate the percent adhesion of the hydrocoat hydrophilic coating on the GALILEO™ Centering Catheter. Tape was firmly applied to the length of the catheter shaft and rapidly removed and inspected for coating removal. The GALILEO™ Centering Catheters passed the Catheter Coating Dry Adhesion Test in that all catheters exhibited 100% coating adhesion.

In addition to the testing described above, the GALILEO™ Centering Catheter has been subjected to accelerated aging testing up to 2 years. Catheters were subjected to accelerated aging conditions and underwent the following tests:

- Source Wire Access Test
- Tip Puncture Test
- Catheter Shaft Puncture Resistance Test
- Balloon Inflation / Deflation Times Test
- Catheter Preparation Test
- Balloon Size Test
- Catheter Extension Tubing Puncture Resistance Test
- Catheter Fatigue Test
- Soft Tip Pull Test
- Distal and Proximal Lap Joint Test
- Connector Joint Test
- Dimensional Tests
- Source Wire Lumen Collapse Test
- Catheter Coating Particulate Test

The GALILEO™ Centering Catheters with Hydrocoat hydrophilic coating passed the accelerated aging testing supporting suitability for use out to 2 years. The GALILEO™ Centering Catheters with Microglide passed real-time aging testing supporting suitability for use out to 1 year.

Biocompatibility testing was conducted on full, sterilized catheters in accordance with ISO 10993 for implanted devices intended for limited (<24 hours) contact with blood. Testing included: Cytotoxicity, Sensitization, Acute Systemic Toxicity, Irritation or Intracutaneous Reactivity, Implantation, Haemocompatibility, and Pyrogenicity. Biocompatibility test results indicated that the materials used in the GALILEO™ Centering Catheters do not present any toxic liabilities to the body and are considered biocompatible.

Packaging Validation Testing was conducted to ensure the integrity of the GALILEO™ Centering Catheter sterile package after 2 years of aging. Testing consisted of visual inspection, leak testing, seal strength testing, and microbial challenge. Testing indicated that the GALILEO™ Centering Catheter package bag, when sealed at nominal sealing parameters, is an acceptable package to protect the device during handling and shipping, and from the environment and microorganisms until the package is opened, for up to two-years shelf life.

The GALILEO™ Centering Catheter passed all hardware, biocompatibility, shelf life, and packaging validation testing and is considered acceptable for use with the GALILEO™ Intravascular Radiotherapy System.

GALILEO™ ³²P Source Wire:

The GALILEO™ ³²P Source Wire, Model GDT-P32-2, was bench tested for acceptability, including mechanical and cyclical testing, dosimetry testing, source uniformity validation, radiation protection testing, radiation exposure rate measurements, and shipping testing. The GALILEO™ ³²P Source Wire passed all testing, is considered acceptable for use with the GALILEO™ Intravascular Radiotherapy System, and is classified as ISO/99/C53211 (Modified Class 2 Impact Test plus Ancillary Cycle Tests).

Mechanical Testing:

A series of environmental and mechanical tests were conducted on the ³²P Source Wire to demonstrate adequacy of sealed source design integrity of the Active wire. This series of testing consisted of subjecting the Source Wires to pressure extremes, temperature extremes, and impacts. The wires passed the requirements of ISO 2919:1980 Sections 7.2 and 7.3, as well as the leak test requirements of ISO 9978:1992(E) Section 5.3.1.

Cyclic Testing:

Cyclic fatigue testing was conducted to verify that the GDT-P32-2 design, which is the same for the Active and InActive wires, met or exceeded the predicated reliability of 0.999 with 95% confidence based on the anticipated service load. Results indicated the fatigue life of the Model GDT-P32-2 design exceeded the product specifications with 0.999 reliability and 95% confidence.

Dose Distribution Validation:

The dose distribution in water for 27-mm GDT-P32-2 sources was characterized at NIST using calibrated radiochromic film dosimetry and Monte Carlo calculations. The overall uncertainty in the determination of the reference dose rate per unit contained activity is estimated to be within $\pm 16\%$ at the 95% confidence interval.

³²P Dosimetry Attenuation Factors:

The 1 mm distal tungsten marker has no effect on the dose distribution in water at depths relevant to coronary Intravascular Radiotherapy (IVRT).

Neither guidewire nor stent attenuation was accounted for during Guidant's clinical trials and Guidant does not recommend attempting to correct for these factors.

Radiation Protection:

Testing was conducted to determine radiation levels to personnel involved in vascular brachytherapy using the GALILEO™ ³²P Source Wire. Measurements show personnel exposure from the Source Wire to be well within yearly limits set by the Nuclear Regulatory Commission.

