

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Intravascular Coronary Stent

Device Trade Name: ACS MULTI-LINK RX DUET® Coronary Stent System
ACS MULTI-LINK OTW DUET® Coronary Stent System
ACS MULTI-LINK RX TRISTAR™ Coronary Stent System
ACS MULTI-LINK OTW TRISTAR™ Coronary Stent System
ACS MULTI-LINK RX ULTRA™ Coronary Stent System
ACS MULTI-LINK OTW ULTRA™ Coronary Stent System
ACS MULTI-LINK RX TETRA™ Coronary Stent System
ACS MULTI-LINK OTW TETRA™ Coronary Stent System
ACS MULTI-LINK RX PENTA™ Coronary Stent System
ACS MULTI-LINK OTW PENTA™ Coronary Stent System
ACS RX MULTI-LINK® Coronary Stent System
ACS MULTI-LINK® Coronary Stent System
ACS RX MULTI-LINK HP™ Coronary Stent System
ACS OTW MULTI-LINK HP™ Coronary Stent System

Applicant's Name and Address: Guidant Corporation Vascular Intervention Group
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Date of Panel Recommendation: Not Panel Reviewed

PMA Supplement Number: P970020/S40

Date of Notice of Approval to Applicant: August 6, 2002

The sponsor submitted this PMA supplement to expand the clinical indications for the ACS MULTI-LINK® Coronary Stent Systems as listed above. The sponsor submitted only clinical data in support of this new indication since there were no changes to the devices themselves; therefore, no further pre-clinical bench or animal study data were required. The clinical data are provided in this summary to support the additional indication for the purpose of restoring coronary flow in patients experiencing acute myocardial infarction (AMI), as confirmed by ST segment elevation or angiographic findings, who present within 12 hours of symptom onset with native coronary artery lesions of length \leq 35 mm with a reference vessel diameter of 2.5 mm to 4.0 mm.

The original PMA for the ACS MULTI-LINK® Coronary Stent Systems, approved October 2, 1997, included ACS RX MULTI-LINK® Coronary Stent System, ACS MULTI-LINK® Coronary Stent System, ACS RX MULTI-LINK HP™ Coronary Stent System, and ACS OTW MULTI-LINK HP™ Coronary Stent System. The ACS MULTI-LINK® Coronary Stent Systems are indicated for use in patients with symptomatic ischemic heart disease due to discrete de novo and restenotic native coronary artery lesions less than 20 mm length with a reference vessel diameter ranging from 3.0 mm to 3.75 mm (MULTI-LINK®, RX MULTI-LINK HP™, OTW MULTI-LINK HP™) and lesions less than 22 mm length with a reference vessel diameter ranging from 3.0 mm to 3.5 mm (RX MULTI-LINK®), and are intended to improve coronary luminal diameter. Long term outcome (beyond six months) for this permanent implant is unknown at present.

For more information on the data that supported the original indication, the summary of safety and effectiveness data for the original PMA should be referenced. Written requests for copies of the summary of safety and effectiveness data can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, Room 1-23, Rockville, MD 20857. This information can also be accessed via the FDA CDRH Internet home page located at <http://www.fda.gov/cdrh/pmepage.html>.

Stent modifications were previously submitted in the following supplements:

S004 - ACS MULTI-LINK RX DUET® Coronary Stent System and ACS MULTI-LINK OTW DUET Coronary Stent System, approved November 5, 1998

S017 - ACS MULTI-LINK RX TRISTAR™ Coronary Stent System and ACS MULTI-LINK OTW TRISTAR Coronary Stent System, approved December 22, 1999

S021 - ACS MULTI-LINK RX ULTRA™ Coronary Stent System and ACS MULTI-LINK OTW ULTRA Coronary Stent System, approved September 8, 2000 for sizes 3.5 mm to 4.0 mm

S023 - ACS MULTI-LINK RX TETRA™ Coronary Stent System and ACS MULTI-LINK OTW TETRA Coronary Stent System, approved October 3, 2000

S027 - ACS MULTI-LINK RX PENTA™ Coronary Stent System and ACS MULTI-LINK OTW PENTA Coronary Stent System, approved May 7, 2001.

New indications were previously added to the PMA in the following supplements:

S005 – Approved February 18, 1999. Approval to add the indication for abrupt or threatened abrupt closure to the product labeling for the ACS MULTI-LINK™ (OTW, RX HP™, and OTW HP™), ACS MULTI-LINK RX, ACS MULTI-LINK (RX and OTW) DUET™ Coronary Stent Systems (CSS); and approval for additional stent sizes for the ACS MULTI-LINK RX (stents with 2.5mm diameter or 35mm length) and ACS MULTI-LINK (RX and OTW) DUET™ (stents with 2.5mm diameter or 38mm length) CSS.

