



P970020

Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20856

OCT - 2 1997

Ms. Sara Toyloy  
Director, Regulatory Affairs  
Guidant Corporation/Advanced Cardiovascular Systems  
3200 Lakeside Drive  
Santa Clara, California 95052-8167

Re: P970020  
ACS Multi-Link™ Coronary Stent System  
Filed: June 12, 1997  
Amended: September 11, 12, 16, and 22, 23 and 30, 1997

Dear Ms. Toyloy:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the ACS Multi-Link™ Coronary Stent System containing ACS Multi-Link™ CSS, ACS RX Multi-Link HP™ CSS, ACS OTW Multi-Link HP™ CSS, and ACS RX Multi-Link™ CSS delivery platforms. The device with ACS Multi-Link™ CSS, ACS RX Multi-Link HP™ CSS and ACS OTW Multi-Link HP™ CSS delivery platforms is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 20 mm) with a reference vessel diameter ranging from 3.0 mm to 3.75 mm and is intended to improve coronary luminal diameter. The device with ACS RX Multi-Link™ CSS delivery platform, however, is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 22 mm) with a reference vessel diameter ranging from 3.0 mm to 3.5 mm and is intended to improve coronary luminal diameter. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the following information:

Further characterization of long-term safety and effectiveness by following for 5 years from implant at least 390 of the 520 patients implanted with the ACS Multi-Link™ stent in the ASCENT study.

The protocol for this study and study time lines will be submitted to the agency for review within 30 days of approval. The final protocol will be developed interactively with the FDA review team.

Summary reports will be submitted to the agency annually and a final report at the end of the study.

Expiration dating for this device has been established and approved at 1 year for the ACS Multi-Link™ CSS and ACS RX Multi-Link HP™ CSS, 2 years for the ACS RX Multi-Link™ CSS, and 3 months for the ACS OTW Multi-Link HP™ CSS. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Blvd.  
Rockville, Maryland 20850

In addition under section 522(a) of the act, manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted device as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

At that time you should submit five (5) copies to:

Postmarket Studies Document Center  
1350 Piccard Drive (HFZ-544)  
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522.

In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the Federal Food, Drug and Cosmetic Act (the act) (21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3)), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA.

If you have any questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639.

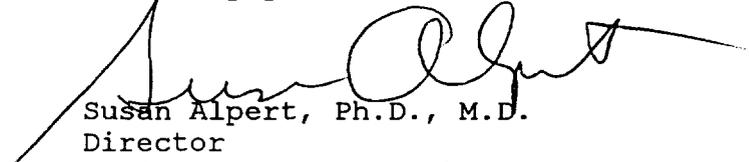
Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health

consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your device is a device that is subject to tracking because it is a permanent implant whose failure would be reasonably likely to have serious adverse consequences.

FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR § 821.20(b) and the devices that FDA has designated for tracking at 21 CFR § 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993)). Pursuant to 21 CFR § 821.20(d), FDA will be adding coronary stents to these lists by publishing a notice in the FEDERAL REGISTER announcing that FDA believes that this device is subject to tracking under section 519(e)(1). This notice will also solicit public comments on FDA's determination.

If you have any questions concerning this approval order, please contact H. Semih Oktay, Ph.D., at (301) 443-8243.

Sincerely yours,



Susan Alpert, Ph.D., M.D.  
Director  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosures

Issued: 3-4-98

#### CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effectuated" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effectuated" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effectuated." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mix-up of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc. Any written report is to be submitted to:

Food and Drug Administration  
Center for Devices and Radiological Health  
Medical Device Reporting  
PO Box 3002  
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW

Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

# **ACS MULTI-LINK™ Coronary Stent Systems**

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# **Summary of Safety and Effectiveness Data**

## **ACS MULTI-LINK™ Coronary Stent Systems**

### **1. General Information**

Device Generic Name: Intravascular Coronary Stent

Device Trade Name: ..... ACS MULTI-LINK™ Coronary Stent System  
ACS RX 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/Advanced Cardiovascular Systems  
3200 Lakeside Drive  
P.O. Box 58167  
Santa Clara, California 95052-8167

PMA Application Number: ..... P970020

Date of Panel Recommendation: ..... not applicable

Date of Notice of Approval to the Applicant: . October 2, 1997

### **2. Indications for Use**

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.

### **3. Contraindications**

ACS MULTI-LINK™ Coronary Stent Systems are contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion, which prevents complete inflation of an angioplasty balloon.

### **4. Warnings and Precautions**

#### **4.1 Warnings**

Since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events, judicious selection of patients is necessary.

Persons allergic to 316L stainless steel may suffer an allergic reaction to this implant.

## 4.2 Precautions

- Implantation of the stent should be performed only by physicians who have received appropriate training.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized ACS MULTI-LINK™ Stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition.

### 4.2.1 Stent Handling - Precautions

- **For single use only.** Do not resterilize or reuse. Note product "Use Before" date.
- **Do not remove stent from its delivery balloon** as removal may damage the stent and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during catheter removal from packaging, placement over guide wire and advancement through hemostasis valve adapter and guiding catheter hub.
- Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

### 4.2.2 Stent Placement - Precautions

- **Do not prepare or pre-inflate balloon prior to stent deployment** other than as directed. Use balloon purging technique described in the Instructions for Use.
- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure as indicated on product label.** (See Balloon Inflated Diameter dimensions in Table 5). Use of pressures higher than specified on product label may result in a ruptured balloon with possible intimal damage and dissection.
- Do not expand the stent if it is not properly positioned in the vessel. (See Stent/System Removal - Precautions)
- **Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgment of the stent from the balloon may occur.**
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
- Placement of a stent has the potential to compromise side branch patency.
- When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the

proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

#### 4.2.3 Stent/System Removal - Precautions

Should **unusual resistance** be felt at any time during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be **removed as a single unit**.

**When removing the Delivery System as a single unit:**

- DO NOT retract the Delivery System into the guiding catheter.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distal as safely possible.
- Tighten the rotating hemostatic valve to secure the Delivery System to the guiding catheter; then remove the guiding catheter and Delivery System as a **single unit**.

Failure to follow these steps and/or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and/or Delivery System components such as the balloon or the elastic membrane.

If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

#### 4.2.4 Post Implant - Precautions

- Great care must be exercised when **crossing a newly deployed stent** with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry.
- Do not perform a **magnetic resonance imaging (MRI)** scan on patients post-stent implantation until the stent has completely endothelialized (eight weeks) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

## 5. Device Description

The ACS MULTI-LINK™ Coronary Stent System (CSS) is comprised of two components: the Stent and the Delivery System. The ACS MULTI-LINK™ 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™ Stent allow ACS to 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 and the ACS OTW MULTI-LINK HP™ CSS. The RX systems are the ACS RX MULTI-LINK™ CSS and the ACS RX MULTI-LINK HP™ CSS.

The Stent is identical despite which Delivery System it is mounted on. 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 0.014 inch diameter guide wires.

Table 1 provides the product labeling specifications for the ACS MULTI-LINK™ Stent and the four Delivery Systems.

**Table 1. Product Labeling Specifications for the ACS MULTI-LINK™ Systems**

Product	Delivery System Type	Stent Diameter (mm)	Stent Length (mm)	Crimped Stent Profile (F)	Minimum Guiding Catheter Inner Diameter (inch)	Stent Deployment Pressure (atm)	Rated Burst Pressure (atm)	Nominal Expanded Stent Length (mm)	Stent Free % Area
ACS MULTI-LINK™ CSS	OTW	3.00	15	5.0	0.075	8	10	14.6	83.10%
		3.25		5.0	0.075			14.5	84.28%
		3.50		5.0	0.075			14.3	85.23%
		3.75		5.7	0.082			14.0	85.96%
ACS RX MULTI-LINK™ CSS	RX	3.00	15	4.4	0.064	6	8	14.6	83.10%
		3.50	15		0.064			14.3	85.23%
		3.00	25	4.3	0.072	7	16	25.1	83.10%
		3.50	25		0.072			24.3	85.23%
ACS RX MULTI-LINK HP™ CSS	RX	3.00	15	4.3	0.064	11	16	14.6	83.10%
		3.50						14.3	85.23%
		3.75						14.0	85.96%
ACS OTW MULTI-LINK HP™ CSS	OTW	3.0	15	4.3	0.064	11	16	14.6	83.10%
		3.5						14.3	85.23%
		3.75						14.0	85.96%

OTW = Over-The-Wire

RX = Rapid Exchange

## 6. Alternative Practices or Procedures

Patients with early coronary artery disease receive exercise, diet and drug therapy. If the disease progresses, PTCA, coronary artery bypass graft (CABG) surgery or stenting may be performed. Stenting may be performed with commercially available stents.

## 7. Marketing History

The ACS MULTI-LINK™ Stent and the four Delivery Systems are legally marketed internationally under the following four trade names:

ACS MULTI-LINK™ Coronary Stent System (CSS)

ACS RX MULTI-LINK™ Coronary Stent System (CSS)

ACS RX MULTI-LINK HP™ Coronary Stent System (CSS)

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## ACS OTW MULTI-LINK HP™ Coronary Stent System (CSS)

The specific countries are as follows:

Argentina	Finland	Lebanon	Singapore
Australia	France	Liechtenstein	Slovenia <sup>1</sup>
Austria	Germany	Luxembourg	South Africa
Belgium	Greece	Malaysia	Spain
Brazil	Hong Kong	Malta	Sweden
Canada	Iceland	Mexico <sup>1</sup>	Switzerland
Chile	India	Netherlands	Syria
Colombia	Indonesia	New Zealand	Turkey
Costa Rica	Iran	Norway	UAE
Croatia	Ireland	Oman	United Kingdom
Czech Republic	Israe <sup>1</sup>	Pakistan	Uruguay
Denmark	Italy	Portugal	Venezuela
Ecuador	Jordon <sup>1</sup>	Philippines	
Egypt <sup>1</sup>	Kuwait <sup>1</sup>	Saudi Arabia	

<sup>1</sup> = ACS RX MULTI-LINK HP™ CSS not included.

Note: The ACS OTW MULTI-LINK HP™ CSS has not yet been released.

### Market Withdrawal

#### ***ACS MULTI-LINK™ Coronary Stent System (CSS):***

The original design of the over-the-wire ACS MULTI-LINK™ CSS was withdrawn from the Australian market in April 1997. The withdrawal was a result of one customer complaint regarding the detachment of the retractable sleeve marker in one patient; there was no patient injury and the stent was not involved. At the request of the Australian Therapeutic Goods Administration (TGA), Guidant ACS withdrew this earlier design of ACS MULTI-LINK™ CSS with the retractable sleeve marker from the Australian market. The design of the ACS MULTI-LINK™ CSS for which Guidant ACS is seeking FDA Premarket approval for in this PMA application is the current design (G950101/S24, December 4, 1996) and does not include the retractable sleeve marker. There have been no market withdrawals on the current design relating to the safety and effectiveness of the device.

#### ***ACS RX MULTI-LINK™ Coronary Stent System:***

The original design of the ACS RX MULTI-LINK™ CSS, with the 15 mm stent length was withdrawn from the French market in August 1996 as a result of a small number of customer complaints pertaining to the alleged detachment of the elastic membrane post stent deployment; the stent was not involved. In cooperation with the French Ministry of Health, Guidant ACS voluntarily withdrew this earlier design of the ACS RX MULTI-LINK™ CSS with the 15 mm stent length from the French market. The design of the ACS RX MULTI-LINK™ CSS with the 15 mm stent length for which Guidant ACS is seeking FDA Premarket approval for in this PMA application is the current modified design (G950101/S23, November 7, 1996) and is no longer

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representative of the design that was withdrawn from the French market. There have been no market withdrawals on the current design relating to the safety and effectiveness of the device.

## 8. Adverse Effects of the Device on Health

A total of 1593 patients were enrolled in five multicenter clinical studies to evaluate the use of the ACS MULTI-LINK™ Stent for treatment of symptomatic coronary artery disease. Of these, 1073 received the ACS MULTI-LINK™ Stent and 520 received the Palmaz-Schatz® Stent. These patients form the basis for the observed events reported.

**Table 2. Summary Of Clinical Study Patient Enrollments (n=1,593)**

	ACS MULTI-LINK STENT	CONTROL STENT	PATIENT TOTALS
Randomized Clinical Study	520	520	1,040
Restenosis Study	201	-	201
RX Study	202	-	202
RX HP Study	101	-	101
Feasibility Study	49	-	49
<b>PATIENT TOTALS:</b>	<b>1,073</b>	<b>520</b>	<b>1,593</b>

Twelve patients (12/1073 or 1.1%) who received the ACS MULTI-LINK™ Stent died during the clinical studies. One of these patients died within 30 days of receiving the stent implant as a result of a transfusion related grand mal seizure<sup>1</sup>. There were 11 late deaths which occurred between 58 and 353 days after stenting. Eight late deaths were cardiac related; congestive heart failure (n=4), chronic astudy fibrillation (n=1), sustained ventricular tachycardia (n=1), biventricular heart failure (n=1), and “sudden death” (n=1). Three late deaths were not cardiac related; ruptured abdominal aortic aneurysm (n=1), metastatic liver cancer (n=1) and suicide (n=1).

<sup>1</sup>One patient death < 30 days from the RX Study

### 8.1 Observed Adverse Events

Thrombosis of the stent up to 30 days post-implant may occur. The incidence of thrombosis in patients stented with the ACS MULTI-LINK™ Stent was 0.6% (3/520) in the randomized comparative clinical study. All of these thromboses occurred within 24 hours of stent implantation. Known major risk factors for stent thrombosis include post-stent dissection, persistence of thrombus at the treatment site, poor distal runoff following stent implantation, and small vessel diameters. Patients who develop stent thrombosis are at a particularly high risk for major complications including death, myocardial infarction, and emergent coronary artery bypass surgery.

The incidence of vascular complications requiring surgical repair after stent placement in the randomized comparative clinical study was 1.5%. The rates for bleeding requiring transfusion were 0.8%.