Cartridge Shipping Package & Emergency Safe Shipping Package Test:

A series of tests was conducted to validate the suitability of design, materials and integrity of the GALILEO™ Cartridge and Emergency Safe shipping package to Type A packaging test defined in 49 CFR 173.465. Testing was also performed to verify compliance of the GALILEO™ Cartridge and Emergency Safe shipping package to Type A package test defined in 49 CFR 173, Subpart I and International Atomic Energy Agency (IAEA) Safety Standards Series ST-1. Additionally, the packaging design was tested per the requirements outlined in 49 CFR 172.310, 49 CFR 173.410 and 49 CFR 173.412. The Cartridge and Emergency Safe shipping packages passed the testing (described below) and met the general requirements outlined in 49 CFR 172 and 49 CFR 173.

Source Wire Uniformity and Active Source Length Shelf Life:

The uniformity and active source length shelf life were tested over a maximum usage period of 30 days plus 30 days allotted for shipping and met specifications.

GALILEO™ Source Delivery Unit

The GALILEO™ Source Delivery Unit (SDU) was subjected to hardware and software testing to verify its acceptability for use. Hardware testing included mechanical testing, electrical testing, electromagnetic compatibility (EMC) testing, reliability testing, safety testing, and shipping and transport testing. Software testing included unit, module testing in addition to code verification and software validation.

Electronic Testing:

Testing was performed to ensure the GALILEO™ SDU met the electronic requirements. Physical tests were conducted in support of suitability of the design and construction of the SDU for use in the GALILEO™ Intravascular Radiotherapy System. Inspection / analysis or functional testing was performed on the electronic components of the SDU. The GALILEO™ SDU electronics were found to meet the specified requirements.

Mechanical & Sensory Testing:

Testing was performed to ensure the SDU met the mechanical and sensory requirements. Physical tests were conducted in support of suitability of the design and construction of the SDU for use in the GALILEO™ Intravascular Radiotherapy System. Inspection / analysis or functional testing was performed on the flowing mechanical and sensory components of the SDU.

- SDU Positioning,
- SDU Cooling,
- SDU Primary Drive Design,
- Manual Retract Function,
- Obstruction Damage Survival,
- Catheter Puncture,
- Catheter Reader,
- Force Sensor,
- Wire Tip Sensor,
- Cartridge Replacement Stability,
- Unintended Motion,
- Base Lock,
- Wire Extension Distance,
- Wire Extension Absolute / Relative Accuracy & Step Increment,
- Drive Speed Envelope, Drive Force,
- Wire Transit Time,
- Emergency Retract,
- Manual Retract,
- Head Height Adjustment,
- Head Rotational Adjustment,
- Display Swivel Adjustment,
- Display Tilt Adjustment,
- Display Touch Screen Force,
- Load Cell Accuracy,
- Catheter / Wire Interface,
- Catheter Key Latch Integrity,
- Head Adjustment Durability,
- Cartridge Insertion Durability,
- Display Tilt Durability,
- Positional Accuracy Durability,
- Wire / Catheter Severance Tools & Emergency Storage Safe,
- Mechanical Drive Stop Integrity,
- Cartridge Security,
- Cartridge / Power Interlock.

The GALILEO™ SDU was found to meet the specified requirements. Additional mechanical testing was conducted to verify software driven mechanical changes to the drive force and wire speed in the distal section of the catheter. The SDU passed the additional testing.

Electromagnetic Compatibility (EMC) Testing:

Testing was performed to ensure compliance with IEC 60601-1-2:1993. Physical tests conducted in support of suitability of the design and construction of the SDU for use in the GALILEO™ Intravascular Radiotherapy System include:

- EN 55011:1991, Radiated / Conducted Emissions,
- IEC 61000-4-3:1995, Radiated Immunity,
- IEC 61000-4-8:1994, Magnetic Radiated Immunity,
- IEC 61000-4-6:1996, Conducted Immunity,
- IEC 61000-4-2:1995, ESD Immunity
- IEC 61000-4-4:1995, Fast Transient / Burst Immunity,
- IEC 61000-4-5:1995, Surge Immunity, and

- IEC 61000-4-11:1994, Mains Variation.

The GALILEO™ Source Delivery Unit passed all testing requirements.

Reliability Testing:

Testing was performed to verify the SDU met its reliability requirements. Reliability demonstration tests conducted in support of suitability of the design and construction of the SDU for use in the GALILEO™ Intravascular Radiotherapy System include:

- Normal operating Cycle Reliability,
- Unknown Component Reliability, and
- Emergency Retract Reliability.

The GALILEO™ Source Delivery Unit passed all testing requirements. In addition, FMEA and Fault Tree Analysis were performed using guidelines established in IEC 812: 1985 and IEC 1025: 1991, respectively, using reliability prediction models established in MIL-HDBK-217F: 1991 and failure rate data from NPRD-95.