S031 – Approved June 5, 2001. Approval for the addition of a new indication for the ACS MULTI-LINK RX and OTW DUET™, TRISTAR™, ULTRA™, TETRA™ Coronary Stent Systems and ACS MULTI-LINK® stent and the four delivery systems. The new additional indication for these devices is for use in patients with symptomatic ischemic heart disease due to lesions in saphenous vein bypass grafts (SVGs) (length ≤ 35 mm) with a reference vessel diameter of 3.0 mm to 4.0 mm.

S035 – Approved January 14, 2002. Approval for the addition of an indication to use the 4.5 mm and 5.0 mm ULTRA™ OTW and RX for the treatment of saphenous vein graft (SVG) lesions. The MULTI-LINK RX ULTRA™ and MULTI-LINK OTW ULTRA™ Coronary Stent System includes the following indication:

1. Patients with symptomatic ischemic heart disease due to discrete de novo or restenotic native coronary artery lesions (length ≤ 25 mm) with reference vessel diameters ranging from 3.5 mm to 5.0 mm;

2. Patients with symptomatic ischemic heart disease due to lesions in saphenous vein bypass grafts (length ≤ 35 mm) with reference vessel diameters ranging from 3.5 mm to 5.0 mm; and
3. Treatment of abrupt or threatened abrupt closure in patients with failed interventional therapy in lesions (≤ 35 mm in length) with reference diameters in the range of 3.5 mm to 5.0 mm. Long term outcome for this permanent implant is unknown at present. Note: 38 mm length stents are solely indicated for use in patients with abrupt or threatened abrupt closure and patients with lesions in saphenous vein bypass grafts

S036 – Approved January 14, 2002. Approval for the addition of an indication to use the 3.0 mm to 4.0 mm ULTRA™ OTW and RX for the treatment of SVG lesions. The MULTI-LINK RX PENTA™ and MULTI-LINK OTW PENTA™ Coronary Stent System will include the following indication:

1. Patients with symptomatic ischemic heart disease due to discrete de novo or restenotic native coronary artery lesions (length ≤ 25 mm) with reference vessel diameters ranging from 3.0 mm to 4.0 mm;
2. Patients with symptomatic ischemic heart disease due to lesions in saphenous vein bypass grafts (length ≤ 35 mm) with reference vessel diameters ranging from 3.0 mm to 4.0 mm; and
3. Treatment of abrupt or threatened abrupt closure in patients with failed interventional therapy in lesions (≤ 35 mm in length) with reference diameters in the range of 2.5 mm to 4.0 mm. Long term outcome for this permanent implant is unknown at present.

Note: The 2.5 mm and 2.75 mm stents are solely indicated for use in patients with abrupt or threatened abrupt closure. The 33 mm and 38 mm length stents are indicated solely for use in patients with abrupt or threatened abrupt closure and patients with lesions in saphenous vein bypass grafts.

II. INDICATIONS

The ACS MULTI-LINK® Coronary Stent Systems as listed above are indicated for improving coronary luminal diameter in the following (see Individualization of Treatment):

- Improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete *de novo* or restenotic native coronary artery lesions length ≤ 25 mm with a reference vessel diameter of 3.0 mm to 4.0 mm.
- Improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to lesions in saphenous vein bypass grafts length ≤ 35 mm with a reference vessel diameter of 3.0 mm to 4.0 mm.
- **Restoring coronary flow in patients experiencing acute myocardial infarction, as confirmed by ST segment elevation or angiographic findings, who present within 12 hours of symptom onset with native coronary artery lesions of length ≤ 35 mm with a reference vessel diameter of 2.5 mm to 4.0 mm.** (Indication added in this application.)
- Treatment of abrupt or threatened abrupt closure in patients with failed interventional therapy in lesions length ≤ 35 mm with a reference vessel diameter of 2.5 mm to 4.0 mm.

Long-term outcome (beyond 6 months) for this permanent implant is unknown at present.

III. CONTRAINDICATIONS

The ACS MULTI-LINK® Coronary Stent Systems as listed above are contraindicated for use in:

- Patients in whom anti-platelet and/or anti-coagulant therapy is contraindicated.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Instructions for Use (IFU,) Guidant MULTI-LINK RX & OTW DUET Coronary Stent System, U.S. (CADILLAC) labeling.

V. DEVICE DESCRIPTION

The ACS MULTI-LINK® Coronary Stent Systems (CSS) as listed above are each comprised of two components: the Stent and the Delivery System. The Stent is fabricated from 316L stainless steel tubing and is comprised of a series of cylindrically oriented corrugated rings aligned along a common longitudinal axis. Each corrugated ring is connected to an adjacent ring by three straight longitudinally oriented bars.

The Stent is mounted on one of four delivery systems. Each Delivery System provides a means for carrying the Stent through the coronary vasculature, and once in the desired location, expands the Stent through balloon inflation. The four Delivery Systems available with the ACS MULTI-LINK® Stents as listed above offer two modes of delivery: Over-The-Wire (OTW) and Rapid Exchange (RX). The Delivery Systems are based upon Guidant ACS PTCA catheter technology.