Initial delivery failure occurred in 2.9% (15/520) of patients as follows: operator was unable to deliver the first stent (n=12); stent was not deployed at the lesion site (n=2); and, inability to post dilate (n=1). Delivery of a second ACS MULTI-LINK™ Stent was successful in all but 1.5% (8/520) of patients.

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**Table 3 - Principal Adverse Events at 6 Months**  
%, [+ 95% confidence interval], Number/Denominator  
Randomized, *de novo* patients and non-randomized restenosis patients (n = 1,241)

Complication	MULTI-LINK™ <i>DE NOVO</i> (n=520)	Palmaz Schatz® <i>DE NOVO</i> (n=520)	MULTI-LINK™ RESTENOSIS (n=201)
Death Total	1.5% [0.7%, 3.0%], 8/520	3.1% [1.8%, 4.9%], 16/520	0.5% [0.0%, 2.7%], 1/201
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
30-Days	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.5% [0.7%, 3.0%], 8/520	1.9% [0.9%, 3.5%], 10/520	0.5% [0.0%, 2.7%], 1/201
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Non-Q-Wave MI	4.0% [2.5%, 6.1%], 21/520	4.6% [3.0%, 6.8%], 24/520	4.0% [1.7%, 7.7%], 8/201
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	4.0% [2.5%, 6.1%], 21/520	4.0% [1.7%, 7.7%], 8/201
Out-of-Hospital	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
CABG Total	2.5% [1.3%, 4.2%], 13/520	2.1% [1.1%, 3.8%], 11/520	1.0% [0.1%, 3.5%], 2/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.9% [0.9%, 3.5%], 10/520	1.3% [0.5%, 2.8%], 7/520	1.0% [0.1%, 3.5%], 2/201
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	1.9% [0.9%, 3.5%], 10/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.2% [0.0%, 1.1%], 1/520	1.0% [0.3%, 2.2%], 5/520	0.0% [0.0%, 1.5%], 0/201
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	1.3% [0.2%, 2.8%], 7/520	0.0% [0.0%, 1.5%], 0/201
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	3.3% [1.9%, 5.2%], 17/520	1.0% [0.1%, 3.5%], 2/201
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/201
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	3.7% [2.2%, 5.6%], 19/520	2.0% [0.5%, 5.0%], 4/201

## 8.2 Potential Adverse Events

Adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries (including those listed in Table 3):

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

## 9. Summary of Preclinical Studies

### 9.1 Biocompatibility Testing

Biocompatibility Testing was conducted on the ACS MULTI-LINK™ Stent and the four Delivery Systems in accordance with the ISO 10993-1 Standard, the May 1994 FDA “Guidance for the Submission of Research and Marketing Applications: Intravascular Stents,” and the Tripartite Biocompatibility Guidance for Medical Devices (April 1987). The three documents are referenced since the actual testing was completed in four separate phases for each of the four Delivery Systems; the more recent Delivery Systems were tested according to the ISO 10993-1 Standard, whereas the older versions were tested according to the Tripartite and the May 1994

FDA Guidance Document. *The May 1994 Guidance Document specifies the number of devices/samples to be tested for each pre-clinical test.* In addition, the Biocompatibility Testing was conducted in accordance with 21 CFR Part 58, Good Laboratory Practices. The ACS MULTI-LINK™ Stent and the four Delivery Systems passed all applicable tests.

## **9.2 Sterilization Testing:**

Sterilization of the ACS MULTI-LINK™ Stent and the four Delivery Systems and its packaging was verified or validated using the fraction-negative method of Stumbo-Murphy-Cochran. The inflation lumens of the catheters were inoculated with spores of *B. subtilis v. niger* and were allowed to dry before being packaged and exposed to an Ethylene Oxide (EtO) cycle. The D-Value was calculated and the SAL was determined. This testing demonstrated that the ACS MULTI-LINK™ Stent and the four Delivery Systems were sterilized according to the specified parameters.

### **9.2.1 EtO Residuals:**

EtO residuals for the ACS MULTI-LINK™ Stent and the four Delivery Systems were determined using the AAMI/ISO 10993-7R, Biologic Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals Standard. Simulated use extraction of the sterilized product sample was used. EtO Standards were made by weighing the chemical into a known volume of water. The standard calibration curves were used to calculate the amounts of the EtO extracted from the sample, that was then used to calculate the amount of EtO residuals. The EtO residuals for the ACS MULTI-LINK™ Stent and the four Delivery Systems met the requirements of the AAMI/ISO 10993-7R, Biologic Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals Standard.

### **9.2.2 In-Vivo Animal Testing:**

*In-vivo* animal testing was conducted on the ACS MULTI-LINK™ Stent and the four Delivery Systems. Chronic studies were conducted to evaluate the functional performance of the Stent and the resulting angiographic and pathologic responses of the coronary vasculature to the Stent.

The Chronic studies included a total of 19 coronary atherosclerotic swine, 19 coronary nonatherosclerotic swine, 43 normal coronary canine, and 7 peripheral atherosclerotic rabbit stent implant procedures for a total of 105 stent implantations. Angiographic analysis immediately following implantation and at the intended end-point confirmed patent stents with excellent intravascular flow. There were no luminal protrusions or filling defects. Angiographic luminal narrowing was minimal, equivalent to baseline or post-stent implantation observations.

There were no incidences of stent migration, sub-acute thrombosis, excessive neointimal proliferation, flow degradation or untoward clinical events. Histological analysis demonstrated no excessive inflammatory reactions or thrombosis, nor significant neointimal proliferation or luminal narrowing.

Additional acute studies were conducted to evaluate Delivery System performance, ease of implantation, and acute angiographic patency. Excellent expansion, vessel conformance and radial strength of the stent were demonstrated by angiography and there was no evidence of excessive vascular injury.

### 9.3 In-Vitro Bench Testing

*In-Vitro* bench testing was conducted on the ACS MULTI-LINK™ Stent and the four Delivery Systems in accordance the May 1994 FDA “Guidance for the Submission of Research and Marketing Applications: Intravascular Stents”.

The relevant tests outlined in the guidance were conducted to demonstrate the functional performance characteristics of the ACS MULTI-LINK™ Stent and the four Delivery Systems. The testing was conducted on units that were sterilized using EtO, which is the sterilization method that will be used for production purposes.

#### 9.3.1 Stent Material Specification and Conformance Testing

##### 9.3.1.1 Chemical Analysis:

The ACS MULTI-LINK™ Stent is fabricated from medical grade 316L stainless steel tubing, which conforms to ASTM F-138-92 Grade 2, in both the chemical analysis and the inclusion/impurity content. The two tests used to determine the chemical content of the stainless steel tubing are ASTM E1086, which detects all elements except nitrogen and in some instances carbon, and ASTM E1019, which detects nitrogen and carbon. The minimum grain size that is accepted in the ACS MULTI-LINK™ Stent tubing will be greater than or equal to ASTM 7.0, which is measured in accordance with ASTM E112. The chemical analysis of the ACS MULTI-LINK™ Stent met the product specifications.

##### 9.3.1.2 Scanning Electron Microscopy (SEM) Analysis:

SEM analysis was conducted to identify and analyze trace surface contaminants, that may be contained in the tubing used to fabricate the ACS MULTI-LINK™ Stent. Samples of tubing were processed according to the manufacturing process instructions and visualized with the SEM. Particulates (if any) were analyzed using an electron dispersive x-ray (EDX). The size and quantity of the particles evaluated do not exceed USP requirements for small volume injections. The SEM analysis of the ACS MULTI-LINK™ Stent met the product specifications.

##### 9.3.1.3 Yield Strength and Elongation:

The tensile strength and elongation test was performed to determine the yield strength and percent elongation of the ACS MULTI-LINK™ Stent tubing. These tests were conducted in accordance with ASTM E345, “Standard Test Methods of Tension Testing of Metallic Foil.” The yield strength and elongation of the ACS MULTI-LINK™ Stent met the product specifications.

##### 9.3.1.4 ASTM Conformance:

The ACS MULTI-LINK™ Stent 316L stainless steel tubing conforms to ASTM F-138-92 Grade 2. To ensure compliance with ASTM F-138-92 Grade 2, the 316L stainless steel tubing is also tested to or required to meet the following ASTM Standards:

**Table 4. ACS MULTI-LINK™ Stent - ASTM Conformance**

ASTM Standard	Title
A751	Practices and Terminology for Chemical Analysis of Steel Products
E1086	Standard Method for Optical Emission Vacuum Spectrometric Analysis of Stainless Steel by the Point to Plane Excitation Technique
E112	Standard for Determining Average Grain Size
A262 Method A & E	Practices for Detecting Susceptibility to Inter-granular Attack in Austenitic Stainless Steel

ASTM Standard	Title
E1019	Standard Test Method for Determination of Carbon, Sulfur, Nickel and Cobalt Alloys
G5-87	Standard Reference Test Method for Making Potentiostatic and Potentiodynamic Anodic Polarization Measurements
F86-84	Standard Practice for Surface Preparation and Marking of Metallic Surgical Implants
G15-93	Terminology Relating to Corrosion and Corrosion Testing
G102-89	Practice for Calculation of Corrosion Rates and Related Information from Electrochemical Measurements

The ACS MULTI-LINK™ Stent met requirements of the aforementioned ASTM Standards.

### 9.3.2 Stent Integrity Testing

#### 9.3.2.1 Corrosion

The corrosion test was conducted to determine the susceptibility of the ACS MULTI-LINK™ Stent to corrosion and pitting under potentiodynamic conditions. Stent samples were placed in an electrolyte solution buffered to a physiological pH and heated to nominal blood temperature. The corrosion test generated a cyclic anodic polarization curve and a cathodic polarization curve, which were used for the analysis of corrosion susceptibility. Faraday's law was used to calculate the corrosion rates. The corrosion resistance of the ACS MULTI-LINK™ Stent met the product specifications.

#### 9.3.2.2 Dimensions

The dimension test was used to evaluate the dimensions of the ACS MULTI-LINK™ Stent. Samples were measured for stent strut width and thickness. All measurements were made under 500x magnification. The dimensions of the ACS MULTI-LINK™ Stent met the product specifications.

#### 9.3.2.3 Stent-Free Area Percentage

The stent-free area percentage was found by subtracting the area of the ACS MULTI-LINK™ Stent from the total stented vessel area, and then divided by the total stented vessel area. The stent-free area percentage of the ACS MULTI-LINK™ Stent met the product specifications.

#### 9.3.2.4 Length Change

The length change test determined the percent shortening of the ACS MULTI-LINK™ Stent when expanded to the nominal diameter. Each stent was measured to 0.001 mm resolution prior to and after expansion in tubing and in air. The length change of the ACS MULTI-LINK™ Stent met the product specifications.

#### 9.3.2.5 Uniformity of Expansion

The uniformity of expansion test measured the uniformity of the ACS MULTI-LINK™ Stent along its length after balloon expansion in tubing. Uniformity was defined as the mean outer diameter plus or minus the standard deviation at five locations along the length of the stent (proximal, mid, distal) after balloon expansion. The ACS MULTI-LINK™ Stent expanded uniformly and maintained this uniformity upon withdrawal of the balloon. The uniformity of expansion of the ACS MULTI-LINK™ Stent met the product specifications.

#### **9.3.2.6 Recoil**

The recoil test determined the percent recoil of the ACS MULTI-LINK™ Stent after balloon expansion. The stent outer diameter was measured using a LASER Micrometer with and without the expanded balloon in place and the percentage was calculated. The recoil of the ACS MULTI-LINK™ Stent met the product specifications.

#### **9.3.2.7 Compression - Stiffness (Flat Plate Test)**

The flat plate compression test determined the resistance of the ACS MULTI-LINK™ Stent after expansion to a compressive force which simulated an eccentric load. The resultant force using an Instron was measured for each loss in diameter and a stiffness curve of load verses displacement was generated. Using the curve generated from the Instron the yield point was determined and used to calculate the elastic modulus, or stiffness, based on the linear regression of the initial displacement to the yield point. The stiffness of the ACS MULTI-LINK™ Stent met the product specifications.

#### **9.3.2.8 Compression - Radial Strength (Pressure Vessel)**

The pressure vessel compression test was used to determine the hoop strength of the ACS MULTI-LINK™ Stent. The stent is expanded in tubing which is then placed in the pressure vessel fixture which radially compresses the stent. The pressures at which the stent irreversibly deformed and fully collapsed were measured. The radial (hoop) strength and irreversible deformation of the ACS MULTI-LINK™ Stent met the product specifications.

#### **9.3.2.9 Accelerated Fatigue**

The accelerated fatigue test was performed to determine the fatigue resistance of the ACS MULTI-LINK™ Stent. Stents were tested for 380 million cycles in a physiologically simulated environment under accelerated conditions. Three hundred and eighty million cycles approximates a ten year fatigue resistance with an assumed heart rate of 72 beats per minute. The ACS MULTI-LINK™ Stent met the 10 year accelerated fatigue resistance requirement of the product specifications.

#### **9.3.2.10 Finite Element Analysis (FEA)**

The FEA evaluated the structural integrity of the ACS MULTI-LINK™ Stent. The simulation was a finite element analysis of the stent subjected to expected load conditions generated in coronary arteries. The analysis took into account static and fatigue loadings at nominal balloon expansion, and ten year radial contractive fatigue cycling for stents with and without “flaws”. The ACS MULTI-LINK™ Stent met the FEA requirement of the product specifications.

#### **9.3.2.11 Magnetic Resonance Imaging (MRI)**

The ACS MULTI-LINK™ Stent is fabricated from 316L stainless steel tubing which has a high nickel content that helps to stabilize iron in a nonmagnetic state thereby diminishing magnetic susceptibility. In addition, to prevent “black hole” artifacts, the Instructions for Use (IFU) booklet includes a WARNING against performing an MRI within eight weeks of stent implantation. The actual WARNING is as follows:

“An MRI scan should not be performed on patients post-stent implantation until the stent has completely endothelialized (eight weeks) to minimize any potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field”.

### **9.3.3 Stent and Delivery System Testing**

#### ***9.3.3.1 Delivery System Profiles and Lengths***

The Delivery System profiles and lengths test was performed to determine the profile and length measurements of the four models of the ACS MULTI-LINK™ CSS. Tests specific to a particular model are indicated in parentheses. The following profiles and lengths were measured:

##### **9.3.3.1.1 Distal retractable sleeve profile (ACS MULTI-LINK™ CSS)**

The diameter of the distal portion of the retractable sleeve, distal to the sleeve junction using a LASER micrometer.