Safety Testing:

Testing was conducted to ensure compliance with UL 2601-1:1994, IEC 60601-1:1988, Amendment 1:1991 and Amendment 2:1995, as well as IEC 60601-2-17: 1989 and Amendment 1:1996, allowing exceptions where appropriate for a non-gamma, non-remote cardiac application. Physical tests conducted in support of suitability of the design and construction of the SDU for use in the GALILEO™ Intravascular Radiotherapy System include, but are not limited to:

- Identification, marking, & documents
- Environmental conditions
- Protection against electrical shock hazards
- Protection against mechanical hazards
- Protection against radiation hazards
- Protection against excessive temperatures
- Cleaning, sterilization, & disinfection
- Interruption of power supply
- Abnormal operation & fault conditions
- Constructional requirements
- Accuracy of operating data
- Power Input

Additional safety requirements were tested as part of the EMC testing and the software validation and is documented in those reports and Risk Analysis was performed per the guidelines established in IEC 1441: 1998 and IEC 60601-1-4: 1996. The GALILEO™ SDU passed all safety testing requirements.

Shipping & Transport Testing:

Testing was conducted to verify compliance with requirements such as temperature, humidity, and pressure exposure as well as exposure to compression, shock, and vibration while the SDU components were contained in their individual shipping containers. Components of the GALILEO™ SDU were tested at an ISTA certified testing laboratory.

The GALILEO™ SDU Head, Base and Cartridge, in their containers for shipping, were exposed to temperature and humidity extremes. All three GALILEO™ SDU components, in their containers for shipping, were also exposed to a reduced pressure. In addition, the Head and the Cartridge, in their shipping containers, were exposed to shipping test procedures (compression, shock and vibration)

established in ISTA 2A "Performance Test for Individual Packaged-Products 150 lb or less." One exception to this test was that the drop height was increased to 30 inches. The Base was exposed to shipping test procedures (impact and vibration) established in ISTA 2B "Performance Test for Individual Packaged-Products Over 150 lbs".

Acceptance criteria required that all samples of each component be free of any gross damage that would compromise the functionality and safety of the device. In addition, all labels and labeling were required to remain legible. All components successfully completed shipping validation testing.

Software Testing:

The GALILEO™ Intravascular Radiotherapy System Software was subjected to, and passed, a software validation test protocol, including unit testing, to test device functionality against the requirements. Revisions of the software were analyzed for regression testing requirements prior to testing. In addition to the validation testing, code verification, including formal code inspections, was performed. The software was developed and tested in compliance with IEC 60601-1-4: 1996 and applicable FDA software guidances and ANSI standards.

Animal Studies

An animal study using the predecessor Guidant Intravascular Radiotherapy System evaluated the efficacy and safety of the intravascular beta irradiation with a 27mm ³²P Source Wire. This study was carried out in porcine coronary restenosis models with both stent-injured ("stented") and balloon-injured ("balloon") coronary arteries. Both short-term (1 month follow-up) and long-term studies (6 month follow-up) were conducted.

The short-term study confirmed the efficacy of intravascular radiation to reduce neointimal proliferation initiated by coronary arterial injury in stented as well as in balloon injured arteries. In the long term study, morphometric analysis indicated a retention of inhibition of neointimal proliferation in vessels treated with intravascular radiation when compared to similarly injured vessels receiving no treatment. These studies supported the use of the Guidant Intravascular Radiotherapy System in clinical investigations using a prescribed dose of 20 Gy at 1 mm beyond the Reference Lumen Diameter.

In addition to these animal studies, a system level animal study was conducted with the GALILEO™ Intravascular Radiotherapy System using a simulated source to ensure the functionality of the GALILEO™ Intravascular Radiotherapy System. Testing indicated that the system functions appropriately.

XII. Summary of Clinical Studies

In the INHIBIT (G980094) clinical investigation, a modified oncology afterloader was used to deliver the treatment. The GALILEO™ SDU provides the same function as the modified oncology afterloader, but was designed specifically for use in intravascular radiotherapy. The GALILEO™ SDU automates many of the functions performed by the user in the INHIBIT trial.

The Guidant Intravascular Radiotherapy System was evaluated in three multi-center studies, which enrolled a total of 626 patients, for the treatment of restenosis. These studies, PREVENT, PREVENT CE, and INHIBIT are summarized below.

PREVENT Trial:

The PREVENT Trial was a prospective, randomized, double-blind, sham controlled Phase I feasibility study intended to demonstrate the safety of delivering a controlled dose of radiation from a beta-emitting source to a target lesion. The treatment was delivered immediately following an interventional procedure with the intention of reducing recurrent restenosis. The PREVENT Study was conducted under an approved Investigational Device Exemption (IDE) at three sites in the United States. Eighty-one (81) patients were enrolled at three sites.