The OTW systems are the ACS MULTI-LINK® CSS, ACS OTW MULTI-LINK HP™ CSS, ACS MULTI-LINK OTW DUET® CSS, ACS MULTI-LINK OTW TRISTAR™ CSS, ACS MULTI-LINK OTW ULTRA™ CSS, ACS MULTI-LINK OTW TETRA™ CSS, and ACS MULTI-LINK OTW PENTA™ CSS. The RX systems are the ACS RX MULTI-LINK® CSS, ACS RX MULTI-LINK HP™ CSS, ACS MULTI-LINK RX DUET® CSS, ACS MULTI-LINK RX TRISTAR™ CSS, ACS MULTI-LINK RX ULTRA™ CSS, ACS MULTI-LINK RX TETRA™ CSS, and ACS MULTI-LINK RX PENTA™ CSS.

The Stents are identical regardless of the Delivery System on which they are mounted. All four Delivery Systems are equipped with an elastic membrane that covers the balloon portion over which the Stent is placed. The elastic membrane aids in the even expansion of the Stent. There are two radiopaque markers placed underneath the balloon between which the Stent is positioned; these markers facilitate the fluoroscopic placement of the Stent. The Delivery Systems are prepared using the double negative aspiration technique and are compatible with 0.024 inch diameter guide wires.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for acute myocardial infarction are PTCA alone, PTCA and stent placement, or medical care without PTCA or stent placement.

VII. MARKETING HISTORY

Guidant Corporation, Vascular Intervention, has never distributed a coronary stent system device with the indication for the treatment of acute myocardial infarction to any region in the world.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The CADILLAC Trial was a prospective randomized study to determine the comparative major adverse cardiac events (MACE) rates defined as the composite of death, disabling stroke, reinfarction and ischemi- driven revascularization by CABG or PTCA related to the target vessel. The study was conducted at 74 centers from eight countries. After satisfying clinical and angiographic criteria, 2,082 patients were randomized equally to one of four reperfusion strategies.

Patients with clinical symptoms of AMI (without cardiogenic shock) of at least 30 minutes in duration but no more than 12 hours were screened for eligibility. Angiographic confirmation was required to assure that the lesion was in a native coronary lesion, not previously stented, and visually estimated to be between 2.5 and 4.0 mm in diameter and < 76 mm in length. Lesions had to be covered by no more than two stents, each of which was \leq 38 mm in length.

The initial statistical comparison was a superiority comparison for the primary endpoint of MACE at six months. The hypothesis was that the ACS MULTI-LINK® Stent had a lower incidence of MACE compared to PTCA. The ACS MULTI-LINK Stent was found to be statistically significantly more effective than PTCA alone as documented by a lower 180-Day MACE rate (Table 1).

The second comparison was an equivalency test, for the primary endpoint of MACE at six months. The hypothesis was that the ACS MULTI-LINK Stent has the same or lower incidence of MACE compared to PTCA plus abciximab. Table 1 demonstrates that reperfusion with the ACS MULTI-LINK Stent alone resulted in a significantly lower 180-Day MACE rate when compared to PTCA plus abciximab.

Table 1 - Principal Adverse Events Through 180 days - CADILLAC Trial
Percent, [95% Confidence Interval], (Number)