##### **9.3.3.1.2 Proximal retractable sleeve profile (ACS MULTI-LINK™ CSS)**

The diameter of the proximal portion of the retractable sleeve, proximal to the sleeve junction using a LASER micrometer.

##### **9.3.3.1.3 Retractable sleeve junction profile (ACS MULTI-LINK™ CSS)**

The diameter of the retractable sleeve proximal/distal junction using a LASER micrometer.

##### **9.3.3.1.4 Crossing profile (ACS MULTI-LINK™ CSS)**

The diameter of the distal flared tip of the retractable sleeve measured using a LASER micrometer.

##### **9.3.3.1.5 Crimped stent outer diameter (OD)**

The diameter of the crimped stent on a balloon with the elastic membrane using a LASER micrometer

##### **9.3.3.1.6 Delivery System Tip outer diameter (OD)**

The diameter of the Delivery System tip including the elastic membrane using a LASER micrometer.

##### **9.3.3.1.7 Balloon with elastic membrane collapsed profile**

The smallest hole in a profile gage block through which one half of the collapsed balloon with elastic membrane passes without resistance.

##### **9.3.3.1.8 Balloon with elastic membrane working length**

The length from shoulder to shoulder of the balloon when expanded to 120 psi (8 atm) measured using a ruler with 0.5 mm resolution.

##### **9.3.3.1.9 Elastic membrane junction outer diameter (OD)**

The diameter of the elastic membrane and distal shaft integrated junction using a digital snap gauge

The profiles and lengths of all models of the ACS MULTI-LINK™ CSS met the product specifications.

#### ***9.3.3.2 Catheter Preparation Test***

The catheter preparation test was performed to evaluate the ease of preparing the four models of the ACS MULTI-LINK™ CSS using the double-negative aspiration method and 60% contrast diluted 1:1 with water. The Delivery System was first aspirated for 30 seconds and repeated until

air was no longer noted in the syringe. The double-negative aspiration method adequately prepares all models of the ACS MULTI-LINK™ CSS.

#### ***9.3.3.3 Retractable Sleeve Flush Test (ACS MULTI-LINK™ CSS)***

The retractable sleeve flush test was performed to evaluate the ease of flushing the retractable sleeve and removing air from the inner chamber of the handle of the ACS MULTI-LINK™ CSS using the procedure outlined in the Instructions for Use booklet. The retractable sleeve was flushed using a syringe filled with saline. The same syringe was used to remove air from the inner chamber of the handle. The retractable sleeve flush test of the ACS MULTI-LINK™ CSS met the product specifications.

#### ***9.3.3.4 Inflation and Deflation Times Test***

The inflation and deflation times test was performed to determine the inflation and deflation times of the four models of the ACS MULTI-LINK™ CSS. The Delivery System was inflated to the rated burst pressure and the inflation time was recorded. The Delivery System was then deflated, and the deflation time was recorded. The inflation and deflation time readings were averaged for each sample. The inflation / deflation times of all four models of the ACS MULTI-LINK™ CSS met the product specifications.

#### ***9.3.3.5 Catheter Bend Integrity Test***

The catheter bend integrity test was performed to determine the bend integrity and stent movement of the four models of the ACS MULTI-LINK™ CSS. The Delivery System was inserted into an rotating hemostatic valve and a guiding catheter until the distal 10 cm of the Delivery System extended beyond the distal tip of the guiding catheter. The Delivery System was then retracted into the guiding catheter. The last two steps were repeated for a specified number of times. At the end, the system was removed from the guiding catheter and inspected for damage. The catheter bend integrity of all four models of the ACS MULTI-LINK™ CSS met the product specifications.

#### ***9.3.3.6 Balloon Rupture, Inner Member Collapse and Stent Compliance Test***

The balloon rupture, inner member collapse and stent compliance test determined the balloon rupture pressure, inflation pressure at which the inner member collapsed, and the inflation pressure/stent diameter relationship of the four models of the ACS MULTI-LINK™ CSS. The Delivery System was inflated incrementally until failure. During this portion of the test, guide wire movement was inspected and inner member collapse was indicated by the restriction of the guide wire movement. The stent outer diameter was measured at each programmed pressure, and the correlation between the inflation pressure and stent outer diameter was determined.

The data analysis indicated with 95% confidence, 99.9% of the balloons will not rupture at or below their rated burst pressure (RBP). No inner member collapses were observed and the stent diameters did not significantly distend with increasing inflation pressures. The balloon rupture pressures (rated burst pressures), inner member collapse and stent compliance of all four models of the ACS MULTI-LINK™ CSS met the product specifications.

#### ***9.3.3.7 Catheter Shaft and Adaptor Maximum Pressure Test***

The catheter shaft and adaptor maximum pressure test determined the pressure integrity of the shaft of the four models of the ACS MULTI-LINK™ CSS. The shafts were pressurized from 0

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psi until failure. The catheter shaft and adaptor maximum pressures of all four models of the ACS MULTI-LINK™ CSS met the product specifications.

#### **9.3.3.8 Junction Pull Test (ACS MULTI-LINK™ CSS)**

The junction pull test determined the tensile strengths of the junctions between the elastic membrane and the distal shaft, the proximal and distal portions of the retractable sleeve, and the proximal and distal portions of the base catheter shaft of the ACS MULTI-LINK™ CSS. All junctions were pulled until failure using an Instron. The junction pull strengths of the ACS MULTI-LINK™ CSS met the product specifications.

#### **9.3.3.9 Elastic Membrane Integrated Junction Shear Strength Test**

The elastic membrane integrated junction shear strength test determined the maximum force exerted (shear strengths) on the junction between the elastic membrane and the distal shaft. The Delivery Systems were pulled through a small diameter ring using an Instron. The elastic membrane junction shear strength of all four models of the ACS RX MULTI-LINK™ CSS met the product specifications.

#### **9.3.3.10 Delivery System In-Stent Balloon Fatigue Test**

The Delivery System In-Stent Balloon Fatigue Test was performed to determine whether the balloon will sustain repeated inflations inside the stent without failure. The Delivery System was pressurized to expand the stent in Tecoflex tubing, and then deflated. A pressure tester was then used to perform subsequent inflations inside the stent. The Delivery System in-stent fatigue of all models of the ACS MULTI-LINK™ CSS met the product specifications.

### **9.3.4 Package Integrity Testing:**

The package integrity testing for the ACS MULTI-LINK™ CSS and the four Delivery Systems was completed on the ACS MULTI-LINK™ CSS and the ACS RX MULTI-LINK™ CSS. This testing was representative of all four packages since the packaging of the ACS RX MULTI-LINK™ CSS, the ACS RX MULTI-LINK HP™ CSS and the ACS OTW MULTI-LINK HP™ CSS are identical.

Packaged devices were exposed to one EtO sterilization cycle with a 72 hour aeration period and then exposed to a transportation simulation. The transportation simulation testing was performed in accordance with the International Safe Transit Association, Preshipment Test Procedure 1A. This testing included a vibration and drop test and environmental conditioning that included exposure to excessive heat and cold cycles. Subsequently the package integrity was tested as follows:

#### **9.3.4.1 Package Leak Test**

The package leak test was used to verify the integrity of the package seal. The sterilized package was pressurized and submerged in water. If the package seal was poor or broken air bubbles would be noticed leaking from the package at a constant rate.

#### **9.3.4.2 Package Seal Strength**

The package seal strength test was used to verify the strength of the package seal. This test was conducted using a tensile tester in accordance with the American Society for Test Materials, D903 guidance document.

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### 9.3.4.3 Microbial Challenge

The microbial challenge test was conducted in accordance with the Microbial Challenge test protocol published by North American Science Associates (NAmsA), a contract test laboratory. The package containing the sterilized device was challenged in a chamber with talcum powder containing  $10^6$  bacterial spores. After the challenge phase was complete, the outside of the package was disinfected and the device was tested for sterility. The presence of a sterile culture indicated that the sterile barrier of the package was not compromised.

The package integrity testing demonstrated that the packaging of the ACS MULTI-LINK™ Stent and the four Delivery Systems met the product specifications.

### 9.3.5 Shelf-Life (Aging) Testing

Shelf-Life testing was conducted on the ACS MULTI-LINK™ Stent and the four Delivery Systems. The test protocol required the packaged devices to first undergo the package integrity test protocol outlined in section 4.0 above. The test units were then exposed to environmental aging conditions including temperature and relative humidity and then tested for functional performance characteristics in addition to the package integrity tests. Based on the acceleration factor used the shelf-life of the devices was determined as follows:

**Table 5. ACS MULTI-LINK™ Stent / Four Delivery Systems -- Shelf-Life**

Product Name	Self-Life
ACS MULTI-LINK™ Coronary Stent System	1 year
ACS RX MULTI-LINK™ Coronary Stent System	2 years
ACS RX MULTI-LINK HP™ Coronary Stent System	1 year
ACS OTW MULTI-LINK HP™ Coronary Stent System	3 months <sup>1</sup>

<sup>1</sup> = The shelf-life of the ACS OTW MULTI-LINK HP™ CSS will be extended in the future based upon testing conducted to the identical protocol.

## 10. Summary of Clinical Studies

The ACS MULTI-LINK™ Stent was evaluated in five multicenter studies which enrolled a total of 1593 patients for the treatment of symptomatic coronary artery disease in *de novo* lesions or in restenosed vessels. Of these, 1073 patients received either the ACS MULTI-LINK™, the ACS RX MULTI-LINK™, or the ACS RX MULTI-LINK HP™ Stent, and 520 patients received the Palmaz-Schatz® Stent. Initial testing of the stent in two studies (West I and (West II) was performed in Europe from 1993-1996. Acceptable acute procedure success, subacute thrombosis, 30-day major adverse cardiac event (MACE) and six month target vessel failure (TVF) rates were noted in these studies. In 1995, the stent was approved in Europe for general clinical use. In addition to the original over-the-wire (OTW) Delivery System, three other Delivery Systems were developed. These systems are a rapid exchange (RX) system with the stent mounted on a standard balloon, an RX system with the stent mounted on a high pressure (HP) balloon, and an OTW system with the stent mounted on an HP balloon. Standard stent technique currently includes a percutaneous transluminal coronary angioplasty (PTCA) catheter exchange for a PTCA catheter with an HP balloon after initial stent deployment. The HP balloon is used to optimize final stent deployment. Mounting the stent directly on an HP balloon has the advantage of eliminating a PTCA catheter exchange since both initial deployment and final

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optimization of deployment can be accomplished with the same balloon. The specific studies are discussed in the following sections.

### **10.1 Gender Bias**

To determine whether gender bias had occurred during the clinical studies, the ratio of women to men treated in the ACS MULTI-LINK™ Stent groups was compared to that of the control group. There were no significant baseline differences in patient characteristics between the groups in any of the studies. This includes percent of males and females, age, incidence of diabetes, and hypertension. The Restenosis Study did have more patients who were hyperlipidemic requiring medication and who had prior myocardial infarctions. The Rapid Exchange/Longer Length Study had more patients with Canadian Cardiovascular Scale (CSS) Class III and IV angina. For the Rapid Exchange/High Pressure balloon study, small differences existed in the incidence of diabetes, hypertension and hyperlipidemia. Statistical analysis of the clinical data did not show an association between gender and the primary or secondary clinical outcomes.

### **10.2 Statistical Analyses**

#### **10.2.1 Analysis Population**

The primary effectiveness endpoint of TVF was reviewed on an intent-to-treat basis. Patients were analyzed according to the assigned randomized treatment and regardless of the subsequent sequence of events. Those patients who met eligibility requirements for the primary endpoint included all patients randomized who were not deregistered and who were available for angiographic or clinical follow-up.

#### **10.2.2 Determination of Treatment Group Equivalency**

All clinically relevant baseline variables were tabulated and compared between the two treatment arms. Categorical variables were tested using appropriate contingency table analyses (exact or chi-square approximations), and continuous variables were tested using unpaired Student's t-test or Wilcoxon rank-sum test, depending on variable distribution.

#### **10.2.3 Determination of Safety and Effectiveness**

The primary and secondary restenosis endpoints were tested using exact contingency table analyses for binary incidence rates (angiographic restenosis, target vessel-related revascularization or failure), or combined non-specific late ischemic endpoints. Coronary restenosis measures by late absolute minimum lumen diameter (MLD) and late percent diameter stenosis was tested using Student's t-test or the Wilcoxon signed-rank test. The incidence of acute and late complications between the ACS MULTI-LINK™ Stent and the control Palmaz-Schatz® Stent arms was tested using chi-square.

#### **10.2.4 Secondary Endpoint Analyses**

Secondary endpoint testing and subgroup hypothesis testing used identical hypothesis testing procedures as in the primary endpoint analysis. Beyond these simple comparisons, sophisticated statistical models (multivariate regression and multivariate survival analysis, and Kaplan-Meier survival analysis), were used to explore the unique advantages of the ACS MULTI-LINK™ Stent, such as mechanisms of action, and effect, or lack of effect, on late patient outcomes. The analyses included:

- Multivariable and multivariate techniques (linear, logistic, general linear modeling, cubic spline modeling, or multiple outcome analysis)
- Failure-time model analyses (Cox proportional hazards regression, parametric and non-parametric survival analysis, competing risks analysis)

#### 10.2.5 The ASCENT Study

For the ASCENT Study, the original proposed sample size of 1040 patients that was calculated with the Blackwelder formula employed the following assumptions:

1. The null hypothesis was that the ACS MULTI-LINK™ Stent would have a *greater* target vessel failure rate than the Palmaz-Schatz® Stent.
2. Rejection of the null hypothesis would signify that the ACS MULTI-LINK™ Stent had an *equivalent or lower* target vessel failure rate than the Palmaz-Schatz® Stent.
3. The nine month clinical target lesion revascularization rate of the control Palmaz-Schatz® Stent and the ACS MULTI-LINK™ Stent would be approximately 20%.
4. The definition of equivalency was based on a delta of  $\pm 7.5\%$ .
5. The power of the study was 90%.
6. The alpha error was 5%.