PREVENT CE Trial:

The PREVENT CE Trial was a trial similar in design and with similar objectives to the PREVENT Trial and was conducted outside the United States. A total of 146 patients were enrolled at seven international sites.

INHIBIT Trial:

The **I**ntimal **H**yperplasia **I**nhibition with **B**eta **I**n-stent **T**rial (INHIBIT), a multicenter, randomized, placebo-controlled trial began in August 1998. The acute and 9-month clinical and angiographic results showed that the procedure success rate, defined as delivery of the randomized study treatment, without in-hospital major adverse cardiac event was 93.4%. Major adverse cardiac event (MACE with TLR) was defined by the protocol as death, Q wave MI, target vessel related non-Q wave MI, and target lesion revascularization. During analysis, additional events were added thereby creating MACE with TVR which was defined as death, Q wave MI, target vessel related non-Q wave MI, and revascularization of the target vessel. The Kaplan-Meier estimate of freedom from MACE with TLR at 9 months was 86% in the radiated arm and 69% in the control arm (p=0.0006). The Kaplan-Meier estimate for freedom from MACE with TVR at 9 months was 77% in the radiated arm and 66% in the control arm (p=0.0410).

A total of 332 patients were enrolled at 24 investigational sites in the U.S., Europe, Asia, and Australia. All 332 of the enrolled patients were randomized to receive either the active ³²P treatment delivered by the Guidant Intravascular Radiotherapy System (n=166) or a sham control treatment using the same equipment but with a non-radioactive wire (n=166). The primary safety endpoint was defined as MACE with TLR at 9 months and the primary efficacy endpoint was angiographic binary restenosis (defined as ≥ 50% diameter stenosis at follow-up angiography). A clinical events committee, masked to the treatment assignment, adjudicated the major safety endpoints.

Eligible patients, with angina or positive functional study, were identified for elective treatment of in-stent (stainless steel) restenosis in a native coronary artery lesion visually estimated to be between 2.4 and 3.7 mm in diameter. These patients underwent successful percutaneous coronary interventions. Placement of a new stent occurred in 30% (n=101) of the cases. A successful pre-intervention was defined as a final diameter stenosis less than 30% with no major ischemic or procedural complications with an injured length ≤ 47 mm. After the successful intervention, the randomized treatment was administered. If deemed necessary by the clinician, further percutaneous intervention was performed after the randomized treatment.

The Guidant Intravascular Radiotherapy System (an automatic afterloader system) was programmed to deliver a 20 Gy dose to a depth of 1 mm beyond the reference lumen diameter. The radiated and sham control patients had a dwell time based on the source activity of the active wire and the reference lumen diameter that was entered into the afterloader by the radiation staff.

The following recommended drug regimen was evaluated in the INHIBIT Clinical Study:

- Aspirin (ASA) 325 mg daily for one year or per institutional standard, and,
- For stented patients: Clopidogrel 75 mg daily for at least 6 months.
- For non-stented patients: Clopidogrel 75 mg daily for at least 3 months or Ticlopidine 500 mg loading dose followed by 250 mg twice-daily for one month.

The antiplatelet/anticoagulant medications administered to the 332 patients in the INHIBIT Trial were as denoted in Table 9. These medications were in addition to aspirin daily for one year.

Table 9. Antiplatelet Therapy

	Duration (Days)				
	< 25	25-99	100-200	> 200	Unknown
Clopidogrel (75 mg/day)	15 (5%)	88 (27%)	54 (16%)	96 (29%)	11 (3%)
Ticlopidine (250-500 mg/day)	10 (3%)	42 (13%)	2 (1%)	3 (1%)	2 (1%)
Total patients	332				
Unconfirmed antiplatelet medication	3				Clopidogrel and Ticlopidine Clopidogrel/Ticlopidine not required 7 (2%)
Patients with data available	329				13 (4%)

Clinical follow-up occurred at in-hospital, 1 month, 6 month, and 9 month time points. Angiographic follow-up occurred at 9 months if the patient was asymptomatic or earlier if cardiac symptoms warranted. The study randomization was successful as both treatment groups were found to be demographically equivalent. All randomized patients were included in the intent-to-treat analysis. The principal safety and efficacy results are presented in Table 10 followed by the freedom from MACE with TLR Kaplan-Meier curve and MACE with TVR Kaplan-Meier curve, Figures 1 and 2. The mean lesion length studied was 17.4 mm for all patients (mean lesion length for single position was 13.6 mm and for tandem position was 22.9 mm).