	PTCA (n=518)	PTCA plus Abciximab (n=528)	Stent (n=512)	Stent plus Abciximab (n=524)
Any Adverse Event	26.4% [22.7%, 30.5%] (137)	22.3% [18.9%, 26.1%] (118)	18.6% [15.3%, 22.2%] (95)	14.9% [11.9%, 18.2%] (78)
Early (In-Hospital)	10.4% [7.9%, 13.4%] (54)	5.7% [3.9%, 8.0%] (30)	10.2% [7.7%, 13.1%] (52)	5.5% [3.7%, 7.9%] (29)
Out-of-Hospital	16.0% [13.0%, 19.5%] (83)	16.7% [13.6%, 20.1%] (88)	8.4% [6.1%, 11.1%] (43)	9.4% [7.0%, 12.2%] (49)
Any MACE	19.7% [16.4%, 23.4%] (102)	16.3% [13.2%, 19.7%] (86)	11.3% [8.7%, 14.4%] (58)	10.1% [7.7%, 13.0%] (53)
Early (In-Hospital)	6.0% [4.1%, 8.4%] (31)	2.7% [1.5%, 4.4%] (14)	4.9% [3.2%, 7.1%] (25)	2.9% [1.6%, 4.7%] (15)
Out-of-Hospital	13.7% [10.9%, 17.0%] (71)	13.6% [10.8%, 16.9%] (72)	6.4% [4.5%, 8.9%] (33)	7.3% [5.2%, 9.8%] (38)
MI	1.7% [0.8%, 3.3%] (9)	2.7% [1.5%, 4.4%] (14)	1.6% [0.7%, 3.1%] (8)	2.1% [1.1%, 3.7%] (11)
Early (In-Hospital)	0.2% [0.0%, 1.1%] (1)	0.0% [0.0%, 0.7%] (0)	0.8% [0.2%, 2.0%] (4)	0.0% [0.0%, 0.7%] (0)
Out-of-Hospital	1.5% [0.7%, 3.0%] (8)	2.7% [1.5%, 4.4%] (14)	0.8% [0.2%, 2.0%] (4)	2.1% [1.1%, 3.7%] (11)
Ischemic TVR-CABG	3.1% [1.8%, 5.0%] (16)	3.0% [1.7%, 4.9%] (16)	2.7% [1.5%, 4.5%] (14)	1.5% [0.7%, 3.0%] (8)
Early (In-Hospital)	1.5% [0.7%, 3.0%] (8)	0.6% [0.1%, 1.7%] (3)	1.2% [0.4%, 2.5%] (6)	0.6% [0.1%, 1.7%] (3)
Out-of-Hospital	1.5% [0.7%, 3.0%] (8)	2.5% [1.3%, 4.2%] (13)	1.6% [0.7%, 3.1%] (8)	1.0% [0.3%, 2.2%] (5)
Ischemic TVR-PTCA	12.0% [9.3%, 15.1%] (62)	10.6% [8.1%, 13.6%] (56)	5.5% [3.7%, 7.8%] (28)	3.4% [2.0%, 5.4%] (18)
Early (In-Hospital)	2.9% [1.6%, 4.7%] (15)	0.9% [0.3%, 2.2%] (5)	1.8% [0.8%, 3.3%] (9)	0.4% [0.0%, 1.4%] (2)
Out-of-Hospital	9.1% [6.7%, 11.9%] (47)	9.7% [7.3%, 12.5%] (51)	3.7% [2.2%, 5.7%] (19)	3.1% [1.8%, 4.9%] (16)
SAT *	1.9% [0.9%, 3.5%] (10)	0.8% [0.2%, 1.9%] (4)	1.0% [0.3%, 2.3%] (5)	0.0% [0.0%, 0.7%] (0)
Early (In-Hospital)	1.4% [0.5%, 2.8%] (7)	0.4% [0.0%, 1.4%] (2)	1.0% [0.3%, 2.3%] (5)	0.0% [0.0%, 0.7%] (0)
Out-of-Hospital	0.6% [0.1%, 1.7%] (3)	0.4% [0.0%, 1.4%] (2)	0.0% [0.0%, 0.7%] (0)	0.0% [0.0%, 0.7%] (0)
Death	4.4% [2.8%, 6.6%] (23)	2.5% [1.3%, 4.2%] (13)	2.9% [1.6%, 4.8%] (15)	4.2% [2.6%, 6.3%] (22)
Early (In-Hospital)	1.5% [0.7%, 3.0%] (8)	1.1% [0.4%, 2.5%] (6)	2.0% [0.9%, 3.6%] (10)	1.9% [0.9%, 3.5%] (10)
Out-of-Hospital	2.9% [1.6%, 4.7%] (15)	1.3% [0.5%, 2.7%] (7)	1.0% [0.3%, 2.3%] (5)	2.3% [1.2%, 4.0%] (12)
Bleeding Complication *	3.1% [1.8%, 5.0%] (16)	2.7% [1.5%, 4.4%] (14)	4.5% [2.9%, 6.7%] (23)	3.2% [1.9%, 5.1%] (17)
Early (In-Hospital)	2.9% [1.6%, 4.7%] (15)	2.7% [1.5%, 4.4%] (14)	3.3% [1.9%, 5.3%] (17)	2.7% [1.5%, 4.4%] (14)
Out-of-Hospital	0.2% [0.0%, 1.1%] (1)	0.0% [0.0%, 0.7%] (0)	1.2% [0.4%, 2.5%] (6)	0.6% [0.1%, 1.7%] (3)
Disabling Stroke (CVA)	0.2% [0.0%, 1.1%] (1)	0.2% [0.0%, 1.1%] (1)	0.4% [0.0%, 1.4%] (2)	0.4% [0.0%, 1.4%] (2)
Early (In-Hospital)	0.0% [0.0%, 0.7%] (0)	0.0% [0.0%, 0.7%] (0)	0.2% [0.0%, 1.1%] (1)	0.0% [0.0%, 0.7%] (0)
Out-of-Hospital	0.2% [0.0%, 1.1%] (1)	0.2% [0.0%, 1.1%] (1)	0.2% [0.0%, 1.1%] (1)	0.4% [0.0%, 1.4%] (2)

- Displayed are 95% exact Clopper-Pearson confidence intervals for one proportion.
- Any Adverse Event includes MI, ischemic TVR - CABG and PTCA, SAT, death, bleeding complication, and CVA.
- TVR = target vessel revascularization by Coronary Artery Bypass Graft Surgery (CABG) or Percutaneous Coronary Intervention (PCI).
- SAT = Any cardiac death < 30 days. Any subacute (outside of cath lab) closure requiring revascularization of the target site < 30 days with presence of thrombus at the target site, any total closure indicated by Quantitative Coronary Angiography (QCA) < 30 days.
- CABG and PTCA are ischemic events at the target vessel, as defined in the study protocol.
- Disabling stroke (CVA) is protocol-defined as an acute, new neurological deficit lasting > 24 hours affecting daily activities, or resulting in death.
- Any Adverse Event counts are straight sums across the individual events. All other counts are patient counts, with patients counted only once at each level of summation.
- Note that only the first occurrence of each event for each patient was recorded in the adjudicated dataset. As a result, only the first of each event is counted for each patient.