In follow-up correspondence between FDA and the sponsor it was agreed that the PMA submission could be powered at 80% allowing for a 720 patient sample size. The PMA presents acute data for the 1040 patient cohort with *de novo* lesions.

The randomized, prospective, multi-center design, and the use of selected clinical markers (i.e. recurrent symptoms or a positive functional study for recurrent ischemia) allowed for a critical evaluation of the restenosis endpoint. A clinical events committee (CEC) blinded to treatment assignment adjudicated all major events including death, non-fatal myocardial infarction, and target vessel revascularization. Participating investigators were not included on this committee. The primary clinical restenosis endpoint, and all secondary endpoints were analyzed on an intent-to-treat basis. Multivariable modeling was applied to acute and late term patient data to determine predictors of restenosis.

Univariate and stepwise logistic regression modeling of TVF were performed. Stepwise logistic regression modeling indicated that post-procedure MLD was the only significant independent predictor of TVF. Randomized treatment assignment was not a significant predictor after adjusting for post-procedure MLD.

#### 10.2.6 Power Estimates for the Restenosis Study

Using the standard calculation methods for required sample size with an alpha of 5% as described by Fleiss (“Statistical Methods for Rates and Proportions”) for equal sized arms, yielded a required sample size of 118 patients per arm or a total of 236 patients. This led to an initial sample size of 113 in order to achieve at least 90% power. Since the *de novo* lesion randomized comparison arm of the ASCENT Study enrolled 520 patients, the resulting power was greater than 90%. The estimated sample size of 201 patients enrolled in the Restenosis Study allowed for additional discrimination ability. These sample size estimates were based on the presumptive use

of a two-tailed test, at the 5% level of the difference between independent proportions, using Gaussian distribution. A traditional approach to the statistical testing was employed since the operating characteristics of the Blackwelder approach for this situation have not been theoretically determined.

### **10.3 Feasibility Study**

#### **10.3.1 Objectives**

The feasibility study was performed prior to initiation of the randomized study and was conducted under an approved investigational device exemptions (IDE) application and used the ACS MULTI-LINK™ Stent with an OTW Delivery System. This was a non-randomized multi-center (3) study of 49 *de novo* and restenotic native coronary artery lesions in reference vessels of 3.0 to 3.5 mm in diameter and  $\leq 12$  mm in length, in which all patients underwent stent deployment at 8 atm with the Delivery System, and mandatory serial post-deployment dilatations at 12 and 16 atm. Angiographic and intravascular ultrasound imaging were used to track the response of the stent. A secondary endpoint, TVF (defined as a composite of death, non-fatal myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass graft surgery (CABG), and repeat PTCA), was assessed at 30 days and 12-14 months post-procedure. Post-stent placement anti-platelet therapy included aspirin 325 mg/day for up to one year and Coumadin to maintain an International Normalized Ratio (INR) at 1.5 for 30 days.

#### **10.3.2 Results**

The mean reference artery diameter was  $3.18 \pm 0.49$  mm. The MLD was  $1.24 \pm 0.46$  which corresponded to a per cent diameter stenosis of  $61 \pm 13\%$  diameter stenosis. The MLD increased to  $2.49 \pm 0.42$  mm ( $22 \pm 11\%$  stenosis) following stent deployment at 8 atm. The maximum MLD was  $2.98 \pm 0.28$  representing a residual stenosis of  $6.9 \pm 9.4\%$  after balloon dilatation at 16 atm. Intravascular ultrasound indicated that intrastent dimension (as assessed by lumen area through tightest stent spot and per cent expansion [lumen cross sectional area stent/lumen cross sectional area reference vessel]) progressively increased as balloon inflation pressure increased from 8 atm to 16 atm. No unexpected complications were detected with serial ultrasonic imaging of the stents.

This study documented a significant increase in intra-stent dimensions at 16 atm with no abrupt closure. Device delivery success and procedural success were achieved in 100% and 98% of patients respectively. There was a 2.0% incidence of post-stent MACE over a one year follow-up period. The study supports the value of high pressure deployment and showed no major problems with the acute mechanical and clinical performance of the stent. On the basis of this pilot study and the European data the sponsor chose to initiate a randomized study.

### **10.4 The Randomized Clinical Study (ACS MULTI-LINK™ Stent vs. Palmaz-Schatz® Stent)**

#### **10.4.1 Objectives**

A total of 1,040 patients were enrolled in the multicenter (n=59) ASCENT study. Patients with *de novo* native coronary artery lesions were randomized equally in a parallel comparison, to demonstrate equivalence between the ACS MULTI-LINK™ Stent (n=520) using an OTW Delivery System, and the Palmaz-Schatz® Stent (n=520).

### 10.4.2 Study Design

Eligible patients, with angina or positive functional study, were identified for elective stenting of a *de novo* native coronary artery lesion < 20 mm in length which would be covered by up to two 15 mm stents. These patients underwent standard PTCA after which a stent Delivery System of the appropriate size was advanced and deployed.

The anticoagulation regimen administered was aspirin 325 mg/day for at least one year and ticlopidine 250 mg bid for at least 30 days. At the discretion of the investigator, alternative therapy was allowed for non-optimal results which were defined as > 2 stents deployed, > 20% residual stenosis, any residual dissection, poor distal runoff or the presence of thrombus.

Follow-up intervals were 2, 4, and 6 weeks and 6, 9, and 12 months. The study randomization was successful as both treatment groups were demographically equivalent. All randomized patients were included in the intent-to-treat efficacy analysis. The primary endpoint was six month TVF.

### 10.4.3 Description of Patients

There were no baseline differences in patient characteristics between the two groups (Table 5). The mean age of the pooled population was 61±11 years, and 68% of the population was male. Nineteen per cent of the patient population had diabetes mellitus, 53% had hypertension requiring treatment, and 29% had hyperlipidemia requiring medical intervention. Previous cardiovascular events included myocardial infarction in 37% of patients, CABG in 7% of patients, and prior target vessel PTCA in 3% of patients. Seventy per cent had CCS Class III or IV angina, 91% had unstable angina, and 46% had a positive functional study demonstrating ischemia.

Baseline angiography did not reveal any differences between the two groups. Seventy-one per cent of patients had single vessel disease, and the mean left ventricular ejection fraction was 56±12%.

**Table 6. ASCENT Study Demographics**  
All Patients Enrolled in the ASCENT Study, N = 1040

	ACS Multi-Link Stent	Palmaz-Schatz Stent	95% CI of Difference
Number Treated	520	520	
Per cent receiving assigned stent	98.5%	96.3%	Calculate
% Male	67%	69%	-8.0, 3.4%
% Diabetic	19%	20%	-5.2, 4.4%
Hypertension	53%	54%	-7.6, 4.6%
Hyperlipidemia	28%	29%	-5.8, 5.3%
Age (yr)	61 ± 11	61 ± 11	-1.34, 1.34
Reference vessel diameter (mm)	2.96 ± 0.49	2.97 ± 0.47	-0.07, 0.05
% DS pre procedure	64 ± 13%	65 ± 13%	-2.5, 0.7%
MLD (mm) pre procedure	1.06 ± 0.40	1.04 ± 0.41	-0.03, 0.07

#### 10.4.4 Results

Device delivery success was achieved in 97.4% and 96.8% of ACS MULTI-LINK™ Stent and the Palmaz-Schatz® Stent patients respectively while procedural success was achieved in 95.2% and 92.8% of ACS MULTI-LINK™ Stent and the Palmaz-Schatz® Stent patients respectively. There was a clinically significant higher incidence of subacute thrombosis in the Palmaz-Schatz® Stent group, 1.9% (10/520) vs. 0.6% (3/520). Six Palmaz-Schatz® Stent patients who suffered subacute thrombosis died within 30 days of stenting giving rise to a significantly higher acute death rate; 1.2% vs. 0%, p=0.02. The six-month MACE rate of 12.7% vs. 16% favored the ACS MULTI-LINK™ Stent, as did the nine month restenosis rate of 15.6% vs. 20.5%.

This study was performed using high pressure balloon inflation to optimize stent deployment when necessary; and with aspirin and ticlopidine, rather than aspirin and coumadin, as the recommended anticoagulation regimen. As a consequence of these changes in stenting technique, the rates of stent thrombosis, bleeding, and vascular complications are lower than rates previously reported in the literature for the original Palmaz-Schatz® Stent study.

The Randomized Study documented equivalence between the ACS MULTI-LINK™ Stent and the Palmaz-Schatz® Stent for the primary variable of TVF (12.3% vs. 13.1%).

Table 7 presents the principal effectiveness and safety results for the Randomized Study.

**Table 7. Principal Effectiveness and Safety Results - Randomized Study**  
Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)  
All Patients Treated (n=1040)

Effectiveness Measures	ACS MULTI-LINK (n=520)	Palmaz-Schatz (n=520)	Difference
Device Success by QCA	97.4% [95.6%, 98.6%] (483/496)	96.8% [95.3%, 98.4%] (482/498)	0.6% [-1.5%, 2.7%]
Procedure Success by QCA	95.2% [92.9%, 96.9%] (472/496)	92.8% [90.1%, 94.9%] (462/498)	2.4% [-0.6%, 5.3%]
In-Stent % DS post procedure, mm*	8 ± 11% [-39%, 42%] (482/520)	10 ± 12% [-34%, 100%] (485/520)	-1.7%* [-3.1%, -0.2%]
In-Stent % DS at 9 month follow-up	32 ± 20% [-16%, 100%] (192/271)	34 ± 20% [-11%, 100%] (171/263)	-2.2% [-6.3%, 1.9%]
In-Stent Restenosis Rate (9 mo)	15.6% [13.5%, 25.0%] (30/192)	20.5% [14.7%, 27.3%] (35/174)	-4.5% [-12.4, 3.4%]
Target Site Revascularization Free (6 mo. K-M)	93.8 % [91.4%, 96.2%]	93.3% [90.9%, 91.4%]	0.5% [-2.6%, 3.5%]
Target Vessel Failure Free (6 mo. K-M)	87.7% [84.8%, 90.6%]	86.9% [84.0%, 89.8%]	0.8% [-3.3%, 4.9%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.8% [3.1%, 7.0%] (25/520)	6.0% [4.1%, 8.4%] (31/520)	-1.2% [-3.9%, 1.6%]
Out-of Hospital Clinical Event Rate	8.3% [6.0%, 11.0%] (43/520)	10.2% [7.7%, 13.1%] (53/520)	-1.9% [-5.4%, 1.6%]
Bleeding Complication Rate	0.8% [0.2%, 2.0%] (4/520)	1.3% [0.5%, 2.8%] (7/520)	-0.6% [-1.8%, 0.7%]
Vascular Event Rate	1.5% [0.7%, 3.0%] (8/520)	3.3% [1.9%, 5.2%] (17/520)	-1.7% [-3.6%, 0.1%]
Subacute Thrombosis Rate	0.6% [0.1%, 1.7%] (3/520)	1.9% [0.9%, 3.5%] (10/520)	-1.3% [-2.7%, 0.0%]
Survival at 30 days (K-M) *	100.0% [99.4%, 100.0%]	98.8% [97.8%, 99.8%]	1.2%* [0.2%, 2.1%]
Survival at 180 days (K-M)	99.4% [98.8%, 100.0%]	98.0% [96.8%, 99.2%]	1.3% [0.0%, 2.7%]
MACE Rate at 6 months	12.7% [10.0%, 15.9%] (66/520)	16.0% [12.9%, 19.4%] (83/520)	-3.3% [-7.5%, 1.0%]
Hospitalization Post-Intervention (days)	1.6 ± 1.6 [1.0, 18] (520/520)	1.7 ± 2.4 [1.0, 32] (520/520)	-0.01 [-0.34, 0.15]

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**Table 7 Definitions:**

- *Device success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device alone (i.e. without the use of other types of stents or new balloon devices).*
  - *Procedure Success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device and any adjunctive device without death, coronary artery bypass surgery (CABG), or myocardial infarction (Q-wave or non-Q-wave) within seven days of the procedure.*
  - *QCA = Quantitative coronary angiography*
  - *% DS = percent diameter stenosis by QCA.*
  - *Target Vessel Failure Free (TVF) = The composite of acute and late-term major events of death, CABG, Q-wave MI or non-Q-wave MI, and percutaneous transluminal coronary angioplasty (PTCA) attributable to the target vessel. (K-M = actuarial freedom-from TVF by Kaplan Meier survival analysis).*
  - *Target Site Revascularization Free (TSR) = Repeat PTCA or CABG to the original site of intervention. (K-M = actuarial freedom-from TSR by Kaplan Meier survival analysis).*
  - *MACE = Major Adverse Cardiac Event of death, Q-wave MI or non-Q-wave MI, CABG, or PTCA to the treated site.*
  - *In-Hospital Clinical Event = Any MACE occurring prior to hospital discharge.*
  - *Out of Hospital Clinical Event = Any MACE occurring from hospital discharge through up to one year of clinical follow-up.*
  - *Bleeding Complication = Blood loss necessitating a transfusion.*
  - *Vascular Event = Any hematoma > 5 cm, arteriovenous fistula, pseudoaneurysm, retroperitoneal bleed, peripheral nerve disorder and surgical repair.*
  - *Subacute Thrombosis = Any cardiac death, subacute closure requiring revascularization of the target site or total closure indicated by QCA within 30 days of the index intervention.*
- \* = difference is statistically significant, p-value < 0.05 (2-tailed) based on t-test or Chi-square analysis as appropriate.

**10.4.5 Survival Analysis**

Table 8 presents the Kaplan Meier Survival Analysis for those patients who were TVF free as determined by angiography. Six month follow-up data was obtained on 842 patients, and 9 month follow-up was completed on 593 patients.