Table 10. Principal Safety and Efficacy Results

Safety and Efficacy Measures	Radiation N = 166	Control N = 166	Relative Risk [95% C.I.]	Difference [95% C.I.]
Follow-up (9 mo) Stent Segment Restenosis Rate	15.0% (19/127)	49.2% (62/126)	0.30 [0.19,0.48]	-34.2% [-45.0%, -23.5%]*
Follow-up (9 mo) Analysis Segment Restenosis Rate	26.4% (34/129)	51.6% (66/128)	0.51 [0.37,0.71]	-25.2% [-36.7%, -13.7%]*
TLR-Free at 290 Days	89.8%	72.3%	1.24 [1.12, 1.38]	17.5% [9.3%, 25.7%]*
TVR-Free at 290 Days	79.5%	68.7%	1.15 [1.02, 1.32]	10.8% [1.5%, 20.2%]*
MACE-Free at 290 Days (TLR)	85.5%	69.3%	1.23 [1.10, 1.39]	16.2% [7.4%, 25.0%]*
MACE-Free at 290 Days (TVR)	76.5%	66.3%	1.15 [1.01, 1.32]	10.2% [0.6%, 19.9%]*
Procedure Success	92.8% (154/166)	93.4% (155/166)	0.99 [0.94, 1.05]	-0.6% [-6.1%, 4.9%]
Device Success	93.4% (155/166)	95.8% (159/166)	0.97 [0.93, 1.03]	-2.4% [-7.3%, 2.5%]
Post-Procedure Stent Segment Minimal Lumen Diameter (MLD, in mm)				
Mean ± SD (N)	2.16 ± 0.45 (158)	2.21 ± 0.46 (159)		-0.05 [-0.15, 0.05]
Range (min, max)	(0.95,3.44)	(1.07,3.91)		
Post-Procedure Analysis Segment Minimal Lumen Diameter (MLD, in mm)				
Mean ± SD (N)	1.92 ± 0.42 (161)	1.96 ± 0.42 (161)		-0.04 [-0.13, 0.06]
Range (min, max)	(0.97,3.14)	(1.07,3.62)		
Post-Procedure Stent Segment Percent Diameter Stenosis (%DS)				
Mean ± SD (N)	20.8% ± 13.8% (158)	19.1% ± 15.6% (159)		1.72% [-1.54%, 4.97%]
Range (min, max)	(-30.1%, 50.7%)	(-42.8%, 50.1%)		
Post-Procedure Analysis Segment Percent Diameter Stenosis (%DS)				
Mean ± SD (N)	29.6% ± 10.9% (161)	28.5% ± 11.2% (161)		1.07% [-1.34%, 3.49%]
Range (min, max)	(6.3%, 57.9%)	(-7.5%, 52.5%)		

Safety and Efficacy Measures	Radiation N = 166	Control N = 166	Relative Risk [95% C.I.]	Difference [95% C.I.]
Follow-Up Stent Segment Minimal Lumen Diameter (MLD, in mm)				
Mean ± SD (N)	1.91 ± 0.75 (127)	1.46 ± 0.66 (126)		0.45 [0.28, 0.63]*
Range (min, max)	(0.00,3.21)	(0.00,3.31)		
Follow-Up Analysis Segment Minimal Lumen Diameter (MLD, in mm)				
Mean ± SD (N)	1.54 ± 0.65 (129)	1.38 ± 0.61 (128)		0.16 [0.01, 0.31]*
Range (min, max)	(0.00,3.21)	(0.00,3.31)		
Follow-Up Stent Segment Percent Diameter Stenosis (%DS)				
Mean ± SD (N)	29.2% ± 27.4% (127)	48.3% ± 21.0% (126)		-19.2% [-25.2%, -13.1%]*
Range (min, max)	(-29.7%, 100%)	(-8.4%, 100%)		
Follow-Up Analysis Segment Percent Diameter Stenosis (%DS)				
Mean ± SD (N)	43.3% ± 21.8% (129)	51.3% ± 18.3% (128)		-8.06% [-13.0%, -3.11%]*
Range (min, max)	(6.4%, 100%)	(11.5%, 100%)		
Safety Measures and Other Clinical Events to 290 Days				
MACE with TLR at 290 Days	14.5% (24/166)	30.7% (51/166)	0.47 [0.30, 0.73]	-16.3% [-25.1%, -7.4%]*
Acute MACE with TLR	2.4% (4/166)	2.4% (4/166)	1.0 [0.25, 3.93]	0.0% [-3.3%, 3.3%]
Late MACE with TLR	12.0% (20/166)	28.3% (47/166)	0.43 [0.26, 0.69]	-16.3% [-24.7%, -7.8%]*
MACE with TVR at 290 Days	23.5% (39/166)	33.7% (56/166)	0.70 [0.49, 0.99]	-10.2% [-19.9%, -0.6%]*
Acute MACE with TVR	2.4% (4/166)	2.4% (4/166)	1.0 [0.25, 3.93]	0.0% [-3.3%, 3.3%]
Late MACE with TVR	21.1% (35/166)	31.3% (52/166)	0.67 [0.46, 0.98]	-10.2% [-19.6%, -0.8%]*
Aneurysm	0% (0/166)	0% (0/166)	na	0.0%
Acute Thrombosis	1.8% (3/166)	0.6% (1/166)	3.0 [0.32, 28.6]	1.2% [-1.1%, 3.5%]
Late Thrombosis	3.0% (5/166)	0.6% (1/166)	5.0 [0.59, 42.3]	2.4% [-0.4%, 5.3%]
Acute Total Occlusions	0.6% (1/166)	0.6% (1/166)	1.0 [0.06, 15.9]	0.0% [-1.7%, 1.7%]
Late Total Occlusions	3.6% (6/166)	1.2% (2/166)	3.0 [0.61, 14.7]	2.4% [-0.9%, 5.7%]