* Counts for SAT and bleeding complications are through 30 days.

Adverse events that may be associated with the use of a coronary stent in native coronary arteries include:

- Acute myocardial infarction
- Arrhythmias, including VF and VT
- Death
- Dissection
- Drug reactions to anti-platelet agents / contrast medium
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent Coronary Artery Bypass Surgery
- Hemorrhage, requiring transfusion
- Hypotension / Hypertension
- Infection and pain at insertion site
- Ischemia, Myocardial
- Perforation
- Pseudoaneurysm, Femoral
- Restenosis of stented segment
- Spasm
- Stent embolization
- Stent thrombosis / occlusion
- Stroke / cerebrovascular accident
- Total occlusion of coronary artery

IX. SUMMARY OF THE CLINICAL STUDY

As described above, the CADILLAC Study provided a prospective randomized comparison of the ACS MULTI-LINK® and ACS MULTI-LINK RX DUET® Coronary Stent Systems in four reperfusion strategies: stent with abciximab; stent without abciximab; PTCA with abciximab; and PTCA without abciximab, in the treatment of patients presenting with an acute myocardial infarction.

Table 2 presents the demographics for patients enrolled in the CADILLAC trial. Men represented 73% of the population, a distribution reflective of the AMI population. Other significant risk factors are also listed. A discussion of differences in outcomes and gender is provided following Table 3.

At 7-month angiographic follow-up, the mean percent diameter stenosis for stented patients was 30.8%. In patients treated with PTCA alone, the diameter stenosis was 45.1%, and for patients treated with PTCA plus abciximab the mean diameter stenosis was 48.6%. Similarly, the mean MLD for stent alone was 1.96 mm compared to 1.57 mm for PTCA alone and 1.48 mm for PTCA plus abciximab. The 7-month binary angiographic Restenosis rates for stenting without (13.8%) or with abciximab (17.9%) were significantly superior to those achieved with PTCA without (34.7%) or with abciximab (44.8%). These late angiographic results were reflected in the clinical results. Stent alone was significantly superior to PTCA alone and PTCA plus abciximab at 180 days, proving both primary hypotheses.

The 180-day MACE rate for stent alone of 11.3% was approximately one half that of PTCA alone, with a rate of 19.69% ($p \leq 0.001$). A total of 19 patients experienced subacute thrombosis within the 30-day follow-up interval following revascularization; 10 (1.9%) received PTCA alone, 4 (0.8%) received PTCA plus abciximab and 5 (1.0%) received stent alone. There were no SATs in the stent plus abciximab treatment group.

Table 3 shows the principal effectiveness and safety results of the CADILLAC Acute Myocardial Infarction (AMI) Trial. Figure 1 is a Kaplan-Meier curve of time to a MACE event through 365 days of follow-up. Table 4 shows Time From Initial Procedure to MACE Event (Days).

Table 2 - CADILLAC Trial Patient Demographics

	Men	Women	P Value
N	1520	562	-
Median Age (years)	58	65	< 0.001
Hypertension	29%	45%	< 0.001
Diabetes	14%	24%	< 0.001
Hyperlipidemia	36%	43%	< 0.001
Killip Class >1	10%	15%	< 0.001
Prior MI	16%	8%	< 0.001

Primary Endpoint First Comparison by Evaluating MACE

The first comparison was one of superiority between stent alone and PTCA alone. The stent alone arm of the trial proved to be significantly superior to PTCA alone (11.3% vs. 19.7, $p < 0.001$).

Primary Endpoint Second Comparison by Evaluating MACE

The second comparison was a test of equivalency between stent alone and PTCA plus Abciximab. The stent alone arm of the trial proved to be not only equivalent, but significantly superior to PTCA plus Abciximab (11.3% vs. 16.3%, $p < 0.001$).