**Table 8. Freedom from Target Vessel Failure - All Randomized Patients**  
difference [95% CI] of 0.8%[-3.3%, 4.9%]

	Time after initial procedure (days)									
	0	7	14	30	60	90	120	180	210	270
<b>ACS MULTI-LINK™</b>										
# At risk	513	492	490	490	469	455	448	418	388	295
# Events	7	26	28	28	29	40	45	62	65	74
% Survived	98.7%	95.0%	94.6%	94.6%	94.4%	92.2%	91.2%	87.7%	87.0%	84.8%
SE	0.5%	1.0%	1.0%	1.0%	1.0%	1.2%	1.3%	1.5%	1.5%	1.6%
<b>Palmaz-Schatz®</b>										
# At risk	506	484	482	482	469	458	450	424	390	298
# Events	14	36	38	38	39	47	54	68	73	84
% Survived	97.5%	93.3%	92.9%	92.9%	92.7%	91.1%	89.7%	86.9%	85.8%	83.0%
SE	0.7%	1.1%	1.1%	1.1%	1.1%	1.3%	1.3%	1.5%	1.6%	1.7%

**Tests Between Groups**

Test	Chi-Square	Deg Frdm	P-value
Log-Rank	1.37	1	0.24
Wilcoxon	1.38	1	0.24

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#### 10.4.6 Stent Delivery Failures

There were 39 stent delivery failures as follows: Palmaz-Schatz® Stent (4.4% or 23/520), ACS MULTI-LINK™ Stent (3.1% or 16/520). A classification of reasons for stent delivery failures (i.e. failure to deliver first stent, balloon rupture, misplacement, stent defective etc..) was performed. There were no obvious differences between the two groups. The assigned stent was ultimately implanted in 98.5% (n=8) of the ACS MULTI-LINK™ Stent patients and 96.3% (n=19) of the Palmaz-Schatz® Stent patients. There were 12 cases of post-deployment dilation in which balloon rupture occurred; 1.7% (9/581) of stents deployed in the Palmaz-Schatz® Stent group and 0.5% (3/587) of stents deployed in the ACS MULTI-LINK™ Stent group. Additionally, there were 11 cases of contained (non-tamponade) vessel perforation; 2.0% (10/494) in the Palmaz-Schatz® Stent group and 0.2% (1/491) in the ACS MULTI-LINK™ Stent group.

#### 10.4.7 Long Term Results

##### 10.4.7.1 Deaths

There were 23 patient deaths. Fifteen (2.9%) occurred in the Palmaz-Schatz® Stent group and 8 (1.5%) occurred in the ACS MULTI-LINK™ group. There were 6 early deaths in the Palmaz-Schatz® Stent group as a result of subacute thrombosis. There were no early deaths in the ACS MULTI-LINK™ group. Each death was summarized in the PMA Clinical Report and additional information was included in the PMA. Review of this information did not reveal any unexpected findings.

##### 10.4.7.2 Myocardial Infarctions

A total of 9 patients had a Q-wave MI: 6 (1.2%) for the Palmaz-Schatz® Stent group and 3 (0.6%) for the ACS MULTI-LINK™ group. A total of 45 patients had non-Q-wave MI, 24 (4.6%) in the Palmaz-Schatz® Stent group and 21 (4.0%) in the ACS MULTI-LINK™ group. Each myocardial infarction was summarized in the PMA Clinical Report and additional information was included in the PMA. Review of this information did not reveal any unexpected findings.

##### 10.4.7.3 Revascularization Procedures

*CABG or Repeat PTCA:* A total of 26 patients underwent CABG, 11 (2.1%) in the Palmaz-Schatz® Stent group and 15 (2.9%) in the ACS group. A total of 89 patients underwent repeat PTCA, 49 (9.4%) in the Palmaz-Schatz® Stent group and 40 (7.7%) in the ACS MULTI-LINK™ group. The cumulative revascularization rates over time were also similar between the two groups. Each CABG and repeat PTCA was summarized in the PMA Clinical Report and additional information was included in the PMA. Review of this information did not reveal any unexpected findings.

#### 10.5 Non-Randomized Restenosis Study

##### 10.5.1 Objectives

A 201 patient non-randomized group comparing the ACS MULTI-LINK™ Stent in restenotic lesions was conducted in parallel to the randomized study with the *a priori* intention of using the 520 patient randomized *de novo* ACS MULTI-LINK™ Stent population as a control group for the analysis, and was also compared to the pooled group of 1040 patients treated with either the

ACS MULTI-LINK™ Stent or the Palmaz-Schatz® Stent. The primary endpoint was six month TVF.

### 10.5.2 Description of Patients

A comparison of baseline demographics between the ACS MULTI-LINK™ Stent *de novo* and restenosis groups showed no difference with regard to age, male/female distribution, or incidence of diabetes, hypertension, or cigarette use. The Restenosis Study did have more patients who were hyperlipidemic requiring medication (45% vs. 28%) and who had prior myocardial infarctions (54% vs. 37%).

**Table 9. Restenosis Study Demographics**  
All Restenosis and ACS ASCENT Patients, N=721

	ACS Multi-Link Stent	ACS data from ASCENT Study	95% CI of Difference
Number Treated	201	520	
% Male	71%	67%	-3.8, 11.2%
% Diabetic	25%	19%	-1.0, 12.9%
Hypertension	56%	53%	-4.4, 11.9%
Hyperlipidemia	45%	28%	9.1, 25.0%
Age (yr)	61 ± 11	61 ± 11	-1.8, 1.9
Reference vessel diameter (mm)	2.96 ± 0.57	2.96 ± 0.49	-0.09, 0.08
% DS pre procedure	64 ± 13%	64 ± 13%	-1.8, 2.7%
MLD (mm) pre procedure	1.04 ± 0.43	1.06 ± 0.41	-0.09, 0.05

### 10.5.3 Results

Device delivery success was achieved in 98.0% and 97.4% of the restenosis and the *de novo* groups respectively, while procedural success was achieved in 94.9% and 95.2% of the restenosis and the *de novo* groups respectively. Lesion length was slightly longer in the restenosis group (12.9 ± 6.9 mm vs. 10.8 ± 5.9 mm). There were no significant differences in baseline lesion and acute procedural results between the restenosis and *de novo* groups, and there were no cases of stent thrombosis or bleeding in the restenosis group. There were two (1.0%) vascular complications. As expected, the six-month MACE rate for the *de novo* group was higher than that of the restenosis group (12.7% vs. 10.4%). There was one death, no Q-wave myocardial infarctions, 8 non-Q-wave myocardial infarctions, 3 CABG procedures, and 16 repeat PTCA procedures. Each of these cases was summarized in the PMA Clinical Report and adjunctive information was included in the PMA. No unexpected problems were found.

The Restenosis Study documented equivalence between restenotic and *de novo* patient populations who received the ACS MULTI-LINK™ Stent for the primary variable of TVF (12.3% vs. 10.9%). Table 10 presents the principal effectiveness and safety results from the non-randomized Restenosis Study.

**Table 10. Principal Effectiveness and Safety Results - Restenosis Study**  
**All Patients Treated (n=721)**  
 Percent, Number/denominator, [95% confidence interval] or Mean ± SD (Number) {range}

Effectiveness Measures	Restenosis ACS MULTI-LINK (n=201)	<i>De novo</i> ACS MULTI-LINK (n=520)	Difference (95% CI's)
Device Success by QCA	98.0%[94.9%, 99.4%] (193/197)	97.4% [95.6%, 98.6%] (483/496)	0.6%[-1.8%, 3.0%]
Procedure Success by QCA	94.9%[90.9%, 97.5%] (187/197)	95.2%[92.9%, 96.9%] (472/496)	0.0%[-3.7%, 3.6%]
In-Stent % DS post procedure, mm	8 ± 11% (-44%, 30%) (182/201)	8 ± 11%{-39%, 42%} (482/520)	-0.3%[-2.2%, 1.5%]
Target Site Revascularization Free (6 mo. K-M)	94.6% [91.3%, 97.9%]	93.8% [91.4%, 96.2%]	0.8%[-3.1%, 4.7%]
Target Vessel Failure Free (6 mo. K-M)	89.1% [84.6%, 93.6%]	87.7% [84.8%, 90.6%]	1.4%[-3.9%, 6.7%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.0%[1.7%, 7.7%] (8/201)	4.8%[3.1%, 7.0%] (25/520)	-0.8%[-4.1%, 2.4%]
Out-of Hospital Clinical Event Rate	7.5%[4.2%, 13.0%] (15/201)	8.3%[6.0%, 11.0%] (43/520)	-0.8%[-5.1% 3.5%]
Bleeding Complication Rate	0.0%[0.0%, 1.5%] (0/201)	0.8% [0.2%, 2.0%] (4/520)	-0.8%[-1.5%, 0.0%]
Vascular Event Rate	1.0%[0.1%, 3.5%] (2/201)	1.5%[0.7%, 3.0%] (8/520)	-0.5%[-2.3%, 1.2%]
Subacute Thrombosis Rate	0.0%[0.0%, 1.5%] (0/201)	0.6%[0.1%, 1.7%] (3/520)	-0.6%[-1.2%, 0.1%]
Survival at 30 days (K-M)	100% [98.5%, 100%]	100% [99.4%, 100%]	0.0% [0.0%, 0.0%]
Survival at 180 days (K-M)	99.4% [98.8%, 100%]	99.4% [98.8%, 100%]	0.0% [0.0%, 0.0%]
MACE Rate at 6 months	10.4%[6.6%, 15.5%] (21/201)	12.7%[10.0%, 15.9%] (66/520)	-2.2%[-7.4%, 2.9%]
Hospitalization Post-Intervention (days)*	1.3±0.7[1.0, 5.0] (201/201)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.30*[-0.53,-0.08]

\*Refer to Table 7 footnotes for definitions.

## 10.6 The Rapid Exchange and Longer Length Stent Study

### 10.6.1 Objectives

This non-randomized, multicenter (n=18) study was conducted using the ACS RX MULTI-LINK™ CSS to treat 202 patients to demonstrate equivalence between the ACS RX MULTI-LINK™ CSS and the ACS MULTI-LINK™ CSS in *de novo* native coronary artery lesions. The main objective of this study was comparison of stent deliverability with the ACS Rapid Exchange (RX) Delivery System versus the OTW system that was used in the ASCENT Study

### 10.6.2 Study Design

The ACS RX MULTI-LINK™ CSS was used to treat lesions of up to 32 mm in length. Symptomatic patients with *de novo* coronary artery lesions visually estimated to be between 3.0 and 3.5 mm in diameter and between 12 and 32 mm long were eligible for stenting with a single 15, 25, or 35 mm ACS MULTI-LINK™ Stent. Short-term (30 day) results were collected. The ASCENT stenting and post-stenting anticoagulation protocols were followed. Clinical follow-up

was conducted at 2 weeks and one month. Angiographic follow-up is planned at six months for all patients. The primary endpoint was one month TVF. In addition, acute ischemic, hemorrhagic, and vascular complications and acute success were evaluated. The *a priori* control group for this study was the randomized *de novo* ACS MULTI-LINK™ Stent population from the ASCENT Study.

### 10.6.3 Description of Patients

Baseline demographics, including age and male/female ratio, were not different between the study and ASCENT ACS populations (Table 11). Qualitative coronary angiography (QCA) analysis was performed on 91 patients. The two populations had comparable baseline and post-procedure reference vessel diameter (RVD), MLD, and per cent diameter stenosis (%DS). There was a significant difference in lesion length (15.9 ± 0.9 mm vs. 10.8 ± 0.6 mm) which was anticipated considering the enrollment criteria for this study.

**Table 11. Rapid Exchange Study Demographics**  
All Rapid Exchange Patients and ACS ASCENT Patients, N=722

	ACS Multi-Link Stent	ACS data from ASCENT Study	95% CI of Difference
Number Treated	202	520	
% Male	67%	67%	-7.7, 7.6%
% Diabetic	21%	19%	-4.9, 8.3%
Hypertension	57%	53%	-3.5, 12.8%
Hyperlipidemia	30%	28%	-6.2, 8.7%
Age (yr)	63 ± 11	61 ± 11	-0.2, 3.5
Reference vessel diameter (mm)	2.92 ± 0.49	2.96 ± 0.49	-0.15, 0.07
% DS pre procedure	65 ± 12%	64 ± 13%	-2.2, 3.5%
MLD (mm) pre procedure	1.03 ± 0.40	1.06 ± 0.40	-0.11, 0.06

### 10.6.4 Results

Device delivery success and procedural success were achieved in 100% and 96.7% of patients respectively. This study documented equivalence between the ACS RX MULTI-LINK™ CSS and the ACS MULTI-LINK™ CSS for all effectiveness and safety measures, as well as the primary variable of 30 day TVF (4.8% vs. 5.0%). The 30 day MACE rate was similar to the ASCENT results (RX = 3.5%, ASCENT = 5.0%, 95% CI = [-4.7%, 1.6%]). Time to hospital discharge was significantly shorter for the 25 mm length ACS MULTI-LINK™ Stent patients (1.06 vs 1.64 days).

There was 1 (0.5%) death, 6 (3.0%) non-fatal myocardial infarctions (1 Q-wave and 5 Non-Q-wave MI), 2 (1.0%) repeat PTCA procedures, and no CABG procedures within the first 30 days. Each of these complications was summarized in the PMA Clinical Report and additional information was included in the PMA. Review of this information revealed no unexpected findings. There were also 3 (1.5%) stent thromboses, 1 (0.5%) bleeding complication, and 4 (2.0%) vascular complications.

#### 10.6.4.1 Patients with 35 MM Stent

In the Rapid Exchange Study, 58 patients received the 15 mm length stent, 92 patients received the 25 mm length stent, and 52 patients received the 35 mm length stent. Analysis of the MACE

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data indicated a higher rate in the 35 mm cohort. The MACE rate was 11.5% in this cohort compared to 3.0% and 2.0% in the respective 25 and 15 mm stent cohorts. FDA previously discussed necessary data requirements for the 35 mm stent with the sponsor (N= 150, Upper confidence limit = 15% ). The sponsor is aware that the current 35 mm data set contained in this study is not adequate for approval and is currently designing an additional study for the 35 mm stent.

#### **10.6.4.2 Comparison of 25 mm length with Two Stents**

A subset analysis was performed on the 92 Rapid Exchange Study patients who received the 25 mm length stent and the 74 ASCENT patients who were treated with two 15 mm stents in the ASCENT Study. Baseline characteristics for the two patient populations were similar except for incidence of CCS angina. Fifty-four per cent of the 25 mm Rapid Exchange Study patients had CCS Class III or IV angina, compared to 72% of the ASCENT patients (95% CI = -32.3, -3.3).