* shows statistically significant difference

Numbers are % (counts/sample size) or Mean ± SD.

C.I. = Confidence Interval

Relative risk = Radiated / Control SE = $\sqrt{\frac{(1-p_1)/n_{11} + (1-p_2)/n_{21}}{n_1 + n_2}}$ C.I. = $RR \cdot \exp(\pm 1.96 \cdot SE)$ Difference = Radiated - Control SE = $\sqrt{p_1 \cdot q_1/n_1 + p_2 \cdot q_2/n_2}$ C.I. = $Diff \pm 1.96 \cdot SE$

Stent Segment (from QCA core lab) = the area confined to the proximal and distal borders of the stent

Analysis Segment (from QCA core lab) = the segment that extends 5 mm proximal and distal to the radiated or injured landmark, whichever was longest in length

Survival estimates from Kaplan-Meier method.

TLR-free = Freedom from target lesion revascularization

TVR = Target vessel revascularization which includes target lesion revascularization

TVR-free = Freedom from target vessel revascularization

MACE-free (TLR) = Freedom from death, Q wave and non-Q wave MI, and target lesion revascularization

MACE-free (TVR) = Freedom from death, Q wave and non-Q wave MI, and target vessel revascularization

Device Success = Successful delivery of the prescribed dose of ³²P radiation

Procedure Success = Device Success and hospital discharge without major adverse cardiac event (MACE)

MACE with TLR = composite of death, Q wave and non-Q wave MI, and target lesion revascularization

MACE with TVR = composite of death, Q wave and non-Q wave MI, and target vessel revascularization

Acute = event occurs within 30 days of index procedure

Late = event occurs 31-290 days after index procedure

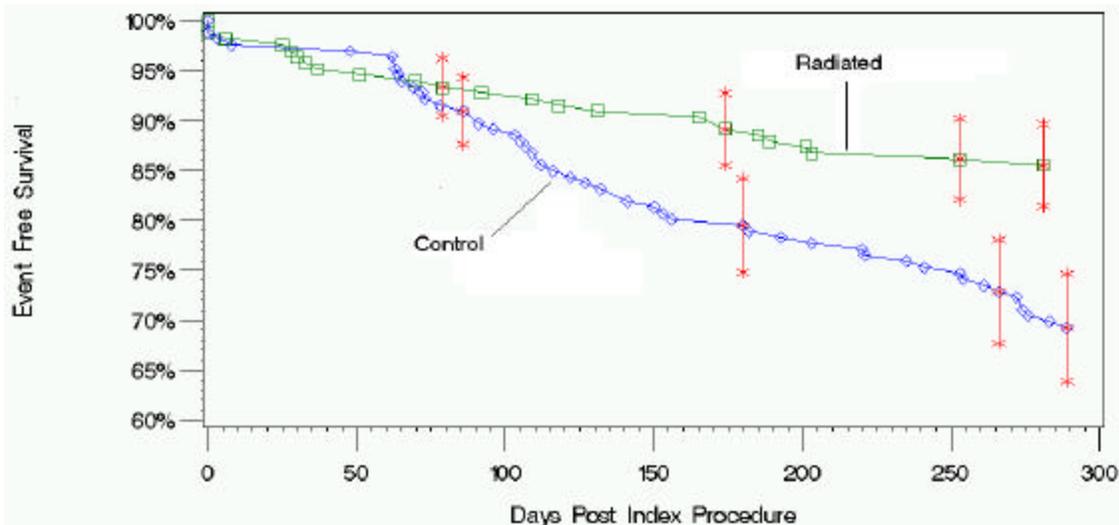
Aneurysm (from QCA core lab) = an expansion of the lumen by at least 20% compared with the normal lumen dimensions in the treatment region (analysis segment) that extends with a wide or narrow mouth beyond the apparent normal contour

Thrombosis (acute or late) = angiographic thrombus or subacute closure within the target vessel at the time of a clinically driven angiographic restudy for documented ischemia (chest pain and ECG changes)