Table 3 - Principal Effectiveness and Safety Results Through 180 Days

	PTCA (n=518)	PTCA plus Abciximab (n=528)	STENT (n=512)	STENT plus Abciximab (n=524)
Efficacy Measures				
Lesion Success by QCA	93.1% (461 / 495)	94.2% (483 / 513)	94.2% (457 / 485)	96.8% (491 / 507)
Clinical Procedure Success by QCA	88.1% (436 / 495)	92.0% (472 / 513)	90.7% (440 / 485)	95.1% (482 / 507)
Post Procedure MLD (mm), in-lesion / in-stent Mean \pm SD (N) Range(min-max)	2.24 \pm 0.50 (501) (0.40, 3.95)	2.21 \pm 0.55 (516) (0.00, 4.86)	2.63 \pm 0.48 (487) (0.00, 4.18)	2.71 \pm 0.48 (507) (0.00, 4.41)
7-Month Follow up in-lesion / in-stent % DS Angiographic Subset Patients Mean \pm SD (N)	45.10 \pm 25.15 (144) (-4.70, 100.0)	48.60 \pm 23.55 (163) (3.30, 100.0)	30.81 \pm 18.87 (138) (-21.3, 100.0)	32.44 \pm 19.63 (162) (-28.5, 100.0)
7-Month Follow up in-lesion / in-stent binary restenosis rate Angiographic Subset Patients	34.7% (50 / 144)	44.8% (73 / 163)	13.8% (19 / 138)	17.9% (29 / 162)
TVR-free Through 6 months	83.8% (434 / 518)	85.6% (452 / 528)	91.4% (468 / 512)	94.5% (495 / 524)
TVF-free Through 6 months	79.3% (411 / 518)	83.0% (438 / 528)	88.3% (452 / 512)	89.5% (469 / 524)
Safety Measures				
In-Hospital MACE Events	6.0% (31 / 518)	2.7% (14 / 528)	4.9% (25 / 512)	2.9% (15 / 524)
Out of Hospital MACE Events Through 180 Days	13.7% (71 / 518)	13.6% (72 / 528)	6.4% (33 / 512)	7.3% (38 / 524)
Bleeding Events	3.1% (16 / 518)	2.7% (14 / 528)	4.5% (23 / 512)	3.2% (17 / 524)
Stent Thrombosis	1.9% (10 / 518)	0.9% (5 / 528)	1.0% (5 / 512)	0.0% (0 / 524)
Survival Through 30 Days	97.5% (505 / 518)	98.9% (522 / 528)	97.9% (501 / 512)	97.3% (510 / 524)
Survival Through 180 Days	95.6% (495 / 518)	97.5% (515 / 528)	97.1% (497 / 512)	95.8% (502 / 524)
MACE rate Through 180 Days *	19.7% (102 / 518)	16.3% (86 / 528)	11.3% (58 / 512)	10.1% (53 / 524)
Length of Hospitalization - US Sites (days) Mean \pm SD (N) Range(min-max)	4.26 \pm 2.78 (418) (1.00, 28.00)	3.74 \pm 2.43 (424) (1.00, 25.00)	4.33 \pm 3.58 (409) (0.00, 39.00)	3.80 \pm 2.51 (423) (1.00, 23.00)
Length of Hospitalization - European Sites (days) Mean \pm SD (N) Range(min-max)	8.10 \pm 4.63 (72) (2.00, 22.00)	8.03 \pm 5.28 (74) (2.00, 24.00)	8.01 \pm 4.65 (73) (3.00, 20.00)	8.52 \pm 6.06 (71) (2.00, 27.00)

CADILLAC Trial Definitions

- Lesion success = Attainment of final result, $< 50\%$ residual stenosis of the target site with TIMI 3 flow, using Guidant MULTI-LINK System or PTCA and any adjunctive device.
- Binary restenosis = $\geq 50\%$ by quantitative coronary analysis
- Target Vessel Failure (TVF) – The composite of death, Q-Wave MI, Non-Q-Wave MI, Target Site Revascularization (TSR) or Target Vessel Revascularization (TVR) by Coronary Artery Bypass Graft Surgery (CABG) or Percutaneous Coronary Intervention (PCI).

* Primary Endpoint

Figure 1 Kaplan–Meier Curve of Time to MACE (to 365 days)