QCA analysis at the time of the PMA submission was performed on 36 of the 92 (39%) 25 mm length stent cases. These data suggest that the two population subsets were comparable at baseline and post-procedure. Acute device and acute lesion success rates on the 36 lesions was 100%, and the acute procedure success rate was 97.2%.

The frequency of MACE at 30 days for patients who received a 25 mm length (2.2%) was similar to the MACE rate for two 15 mm stents in the ASCENT Study (5.4%), [95% CI = -9.2%, 2.7%]. Additionally, there were no differences in the rates of stent thrombosis, bleeding, or vascular complications either acutely or at 30 days.

### **10.7 The High Pressure Study**

#### **10.7.1 Objectives**

The High Pressure Study conducted using the ACS RX MULTI-LINK HP™ CSS was a 101 patient non-randomized, multi-center (n=11) study which was designed to demonstrate equivalence between the ACS RX MULTI-LINK HP™ CSS and the ACS MULTI-LINK™ CSS in *de novo* native coronary artery lesions of  $\leq 20$  mm in length. The 15 mm length ACS MULTI-LINK™ Stent was used in this study. The main objective of this study was comparison of stenting technique with the rapid exchange high pressure (RX HP) balloon system versus the OTW system that was used in the ASCENT Study.

#### **10.7.2 Study Design**

Symptomatic patients with *de novo* coronary artery lesions visually estimated to be between 3.0 and 3.75 mm in diameter and not requiring placement of more than two 15 mm ACS MULTI-LINK™ Stents were eligible. The ACS RX Multi-Link HP™ CSS was advanced and the stent deployed at up to 11 atm, and up to four post-deployment dilatations, up to its rated burst pressure of 16 atm to achieve optimal stent deployment. The *a priori* control group for this study was the randomized *de novo* ACS MULTI-LINK™ Stent population from the ASCENT Study.

Standard post-stenting anticoagulation protocols were followed. Clinical follow-up was collected at 2 weeks and one month. Angiographic follow-up is planned at six months for all patients. The primary endpoint was one month TVF. In addition, acute ischemic, hemorrhagic, and vascular complications and acute success were evaluated.

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### 10.7.3 Description of Patients

Age and male/female ratio were not different between the High Pressure Study and ASCENT ACS populations (Table 12). There were small differences in the incidence of diabetes, hypertension, and hyperlipidemia. There was a similar distribution of LAD (47%) and circumflex (24%) lesions and a small difference in RCA lesions (RX HP = 29% vs. ASCENT = 35%, 95% CI = [-11.3, -1.3] ).

**Table 12. Rapid Exchange High Pressure Dilatation System (RX HP) Study**  
All RX patients and ACS ASCENT Patients, N=621

	RX HP	ACS data from ASCENT Study	95% CI of Difference
Number Treated	101	520	
% Male	64%	67%	-7.8, 3.4%
% Diabetic	25%	19%	0.9, 10.2%
Hypertension	59%	53%	1.0, 11.8%
Hyperlipidemia	23%	28%	-10.1, 0.8%
Age (yr)	62 ± 12	61 ± 11	-0.8, 1.2

### 10.7.4 Results

There were two stent delivery failures with the ACS RX MULTI-LINK HP™ CSS. Two patients had non-Q-wave myocardial infarctions in the first 24 hours post-intervention. One of the non-Q-wave myocardial infarction patients had an urgent CABG. Acute procedure success (final result < 50% residual stenosis and absence of death, CABG, or non-fatal myocardial infarction within 7 days of the procedure) was similar in the two cohorts (RX HP = 98% (99/101), ASCENT = 95.2%, 95% CI = [-0.5, 6.2]). There were no other in-hospital or out-of-hospital complications reported. The 30 day MACE rate was similar to the MACE rate reported for the ACS MULTI-LINK™ Stent in the ASCENT Study (RX HP = 2.0% vs. ASCENT = 5.0%, 95% CI = -6.3%, 0.3%).

Sixty-five per cent (79/122) of the ACS MULTI-LINK™ Stents were deployed at ≤ 11 atm and 98.0% (120/122) of ACS MULTI-LINK™ Stents were deployed at ≤ 16 atm; the rated burst pressure of the balloon. The median post-deployment dilatation pressure with the RX HP balloon was 14 atm and 96% (117/122) of patients received further dilatation at ≤ 16 atm. The ACS RX MULTI-LINK HP™ CSS's high pressure balloon was successfully used in 78% (79/101) of cases for final optimization of stent deployment. The remaining 22 patients, who received 36 ACS MULTI-LINK™ Stents, required additional post-dilatations with alternate balloons. Seventy-two per cent (26/36) of these post-dilatations were ≤ 16 atm. Final dilatations for the remaining 10 ACS MULTI-LINK™ Stents occurred at pressures between 17 and 22 atm. The main reasons for switching to another high pressure balloon were that inadequate stent apposition (n = 12 stents) or unacceptable residual stenosis (n = 10 stents) was obtained with the RX HP balloon.

This study documented equivalence between the ACS RX MULTI-LINK HP™ CSS and the ACS MULTI-LINK™ CSS for all effectiveness and safety measures as well as the primary variable of

30 day TVF (2.0% vs. 5.0%), and demonstrated acceptable deliverability, post-stent deployment characteristics, and 30-day results.

## **10.8 Non-US Clinical Studies**

### **10.8.1 Objectives**

The ACS MULTI-LINK™ Stent was also evaluated in three multi-center study studies in which 380 patients were enrolled. These studies were conducted using both the ACS MULTI-LINK™ CSS and the ACS RX MULTI-LINK CSS. Two of the registries were conducted primarily in western Europe, WEST I (n=102) and WEST II (n=165) and included de novo native coronary artery lesions in reference vessels of 2.75 to 3.5 mm in diameter and ≤ 12 mm in length. The third, The Japanese Study (n=113) included de novo and restenotic native coronary artery lesions in reference vessels of 3.0 to 3.5 mm in diameter and ≤ 12 mm in length, elective procedures and abrupt and threatened abrupt closures. Clinical follow-up periods were six to twelve months while angiographic follow-up was completed at six months. Results of these studies have not been included in any of the analyses.

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

### **11.1 Safety**

The preclinical studies conducted on the ACS MULTI-LINK™ Stent and the four Delivery Systems included biocompatibility, sterilization, and *in vitro* bench testing (stent material specifications and conformance, stent integrity, stent and Delivery System performance, package integrity and shelf-life). The results of biocompatibility testing demonstrated that the stent is acceptable for long-term (implant, circulating blood) invasive use in the cardiovascular system. The results of *in-vitro* bench testing demonstrated that the performance characteristics of the stent and its four Delivery Systems met product specifications and that they are safe for clinical use.

The results of *in-vivo* animal testing that was conducted on the ACS MULTI-LINK™ Stent and its four Delivery Systems demonstrated that acute and chronic *in vivo* performance characteristics, and sterility are safe for clinical use.

### **11.2 Effectiveness**

The results of the clinical studies indicate that the objectives of each study were met, the MACE rates between groups are comparable, the TVF rates are low, and that the data support the indications for use of the ACS MULTI-LINK™ Stent and the four Delivery Systems.

Data from the randomized ASCENT study indicate that the ACS Multi-Link™ Stent performs both acutely and chronically at least as well as the Palmaz-Schatz® Stent. The acute, 30 day, and six month clinical and angiographic point estimates obtained for major safety and effectiveness variables all tend to favor the ACS Multi-Link™ Stent. Additional data obtained from the RX and RX HP studies also support the safety and effectiveness of the ACS Multi-Link™ Stent.

The ASCENT study provides data supporting enhanced indications for coronary stenting. The original Palmaz-Schatz® Stent studies focused on a narrow group of patients with short (≤ 15 mm), *de novo* lesions in the proximal to midportions of native coronary arteries. The current PMA included longer lesions requiring up to two 15 mm length stents and restenotic lesions.

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Analysis of chronic data from these two subsets showed acceptable results that would justify labeling the ACS Multi-Link™ Stent for a wider indication. In addition, enough safety and effectiveness data were obtained for the 25 mm length stent to support approval of this device.

Multivariate analysis indicated that the luminal diameter after the procedure was the most powerful predictor of long term results. This result was similar to the result obtained in the original stent vs. balloon angioplasty studies and supports the “bigger is better” hypothesis.

### **11.3 Complication Rates**

The high bleeding and vascular complication rates associated with stenting that were reported in the original Palmaz-Schatz® Stent studies were mainly due to the aggressive anticoagulation regimen employed after stenting to reduce the rate of subacute thrombosis. There has been a major shift during the last two years to the use of aspirin/ticlopidine rather than aspirin/coumadin. The risk/benefit ratio associated with stenting has been favorably altered as a result of changes in drug therapy. In this PMA, the subacute thrombosis rate was low, and bleeding and vascular complications rates were substantially reduced in comparison to the early stent experience.

The rate of device deployment complications was acceptable when compared to the Palmaz-Schatz® Stent.

### **11.4 Delivery Systems**

Sufficient data have been presented to FDA to justify approval of two rapid exchange Delivery Systems (RX and RX HP) in addition to the over-the-wire (OTW) system. FDA believe that the essential components of the fourth delivery system, the over-the-wire system with stent mounted on high pressure balloon, have been tested during the studies that involved the other three delivery systems. It is, therefore, felt that this fourth system can be evaluated on the basis of preclinical data and prior experience with the other three systems.

### **11.5 Labeling**

To provide additional insight in selecting and treating patients with a coronary artery stent, labeling for this device will contain the following statements:

- The risks and benefits described above should be considered for each patient before use of the ACS MULTI-LINK™ CSS. Patient selection factors to be assessed should include a judgment regarding risk of antiplatelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.
- Premorbid conditions that increase the risk of a poor initial result or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed. A review of the vessel location, reference vessel size, lesion length, qualitative target lesion characteristics, and the amount of myocardium in jeopardy from acute or subacute thrombosis must also be considered.
- Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3 mm, intra-procedural thrombus, or poor distal runoff and/or dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of a thrombus or dissection should be considered

a marker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation.

- The safety and effectiveness of the ACS MULTI-LINK™ Stent have not been established in the following patient populations:
  - Patients with **unresolved vessel thrombus at the lesion site.**
  - Patients with coronary artery **reference vessel diameter < 3 mm.**
  - Patients with lesions located in the left main coronary artery, ostial lesions or lesions located at a bifurcation.
  - Patients with diffuse disease or **poor outflow distal** to the identified lesions.
  - Patients with a **recent acute myocardial infarction** where there is evidence of thrombus or poor flow.
  - Patients with **more than two overlapping stents** due to risk of thrombosis and restenosis.
- The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters to treat in-stent stenosis has not been established.

### **11.6 Post-Approval Studies**

Although enough information has been presented for approval purposes, there is much that can be gained from continued analysis of the sponsor's data. Conditions of approval should indicate that complete follow-up of the randomized patient cohort be obtained at six months, one year, and then yearly thereafter for a total of five years, and that the sponsor make a concerted effort to obtain autopsies on patients who die.

Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

### **12. Panel Recommendation**

Pursuant to section 515(c)(2) of the Federal Food, Drug, and Cosmetic 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 panel, for review and recommendation because the information in the PMA substantially duplicated information previously reviewed by this panel.

### **13. FDA Decision**

The FDA issued an approval order to Guidant Corporation/Advanced Cardiovascular Systems on October 2, 1997. The approval order stipulated that in addition to the standard postapproval requirements, the following information must be submitted: (1) the postapproval reports must

include information further characterizing long-term safety and effectiveness by following for 5 years from implant at least 390 of the 520 patients implanted with the ACS Multi-Link™ Stent in the ASCENT study; (2) the protocol for this study and study time lines will be submitted to the agency for review within 30 days of approval, and the final protocol will be developed interactively with the FDA review team; and, (3) summary reports will be submitted to the agency annually and a final report at the end of the study. FDA inspection of Guidant Corporation/Advanced Cardiovascular Systems' manufacturing facility determined it was in compliance with the Device Good Manufacturing Practices Regulation (21 CFR part 820).

#### **14. Approval Specifications**

Directions for use: See the labeling.

Hazards to health from use of the device: See indications, contraindications, warnings, precautions and adverse events in the labeling.

Postapproval requirements and restrictions: See approval order.

The Approval Order, Summary of Safety and Effectiveness Data, and labeling can be found on the Internet at address <http://www.fda.gov/cdrh/pmapage.html>.

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**ACS MULTI-LINK™ Coronary Stent System**

**Instructions For Use**

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**ACS MULTI-LINK™ Coronary Stent System**

**ACS Draft version 3.1, revised 9/29/97**

**Information for Prescribers**

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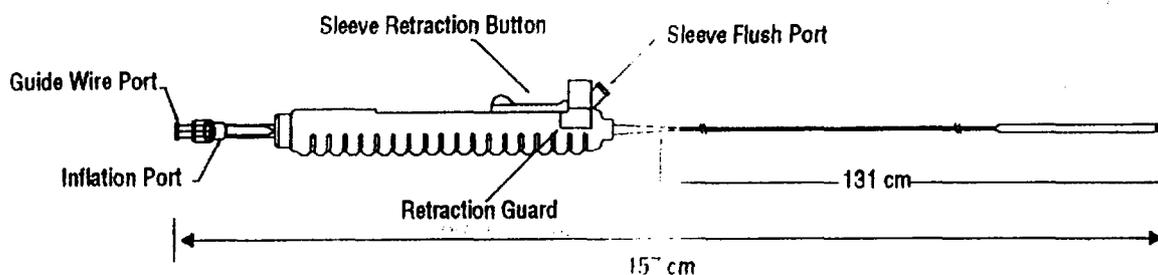
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**ACS MULTI-LINK™ Coronary Stent System (CSS)**  
**Information for Prescribers**

**1. DEVICE DESCRIPTION**

The ACS MULTI-LINK™ Coronary Stent System includes

- A pre-mounted 316L stainless steel stent
- An elastic membrane underneath the stent to aid in even stent expansion.
- Two radiopaque markers, located underneath the balloon, which fluoroscopically mark the ends of the stent.
- Two proximal Delivery System shaft markers (95 and 105 cm from the distal tip).
- A retractable sleeve which covers the entire catheter. A delivery handle that directly connects to the proximal sleeve and accommodates an inflation port, a guide wire port, and a sleeve flush port.