Total Occlusion (acute or late) = an MLD of zero at follow-up as assessed by QCA core lab

Figure 1. Adverse Events: Death, MI, or TLR - Survival to 290 Days

Event-free Survival \pm 1.5 SEM, All Patients Treated (N=332)

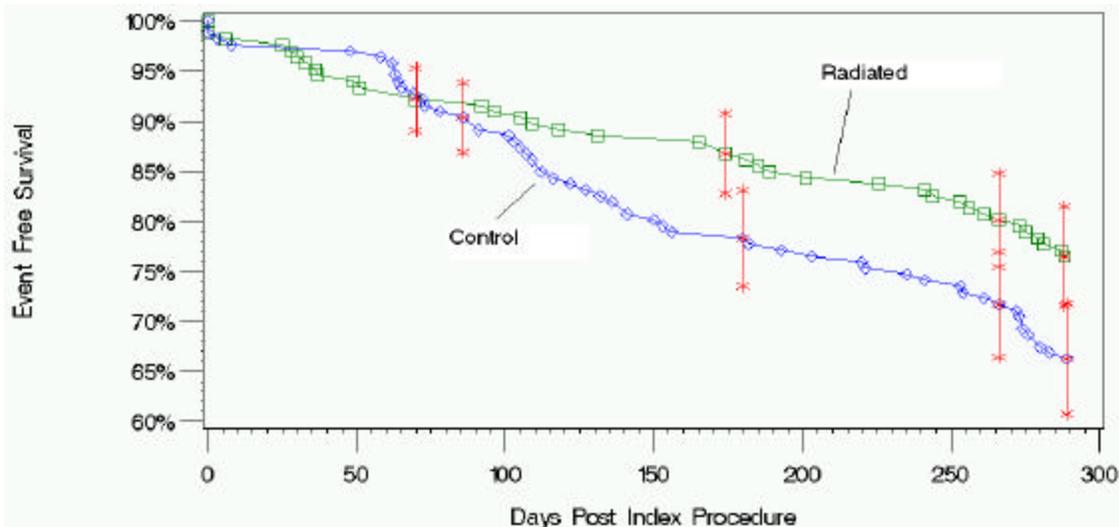


Time After Initial Procedure (days)								
	0	7	14	30	90	180	270	290
Radiated Group								
# At Risk	166	163	163	160	155	148	143	142
# Events	0	3	3	6	11	18	23	24
% Survived	100%	98%	98%	96%	93%	89%	86%	86%
% SEM	0%	1.3%	1.3%	1.5%	1.9%	2.4%	2.7%	2.7%
Control Group								
# At Risk	166	163	162	162	151	132	121	115
# Events	0	3	4	4	15	34	45	51
% Survived	100%	98%	98%	98%	91%	80%	73%	69%
% SEM	0%	1.0%	1.2%	1.2%	2.2%	3.1%	3.5%	3.6%
Tests Between Groups								
	Test	Chi-Square	Degrees Freedom	p-value				
	Log-Rank	11.749	1	0.0006				
	Wilcoxon	10.840	1	0.0010				

Survival percent via product-limit estimates
 Between group assessment by both Log-Rank and Wilcoxon Chi-Square

Figure 2. Adverse Events: Death, MI, or TVR - Survival to 290 Days

Event-free Survival \pm 1.5 SEM, All Patients Treated (N=332)



Time After Initial Procedure (days)								
	0	7	14	30	90	180	270	290
Radiated Group								
# At Risk	166	163	163	160	153	144	133	127
# Events	0	3	3	6	13	22	33	39
% Survived	100%	98%	98%	96%	92%	87%	80%	77%
% SEM	0%	1.0%	1.0%	1.5%	2.1%	2.6%	3.1%	3.3%
Control Group								
# At Risk	166	163	162	162	150	130	119	110
# Events	0	3	4	4	16	36	47	56
% Survived	100%	98%	98%	98%	90%	78%	72%	66%
% SEM	0%	1.0%	1.2%	1.2%	2.3%	3.2%	3.5%	3.7%
Tests Between Groups								
	Test	Chi-Square	Degrees Freedom	p-value				
	Log-Rank	4.176	1	0.0410				
	Wilcoxon	3.978	1	0.0461				

Survival percent via product-limit estimates
 Between group assessment by both Log-Rank and Wilcoxon Chi-Square

Gender Bias and Demographics

The male:female ratio of approximately 70% to 30% is consistent with the incidence within the in-stent restenosis population. No selection bias on the basis of gender was identified. The following major treatment result differences were observed in comparing male patients versus female patients:

- The rate of target vessel revascularization, which is inclusive of target lesion and adjacent to target lesion revascularization, was significantly higher in the radiated female population (32.0%) when compared to the radiated male population (15.5%). When logistic regression was performed for predictors of target vessel revascularization (radiated and control populations), the female gender was twice as likely to have an event as the male gender.
- The other event that had female gender as a predictor was binary angiographic restenosis of the analysis segment. This difference showed that females were half as likely to have analysis segment restenosis, again when the entire radiated and control populations were considered. There was no

significant difference noted when the results were radiated populations were compared directly (radiated female 24.3%, radiated male 27.2%).