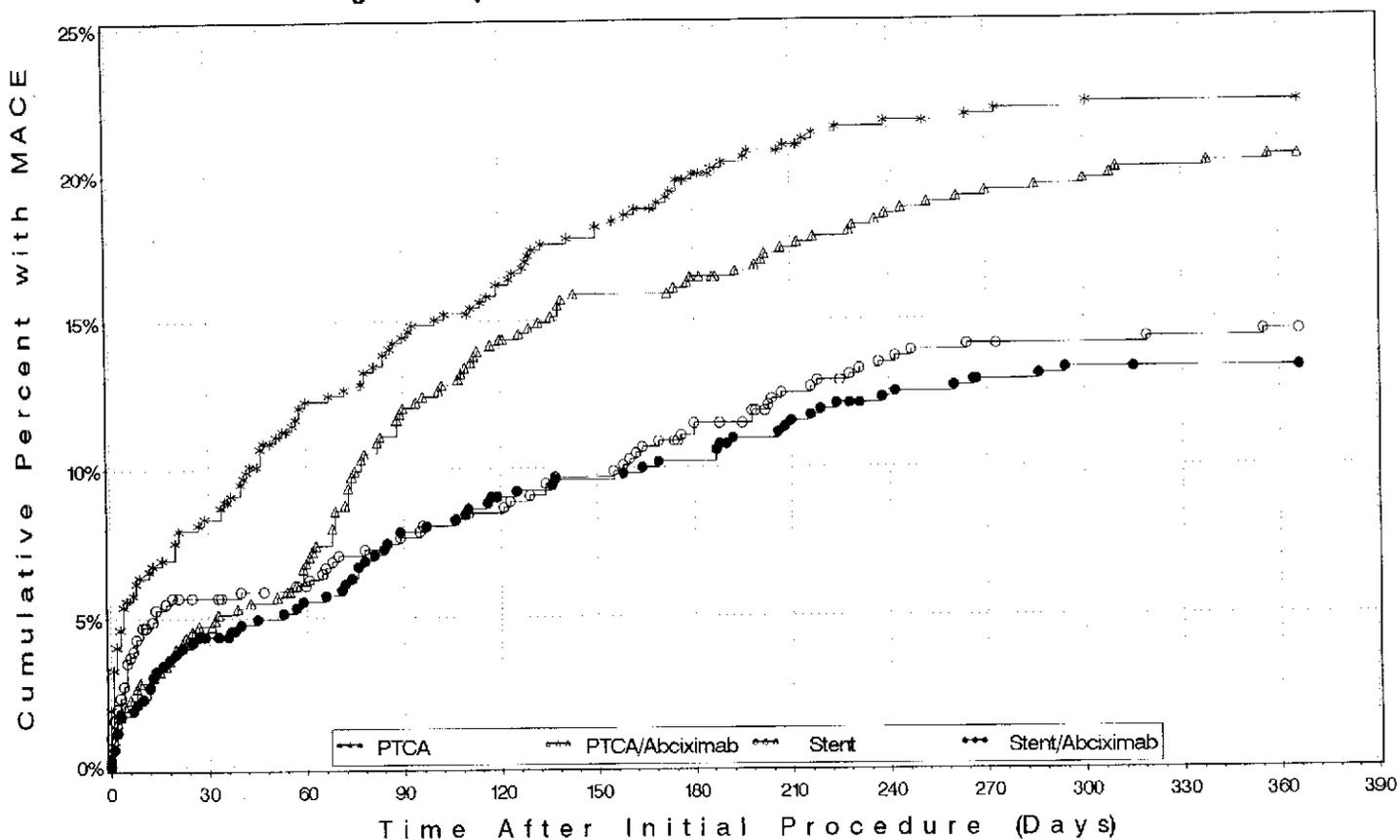


Table 4 – Time From Initial Procedure to MACE Event (Days)

Treatment	Parameter	0 days	14 days	30 days	90 days	180 days	270 days	365 days
PTCA	# At Risk	518	505.5	478	467	431	398.5	386
	# Events	10	35	43	74	102	112	114
	% with Event	1.93	6.78	8.34	14.43	19.98	21.99	22.4
	% SEM	0.6	1.11	1.22	1.55	1.77	1.84	1.85
PTCA plus Abciximab	# At Risk	528	525	508.5	497	457	431	414
	# Events	2	16	25	63	86	101	107
	% with Event	0.38	3.04	4.75	12.03	16.46	19.37	20.54
	% SEM	0.27	0.75	0.93	1.42	1.62	1.73	1.77
Stent	# At Risk	512	504.5	479	474	461	438	421.5
	# Events	5	27	29	39	58	71	73
	% with Event	0.98	5.29	5.69	7.68	11.48	14.11	14.52
	% SEM	0.43	0.99	1.03	1.18	1.42	1.55	1.57
Stent plus Abciximab	# At Risk	524	523	505.5	496	475.5	461	444.5
	# Events	1	17	23	41	53	67	69
	% with Event	0.19	3.24	4.39	7.86	10.19	12.92	13.31
	% SEM	0.19	0.77	0.9	1.18	1.33	1.47	1.49
Tests Between Groups	Test	Chi-Square	Deg Frdm	P-value				
Stent vs. PTCA	Log-Rank	10.9987	1	0.0009				
Stent vs. PTCA plus Abciximab	Log-Rank	6.0671	1	0.0138				

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GENDER BIAS

Much research has been conducted to study the clinical outcomes between men and women after AMI. Although the finding that gender as an independent predictor of mortality after thrombolysis is not conclusive, it has been widely established that there is a distinct bias in the populations skewed by cultural denominators. The trends, varying in decisive ratios, have been recurrent to the extent that women seek medical care later and present with higher or greater risks at the time that attention is sought. Common examples are cardiogenic shock and higher incidences of other complications such as diabetes and hypertension.

A quantitative overview of the research from numerous studies looking at sex-based differences in clinical and angiographic outcomes after AMI¹ reveals findings that parallel to CADILLAC, which attests to the randomness of the CADILLAC population selection process. The benefit of stenting is similar in men and women.

In the general population, the unadjusted mortality for women experiencing an AMI is 1.5 – 2 times greater in women than in men.² This is accounted for by the older age and higher risk factors in women, such as a greater incidence of diabetes, hypertension, and cardiogenic shock.¹ This same trend was found in the analysis of the CADILLAC data, where women had a 2.65 times greater mortality rate at one-year than men. Table 5 depicts “Counts of Death Through 365 Days, Overall and By Type, By Treatment and Gender.” The information illustrates that CADILLAC found the same trends for risk factors and MACE rates as other cardiovascular trials, however, the stent arms versus the PTCA arms had reduced overall composite MACE rates for women.