**Table 1. Device specifications**

Stent Diameter	Stent Length	Minimum Guiding Catheter Inner Diameter *	Stent Deployment Pressure	Rated Burst Pressure	Nominal Expanded Stent Length	Stent Free % Area
3.0 mm	15 mm	0.075 inch	8 atm	10 atm	14.6 mm	83.10 %
3.25 mm	15 mm	0.075 inch	8 atm	10 atm	14.5 mm	84.28 %
3.5 mm	15 mm	0.075 inch	8 atm	10 atm	14.3 mm	85.23 %
3.75 mm	15 mm	0.082 inch	8 atm	10 atm	14.0 mm	85.96 %

\* See individual manufacturer specifications for (Fr.) equivalent.

**2. INDICATIONS**

The ACS MULTI-LINK™ Coronary Stent System is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 20 mm) with a reference vessel diameter ranging from 3.0 mm to 3.75 mm and is intended to improve coronary luminal diameter (See Individualization of Treatment). Long term outcome (beyond six months) for this permanent implant is unknown at present.

**3. CONTRAINDICATIONS**

ACS MULTI-LINK™ Coronary Stent System is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion which prevents complete inflation of an angioplasty balloon.

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#### 4. WARNINGS

- Since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events, judicious selection of patients is necessary.
- Persons allergic to 316L stainless steel may suffer an allergic reaction to this implant.

#### 5. PRECAUTIONS

*(see also Individualization of Treatment)*

- Only physicians who have received appropriate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized ACS MULTI-LINK™ Stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition.

##### 5.1. *Stent Handling - Precautions*

- **For single use only.** Do not resterilize or reuse. Note product "Use Before" date.
- **Do not remove stent from its delivery balloon** as removal may damage the stent and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during catheter removal from packaging, placement over guide wire and advancement through hemostasis valve adapter and guiding catheter hub.
- Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

##### 5.2 *Stent Placement - Precautions*

- **Do not prepare or pre-inflate balloon prior to stent deployment other than as directed.** Use balloon purging technique described in the Instructions for Use.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

- Do not expand the stent if it is not properly positioned in the vessel. (See Stent/System Removal - Precautions)
- Placement of a stent has the potential to compromise side branch patency.
- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure as indicated on product label.** (See Balloon Inflated Diameter dimensions in Table 5). Use of pressures higher than specified on product label may result in a ruptured balloon with possible intimal damage and dissection.
- **Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgment of the stent from the balloon may occur.**
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

### 5.3 *Stent/System Removal - Precautions*

Should unusual resistance be felt at any time during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be removed as a single unit.

When removing the Delivery System as a single unit:

- DO NOT retract the Delivery System into the guiding catheter.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating hemostatic valve to secure the Delivery System to the guiding catheter; then remove the guiding catheter and Delivery System as a single unit.

Failure to follow these steps and/or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and/or delivery system components such as the balloon or the elastic membrane.

If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

### 5.4 *Post Implant - Precautions*

- Great care must be exercised when crossing a newly deployed stent with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry.
- Do not perform a magnetic resonance imaging (MRI) scan on patients post-stent implantation until the stent has completely endothelialized (eight weeks) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

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## 6. ADVERSE EVENTS

A total of 1593 patients were enrolled in five multicenter clinical trials to evaluate the use of the ACS MULTI-LINK™ Stent for treatment of symptomatic coronary artery disease. Of these, 1073 received the ACS MULTI-LINK™ Stent and 520 received the Palmaz-Schatz Stent. These patients form the basis for the observed events reported (see Clinical Studies).

### SUMMARY OF CLINICAL TRIAL PATIENT ENROLLMENTS (n=1,593)

	ACS MULTI-LINK STENT	CONTROL STENT	PATIENT TOTALS
Randomized Clinical Trial	520	520	1,040
Restenosis Registry	201	-	201
RX Registry	202	-	202
RX HP Registry	101	-	101
Feasibility Study	49	-	49
<b>PATIENT TOTALS:</b>	<b>1,073</b>	<b>520</b>	<b>1,593</b>

Twelve patients (12/1073 or 1.1%) who received the ACS MULTI-LINK™ Stent died during the clinical studies. One of these patients died within 30 days of receiving the stent implant as a result of a transfusion related grand mal seizure<sup>1</sup>. There were 11 late deaths which occurred between 58 and 353 days after stenting. Eight late deaths were cardiac related; congestive heart failure (n=4), chronic atrial fibrillation (n=1), sustained ventricular tachycardia (n=1), biventricular heart failure (n=1), and "sudden death" (n=1). Three late deaths were not cardiac related; ruptured abdominal aortic aneurysm (n=1), metastatic liver cancer (n=1) and suicide (n=1).

<sup>1</sup>One patient death < 30 days from the RX Registry

### 6.1 Observed Adverse Events

In the randomized comparative clinical trial (the ASCENT trial), the incidence of thrombosis in patients stented with the ACS MULTI-LINK™ Stent was 0.6% (3/520). All of these thromboses occurred within 24 hours of stent implantation. The incidence of vascular complications requiring surgical repair after stent placement in the randomized comparative clinical trial was 1.5% (8/520). The rate for bleeding requiring transfusion was 0.8% (4/520).

Initial delivery failure occurred in 2.9% (15/520) of patients as follows: operator was unable to deliver the first stent (n=12), stent was not deployed at the lesion site (n=2), and inability to post dilate (n=1). Delivery of a second ACS MULTI-LINK™ Stent was successful in all but 1.5% (8/520) of patients.

**Table 2 - Principal Adverse Events at 6 Months**  
%, [+ 95% confidence interval]. Number/Denominator

Randomized, *de novo* patients and non-randomized restenosis patients (n = 1,241)

Complication	MULTI-LINK™ DE NOVO (n=520)	Palmaz Schatz® DE NOVO (n=520)	MULTI-LINK™ RESTENOSIS (n=201)
Death Total	1.5% [0.7%, 3.0%], 8/520	1.1% [1.8%, 4.9%], 16/520	0.5% [0.0%, 2.7%], 1/201
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
30-Days	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.5% [0.7%, 3.0%], 8/520	1.9% [0.9%, 3.5%], 10/520	0.5% [0.0%, 2.7%], 1/201
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	4.6% [3.0%, 6.8%], 24/520	4.0% [1.7%, 7.7%], 8/201
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	4.0% [2.5%, 6.1%], 21/520	4.0% [1.7%, 7.7%], 8/201
Out-of-Hospital	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
CABG Total	2.5% [1.3%, 4.2%], 13/520	2.1% [1.1%, 3.8%], 11/520	1.0% [0.1%, 3.5%], 2/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.9% [0.9%, 1.5%], 10/520	1.3% [0.5%, 2.8%], 7/520	1.0% [0.1%, 3.5%], 2/201
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	1.0% [0.9%, 3.5%], 10/520 <sup>1</sup>	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.2% [0.0%, 1.1%], 1/520	1.0% [0.3%, 2.2%], 5/520	0.0% [0.0%, 1.5%], 0/201
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	1.3% [0.2%, 2.8%], 7/520	0.0% [0.0%, 1.5%], 0/201
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	1.1% [1.9%, 5.2%], 17/520	1.0% [0.1%, 3.5%], 2/201
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/201
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	3.7% [2.2%, 5.6%], 19/520	2.0% [0.5%, 5.0%], 4/201

<sup>1</sup> = One patient had two events; one in-hospital and one out of-hospital

## 6.2 Potential Adverse Events

Adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries (including those listed in Table 2):

- Acute myocardial infarction
- Arrhythmias, including VF and VT
- Death
- Dissection
- Drug reactions to antiplatelet 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

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## 7. CLINICAL STUDIES

A total of 1,241 patients were enrolled at 59 North American investigational sites in the multicenter ASCENT trial. Of these, 1040 patients with *de novo* native coronary artery lesions were randomized equally to receive the ACS MULTI-LINK™ Stent (n=520) and the Palmaz-Schatz Stent (n=520) in a parallel comparison, while an additional 201 primary restenosis patients were enrolled in a non-randomized arm to receive the ACS MULTI-LINK™ Stent. The primary endpoint of six month clinical target vessel failure was defined as the composite of death, myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass surgery (CABG), and percutaneous transluminal coronary angioplasty (PTCA), attributed to the target vessel. All major endpoints were adjudicated by a clinical events committee blinded to treatment assignment.

Eligible patients, with angina or positive functional study, were identified for elective stenting of a *de novo* native coronary artery lesion visually estimated to be between 3.0 and 3.75 mm in diameter and < 20 mm in length which would be covered by up to two 15 mm stents. These patients underwent standard balloon angioplasty after which a stent delivery system of the appropriate size was advanced and deployed. Additional non-compliant high pressure balloons with a balloon to artery ratio of 1.0-1.1:1.0 were utilized to attain optimal stent apposition.

The anticoagulation regimen administered to 98.8% of patients was aspirin 325 mg/day for at least one year and ticlopidine 250 mg bid for at least 30 days. At the discretion of the investigator, alternative therapy was allowed for non-optimal results which were defined as > 2 stents deployed, > 20% residual stenosis, any residual dissection, poor distal runoff or the presence of thrombus.

Follow-up intervals were 2, 4, and 6 weeks and 6, 9, and 12 months. The study randomization was successful as both treatment groups were demographically equivalent. All randomized patients were included in the intent-to-treat efficacy analysis.

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**Table 3. Principal Effectiveness and Safety Results - Randomized Trial**  
 Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)  
 All Patients Treated (n=1040)

Effectiveness Measures	ACS MULTI-LINK (n=520)	Palmaz-Schatz (n=520)	Difference
Device Success by QCA	97.4% [95.6%, 98.6%] (483/496)	96.8% [95.3%, 98.4%] (482/498)	0.6% [-1.5%, 2.7%]
Procedure Success by QCA	95.2% [92.9%, 96.9%] (472/496)	92.8% [90.1%, 94.9%] (462/498)	2.4% [-0.6%, 5.3%]
In-Stent % DS post procedure, mm*	8 ± 11% [-3.9%, 42%] (482/520)	10 ± 12% [-34%, 100%] (485/520)	-1.7%* [-3.1%, -0.2%]
In-Stent % DS at 9 month follow-up	32 ± 20% [-1.6%, 100%] (192/271)	34 ± 20% [-1.1%, 100%] (171/263)	-2.2% [-6.3%, 1.9%]
In-Stent Restenosis Rate (9 mo)	15.6% [13.5%, 17.0%] (30/192)	20.5% [14.7%, 27.3%] (35/174)	-4.5% [-12.4, 3.4%]
Target Site Revascularization Free (6 mo. K-M)	93.8% [91.4%, 96.2%]	93.3% [90.9%, 91.4%]	0.5% [-2.6%, 3.5%]
Target Vessel Failure Free (6 mo. K-M)	87.7% [84.8%, 90.6%]	86.9% [84.0%, 89.8%]	0.8% [-3.3%, 4.9%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.8% [3.1%, 7.0%] (25/520)	6.0% [4.1%, 8.4%] (31/520)	-1.2% [-3.9%, 1.6%]
Out-of-Hospital Clinical Event Rate	8.3% [6.0%, 11.0%] (43/520)	10.2% [7.7%, 13.1%] (53/520)	-1.9% [-5.4%, 1.6%]
Bleeding Complication Rate	0.8% [0.2%, 2.0%] (4/520)	1.3% [0.5%, 2.8%] (7/520)	-0.6% [-1.8%, 0.7%]
Vascular Event Rate	1.5% [0.7%, 3.0%] (8/520)	3.3% [1.9%, 5.2%] (17/520)	-1.7% [-3.6%, 0.1%]
Subacute Thrombosis Rate	0.6% [0.1%, 1.7%] (3/520)	1.9% [0.9%, 3.5%] (10/520)	-1.3% [-2.7%, 0.0%]
Survival at 30 days (K-M) *	100.0% [99.4%, 100.0%]	98.8% [97.8%, 99.8%]	1.2%* [0.2%, 2.1%]
Survival at 180 days (K-M)	99.4% [98.8%, 100.0%]	98.0% [96.8%, 99.2%]	1.3% [0.0%, 2.7%]
MACE Rate at 6 months	12.7% [10.0%, 15.9%] (66/520)	16.0% [12.9%, 19.4%] (83/520)	-3.3% [-7.5%, 1.0%]
Hospitalization Post-Intervention (days)	1.6 ± 1.6 [1.0, 18] (520/520)	1.7 ± 2.4 [1.0, 32] (520/520)	-0.01 [-0.34, 0.15]

*Device success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device alone (i.e. without the use of other types of stents or new balloon devices).*

*Procedure Success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device and any adjunctive device without death, coronary artery bypass surgery (CABG), or myocardial infarction (Q-wave or non-Q-wave) within seven days of the procedure.*

*QCA = Quantitative coronary angiography*

*% DS = percent diameter stenosis by QCA.*

*Target Vessel Failure (TVF) = The composite of acute and late-term major events of death, CABG, Q-wave MI or non-Q-wave MI, and percutaneous transluminal coronary angioplasty (PTCA) attributable to the target vessel. (K-M = actuarial freedom-from TVF by Kaplan Meier survival analysis).*

*Target Site Revascularization (TSR) = Repeat PTCA or CABG to the original site of intervention. (K-M = actuarial freedom-from TSR by Kaplan Meier survival analysis).*

*MACE = Major Adverse Cardiac Event of death, Q-wave MI or non-Q-wave MI, CABG, or PTCA to the treated site.*

*In-Hospital Clinical Event = Any MACE occurring prior to hospital discharge.*

*Out of Hospital Clinical Event = Any MACE occurring from hospital discharge through up to one year of clinical follow-up.*