The composite endpoint of Major Adverse Cardiac Events (MACE) defined as death, MI, or target lesion revascularization showed no significant difference due to gender. Also the composite endpoint of MACE when defined as death, MI, or target vessel revascularization showed no difference due to gender.

An analysis was done to determine if any demographic variables including gender were predictors of clinical adverse events. Both univariable and multivariable logistic regression models were fit to MACE with TLR (primary safety endpoint) and analysis segment restenosis (primary efficacy endpoint), using the SAS® LOGISTIC procedure. The model was set up to determine what factors predict that a patient would have an event through follow-up of 290 days.

For the univariable analyses each of the following fifteen variables were individually tested for their ability to predict each of the above two dependent variables:

- a) pre-procedure patient demographic and health measures: gender, age, smoking (y/n), diabetes (y/n), hypertension (y/n), hyperlipidemia (y/n), prior MI (y/n)
- b) pre-procedure lesion characteristics: RVD pre-procedure, MLD pre-procedure, stenosis pre-procedure, lesion length, ACC lesion class
- c) the treatment the patient received
- d) post-procedure lesion characteristics: RVD post procedure, MLD post procedure, and stenosis post procedure.

For the multivariable analyses all of the above variables were allowed to enter each model using the stepwise logistic procedure with a p-value to enter of 0.05.

The multivariable predictors of the primary safety endpoint (MACE with TLR) were post-procedure MLD ($p=0.004$, odds ratio of increasing MLD=0.32) and randomized assignment ($p=0.0004$, odds ratio of radiated vs. control=2.96).

The multivariable predictors of the primary efficacy endpoint (binary angiographic restenosis in the analysis segment) were baseline RVD ($p=0.01$, odds ratio of increasing RVD=0.53), baseline lesion length ($p=0.0005$, odds ratio of increasing length=1.06) and randomized assignment ($p=0.0001$, odds ratio of radiated vs. control=2.99).

The odds ratio compares the odds that a patient with the independent variable will have the event (dependent variable) to the odds that a patient without the independent variable will have the event. For example, the odds ratio result shows that a patient with a randomized assignment of control is 2.96 times more likely to have a MACE with TLR event than a patient with a randomized assignment of radiation. Likewise, a patient with a large post-procedure MLD is 0.32 times more likely (same as 3.1 times less likely) to have a MACE with TLR event as a patient with a small post-procedure RVD.

Only angiographic measurements and randomized assignment were significant predictors of event occurrence. No gender bias or other demographic predictor was found.

Device Accountability:

Upon conclusion of enrollment, all sites were notified to secure investigational devices. Investigational device records were verified, the device inventory reconciled and all unused inventory was returned to

Guidant Corporation. Throughout the trial, source wires were installed, removed when the activity decayed below 35 mCi and replaced with new source wires with adequate activity. All source wires were returned to Guidant Corporation when removed from the afterloader and at the end of patient enrollment. The afterloaders were removed from the sites and returned to Nucletron.

Risk / Benefit Analysis:

The primary benefit of intravascular radiotherapy treatment is a decreased incidence of restenosis of the target lesion.

The known risks associated with an intravascular radiotherapy system include the typical risks associated with cardiac catheterization and percutaneous transluminal coronary angioplasty (PTCA). Additional risks include, but are not limited to, accidental exposure to additional beta radiation due to breakage of the ³²P Source Wire, or failure of the wire to retract properly, requiring manual retraction of the wire or removal of the Centering Catheter. Also, treatment with the GALILEO™ Intravascular Radiotherapy System will result in a slight increase in the amount of radiation to a patient due to the slightly longer fluoroscopy time needed to check the position of the Centering Catheter and Source Wire.

XIII. Conclusions Drawn from Studies

The results of the laboratory testing of the GALILEO™ Intravascular Radiotherapy System in combination with the results of the animal studies and INHIBIT clinical studies provide reasonable assurance that the GALILEO™ Intravascular Radiotherapy System performs according to its design intent and is safe and effective for treating in-stent restenosis when used according to device labeling.

XIV. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by the panel.

IX. FDA Decision

FDA issued a PMA approval letter to Guidant Corporation, Inc. on November 2, 2001. FDA also performed an inspection of the manufacturing facilities and found the applicant in compliance with the Quality System Regulation (21 CFR Part 820).

X. Approval Specifications

Instructions for Use: See the labeling

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

Postapproval Requirements and Restrictions: See approval order.