The gender selection was completely random, and solely based upon exclusion and inclusion criteria. In the CADILLAC study, men (mean age 58 years) represented 73% of this population and women (mean age 65 years) represented 27%. For patients who qualified for the study, the gender distribution within the patient population was commensurate with literature for the occurrence of acute myocardial infarction. At various stages during the trial, the Data Safety Monitoring Board reviewed patient demographics to identify any irregularities that could affect the planned conduct of the trial. No gender bias in selection was found.

The MACE rates at 180 days and 365 days between men and women were different only to the extent that women had a higher death rate (a component of MACE).

MACE at 180 days	Females with PTCA	Females with Stents
	25.26%	15.16%
MACE at 365 days	Males with PTCA	Males with Stents
	15.24%	9.09%
MACE at 180 days	Females with PTCA	Females with Stents
	28.07%	19.13%
MACE at 365 days	Males with PTCA	Males with Stents
	18.53%	11.73%

The higher mortality rates in women appear to be unrelated to the therapy received. The findings of the CADILLAC study did not raise any concerns related to a higher risk of death in women who received stents.

**Table 5 – CADILLAC Study, Counts of Death Through 365 Days,
Overall and By Type, By Treatment and Gender**

All Patients	PTCA 1046	Stent 1036	Total 2082
All Deaths	44 (4.21%)	45 (4.34%)	89 (4.27%)
Non-Cardiac Death	15 (1.43%)	13 (1.25%)	28 (1.34%)
Other Cardiac Death	7 (0.67%)	9 (0.87%)	16 (0.77%)
Unknown	4 (0.38%)	8 (0.77%)	12 (0.58%)
Sudden Death	6 (0.57%)	5 (0.48%)	11 (0.53%)
Arrhythmic Death	5 (0.48%)	4 (0.39%)	9 (0.43%)
Acute Myocardial Infarction	5 (0.48%)	2 (0.19%)	7 (0.34%)
Heart Failure	2 (0.19%)	3 (0.29%)	5 (0.24%)
Stroke	0 (0.00%)	1 (0.10%)	1 (0.05%)
Male Patients	761	759	1520
All Deaths	23 (3.02%)	22 (2.90%)	45 (2.96%)
Non-Cardiac Death	8 (1.05%)	6 (0.79%)	14 (0.92%)
Other Cardiac Death	3 (0.39%)	3 (0.40%)	6 (0.39%)
Unknown	2 (0.26%)	4 (0.53%)	6 (0.39%)
Sudden Death	4 (0.53%)	3 (0.40%)	7 (0.46%)
Arrhythmic Death	4 (0.53%)	3 (0.40%)	7 (0.46%)
Acute Myocardial Infarction	2 (0.26%)	1 (0.13%)	3 (0.20%)
Heart Failure	0 (0.00%)	2 (0.26%)	2 (0.13%)
Stroke	0 (0.00%)	0 (0.00%)	0 (0.00%)
Female Patients	285	277	562
All Deaths	21 (7.37%)	23 (8.30%)	44 (7.83%)
Non-Cardiac Death	7 (2.46%)	7 (2.53%)	14 (2.49%)
Other Cardiac Death	4 (1.40%)	6 (2.17%)	10 (1.78%)
Unknown	2 (0.70%)	4 (1.44%)	6 (1.07%)
Sudden Death	2 (0.70%)	2 (0.72%)	4 (0.71%)
Arrhythmic Death	1 (0.35%)	1 (0.36%)	2 (0.36%)
Acute Myocardial Infarction	3 (1.05%)	1 (0.36%)	4 (0.71%)
Heart Failure	2 (0.70%)	1 (0.36%)	3 (0.53%)
Stroke	0 (0.00%)	1 (0.36%)	1 (0.18%)

¹ Sex-Based Differences in Clinical and Angiographic Outcomes After Primary Angioplasty or Stenting for Acute Myocardial Infarction, American Journal of Cardiology 2001; 87: 289-93

² Chapter entitled "Cardiovascular Disease in Women", by Alexandra Lansky, published in "The Manual of Cardiovascular Medicine", by Mark Freed and Robert Safian.

X. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The results of the clinical studies of the ACS MULTI-LINK® Coronary Stent Systems demonstrated that the device is safe and effective when used in acute myocardial infarction.

XI. 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 this panel.

XII. CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH) DECISION

CDRH approval of the Guidant Corporation PMA P970020 supplement 40 is based on the safety and effectiveness of the device demonstrated by the clinical data contained in this supplement. The clinical data obtained from the CADILLAC Trial are provided in this summary to support the additional indication for the purpose of restoring coronary flow in patients experiencing acute myocardial infarction, as confirmed by ST segment elevation or angiographic findings, who present within 12 hours of symptom onset with native coronary artery lesions of length \leq 35 mm with a reference vessel diameter of 2.5 mm to 4.0 mm.

XIII. 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.

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