*Bleeding Complication = Blood loss necessitating a transfusion.*

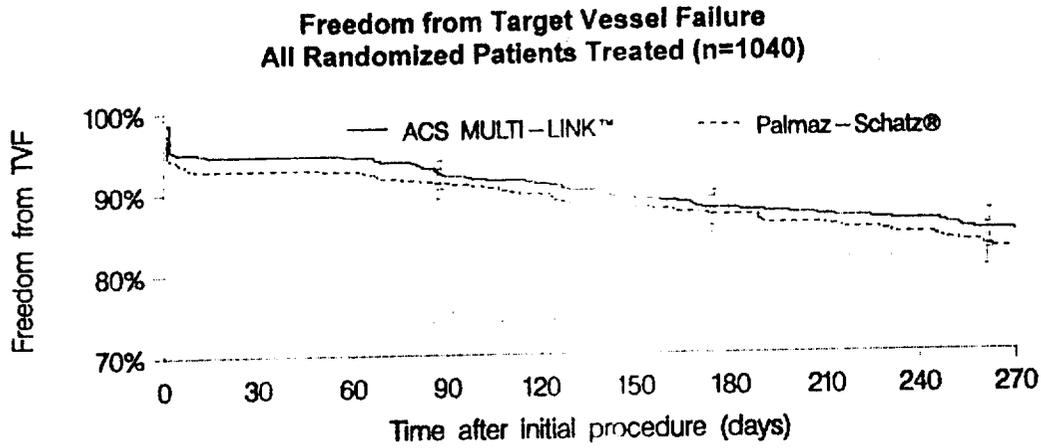
*Vascular Event = Any hematoma > 5 cm, arteriovenous fistula, pseudoaneurysm, retroperitoneal bleed, peripheral nerve disorder and surgical repair.*

*Subacute Thrombosis = Any cardiac death, subacute closure requiring revascularization of the target site or total closure indicated by QCA within 30 days of the index intervention.*

*\* = difference is statistically significant, p-value < 0.05 (2-tailed) based on t-test or Chi-square analysis as appropriate.*

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**Figure 1. Freedom from Target Vessel Failure - All Randomized Patients**



Kaplan Meier Survival Analysis - TVF free at 6 months difference [95% CI] of 0.8%[-3.3%, 4.9%]

	Time after initial procedure (days)									
	0	7	14	30	60	90	120	180	210	270
<b>ACS MULTI-LINK™</b>										
# At risk	513	492	490	490	469	455	448	418	388	295
# Events	7	26	28	28	29	40	45	62	65	74
% Survived	98.7%	95.0%	94.6%	94.6%	94.4%	92.2%	91.2%	87.7%	87.0%	84.8%
SE	0.5%	1.0%	1.0%	1.0%	1.0%	1.2%	1.3%	1.5%	1.5%	1.6%
<b>Palmaz-Schatz®</b>										
# At risk	506	484	482	482	469	458	450	424	390	298
# Events	14	36	38	38	39	47	54	68	73	84
% Survived	97.5%	93.3%	92.9%	92.9%	92.7%	91.1%	89.7%	86.9%	85.8%	83.0%
SE	0.7%	1.1%	1.1%	1.1%	1.1%	1.3%	1.3%	1.5%	1.6%	1.7%

**Tests Between Groups**

Test	Chi-Square	Deg Frdm	P-value
Log-Rank	1.37	1	0.24
Wilcoxon	1.38	1	0.24

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**Table 4. Principal Effectiveness and Safety Results - Restenosis Registry**

**All Patients Treated (n=721)**  
**Percent, Number/denominator, [95% confidence interval] or Mean ± SD (Number) {range}**

Effectiveness Measures	Restenosis	<i>De novo</i>	Difference (95% CI's)
	ACS MULTI-LINK (n=201)	ACS MULTI-LINK (n=520)	
Device Success by QCA	98.0%[94.9%, 99.4%] (193/197)	97.4% [95.6%, 98.6%] (483/496)	0.6%[-1.8%, 3.0%]
Procedure Success by QCA	94.9%[90.9%, 97.5%] (187/197)	95.2%[92.9%, 96.9%] (472/496)	0.0%[-3.7%, 3.6%]
In-Stent % DS post procedure, mm	8 ± 11% (-44%, 40%) (182/201)	8 ± 11% (-39%, 42%) (482/520)	-0.3%[-2.2%, 1.5%]
Target Site Revascularization Free (6 mo. K-M)	94.6% [91.3%, 97.9%]	93.8% [91.4%, 96.2%]	0.8%[-3.1%, 4.7%]
Target Vessel Failure Free (6 mo. K-M)	89.1% [84.6%, 93.6%]	87.7% [84.8%, 90.6%]	1.4%[-3.9%, 6.7%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.0%[1.7%, 7.2%] (8/201)	4.8%[3.1%, 7.0%] (25/520)	-0.8%[-4.1%, 2.4%]
Out-of-Hospital Clinical Event Rate	7.5%[4.2%, 11.0%] (15/201)	8.3%[6.0%, 11.0%] (43/520)	-0.8%[-5.1%, 3.5%]
Bleeding Complication Rate	0.0%[0.0%, 1.5%] (0/201)	0.8% [0.2%, 2.0%] (4/520)	-0.8%[-1.5%, 0.0%]
Vascular Event Rate	1.0%[0.1%, 3.8%] (2/201)	1.5%[0.7%, 3.0%] (8/520)	-0.5%[-2.3%, 1.2%]
Subacute Thrombosis Rate	0.0%[0.0%, 1.5%] (0/201)	0.6%[0.1%, 1.7%] (3/520)	-0.6%[-1.2%, 0.1%]
Survival at 30 days (K-M)	100% [98.5%, 100%]	100% [99.4%, 100%]	0.0% [0.0%, 0.0%]
Survival at 180 days (K-M)	99.4% [98.8%, 100%]	99.4% [98.8%, 100%]	0.0% [0.0%, 0.0%]
MACE Rate at 6 months	10.4%[6.6%, 15.5%] (21/201)	12.7%[10.0%, 15.9%] (66/520)	-2.2%[-7.4%, 2.9%]
Hospitalization Post-Intervention (days)*	1.3±0.7 [1.0, 5.0] (201/201)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.30*[-0.53,-0.08]

Refer to Table 3 footnotes for definitions.

## 8. INDIVIDUALIZATION OF TREATMENT

The risks and benefits described above should be considered for each patient before use of the ACS MULTI-LINK™ CSS. Patient selection factors to be assessed should include a judgment regarding risk of antiplatelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

Premorbid conditions that increase the risk of a poor initial result or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed. The relationship of baseline and procedural variables to TVF was examined. The only statistically significant predictor of TVF was post-procedural Minimum Lumen Diameter (MLD), that is, TVF was less likely with larger MLD's.

Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3 mm, intra-procedural thrombus, or poor distal runoff and/or dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of a thrombus or dissection should be considered a marker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation.

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## 8.1 Use in Special Populations

The safety and effectiveness of the ACS MULTI-LINK™ Stent have not been established in:

- Patients with **unresolved vessel thrombus at the lesion site.**
- Patients with **coronary artery reference vessel diameter < 3 mm.**
- Patients with lesions located in the left main coronary artery, ostial lesions or lesions located at a bifurcation.
- Patients with diffuse disease or **poor outflow distal to the identified lesions.**
- Patients with a recent **acute myocardial infarction** where there is evidence of thrombus or poor flow.
- Patients with **more than two overlapping stents** due to risk of thrombosis and restenosis.
- Patients for longer than six months.

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters to treat in-stent stenosis has not been established.

## 9. HOW SUPPLIED

**STERILE.** This device is sterilized with ethylene oxide. Non-pyrogenic. Do not use if the package is opened or damaged.

**CONTENTS.** One (1) ACS MULTI-LINK™ Coronary Stent System

**STORAGE.** Store in a cool, dry, dark place.

## 10. OPERATOR'S MANUAL

### 10.1 INSPECTION PRIOR TO USE

Prior to using the ACS MULTI-LINK™ Coronary Stent System, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is centered on the balloon or located between the radiopaque balloon markers. Do not use if any defects are noted. Verify that the distal tip of the retractable sleeve completely covers the stent but does not extend beyond the distal tip of the Delivery System. Do not move the retractable sleeve to visualize the stent. Movement of the retractable sleeve without a guide wire or prior to stent deployment may result in stent damage or dislodgment.

### 10.2 MATERIALS REQUIRED

Quantity	Material
	Appropriate guiding catheter(s)
2 - 3	10-20 cc syringes
1,000 u /500 cc	Heparinized Normal Saline (HepNS)
1	0.014 inch X 175 cm extendible or 0.014 inch X 300 cm guide wire
1	Rotating hemostatic valve with 0.096 inch minimum inner diameter
	60% contrast diluted 1:1 with normal saline
1	Inflation device
1	Three-way stopcock
1	Torque device
1	Guide wire introducer

### 10.3 PREPARATION

#### Guide Wire Lumen Flush

Step	Action
1.	Attach syringe with HepNS to guide wire port.
2.	Flush until fluid exits distal tip.

#### Balloon Preparation

Step	Action
1.	Prepare inflation device / syringe with diluted contrast medium.
2.	Attach inflation device / syringe to stopcock; attach to inflation port.
3.	With tip down, orient Delivery System vertically.
4.	Open stopcock to Delivery System; pull negative for 30 seconds; release to neutral for contrast fill.
5.	Close stopcock to Delivery System; purge inflation device / syringe of all air.
6.	Repeat steps 3 through 5 until all air is expelled.  NOTE. If air is seen in shaft, repeat Balloon Preparation steps 3 through 5 to prevent uneven stent expansion.
7.	If a syringe was used, attach a prepared inflation device to stopcock.
8.	Open stopcock to Delivery System.
9.	Leave on neutral.

#### Retractable Sleeve Flush

Step	Action
1.	Attach 10 cc syringe with HepNS to flush port of delivery handle.
2.	Vertically orient delivery handle, shaft up.
3.	Flush until fluid exits distal tip of retractable sleeve.
4.	Pull negative to remove any air in delivery handle chamber.
5.	Repeat steps 3 and 4 until all air is expelled.  NOTE. If air is seen in the delivery handle chamber, repeat Retractable Sleeve Flush steps 2 through 6 to prevent air introduction into patient.
6.	Flush retractable sleeve with HepNS  NOTE. Do not flush retractable sleeve after system introduction into patient.
7.	Remove syringe prior to system introduction into patient.  NOTE. Do not use retractable sleeve for hemodynamic monitoring or contrast injection.

10.4 **DELIVERY PROCEDURE**

Step	Action
1.	Prepare vascular access site according to standard practice.
2.	Predilate lesion with PTCA catheter.
3.	Prepare guide wire for extension.
4.	Maintain neutral pressure on inflation device. Open rotating hemostatic valve as widely as possible.
5.	Backload Delivery System onto proximal portion of guide wire while maintaining guide wire position across target lesion.  <b>CAUTION.</b> Sleeve retraction button should never be moved until stent is ready for deployment. Should it move prematurely, resulting in sleeve retraction, stent deployment should be abandoned. See Stent/System Removal - Precautions section for specific Delivery System removal instructions.
6.	Advance Delivery System over guide wire to target lesion. Utilize radiopaque balloon markers to position stent across lesion; perform angiography to confirm stent position.  <b>NOTE.</b> Should <b>unusual resistance</b> be felt <b>at any time</b> during either lesion access or removal of Delivery System post-stent implantation, the entire system should be removed as a single unit. See Stent/System Removal - Precautions section for specific Delivery System removal instructions.
7.	Tighten rotating hemostatic valve. Stent is now ready to be deployed.

10.5 **DEPLOYMENT PROCEDURE**

Step	Action
1.	Open rotating hemostatic valve slightly.
2.	Slowly retract the sleeve retraction button until it locks.  <b>NOTE.</b> Do not readvance the retractable sleeve prior to removal.  <b>NOTE.</b> Should any uncertainty exist regarding stent position or functionality of the retractable sleeve as it is retracted, abandon procedure and remove the guiding catheter and Delivery System as a single unit. See Stent/System Removal - Precautions section for specific Delivery System removal instructions.
3.	Maintain stent position, using radiopaque balloon markers as guide, by coordinating sleeve retraction with movement of Delivery System.
4.	Tighten rotating hemostatic valve  <b>CAUTION.</b> Refer to Table 5 for <i>in vitro</i> stent outer diameter, deployment pressure, and RBP.
5.	Deploy stent slowly by pressurizing Delivery System in 2 atm increments, every 5 seconds, until stent is completely expanded. Maintain pressure for 30 seconds. <b>Do not exceed RBP or expand stent beyond 4.1 mm.</b>
6.	Deflate balloon by pulling negative on inflation device for 30 seconds.

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10.6 **REMOVAL PROCEDURE**

Step	Action
1.	Ensure balloon is fully deflated.
2.	Fully open rotating hemostatic valve.
3.	While maintaining guide wire position and negative pressure on inflation device, withdraw Delivery System.  NOTE. Do not readvance the retractable sleeve prior to removal.  NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be removed as a <b>single unit</b> . See Stent/System Removal - Precautions section for specific Delivery System removal instructions.  NOTE. If elastic membrane has stretched beyond distal tip post-stent implantation, it does not indicate any problem.
4.	Tighten rotating hemostatic valve.
5.	Repeat angiography to assess stented area.  If necessary, post dilate within stent using PTCA catheter. Balloon inflations should incorporate balloon size closely matching vessel.
6.	Final stent diameter should match reference vessel. <b>ASSURE STENT IS NOT UNDERDILATED.</b>

10.7 **IN VITRO INFORMATION**

**Table 5. Stent Outer Diameters for the ACS MULTI-LINK™ Coronary Stent System**  
Deployment pressures are highlighted and rated burst pressures (RBP) are marked.

Inflation Pressure (atm)	Stent Diameter (mm)			
	3.0	3.25	3.5	3.75
4	2.81	3.03	3.12	3.45
5	2.90	3.10	3.35	3.59
6	2.96	3.18	3.45	3.68
7	3.03	3.27	3.55	3.78
8	3.10	3.36	3.66	3.89
9	3.17	3.47	3.76	3.99
10	3.23 (RBP)	3.58 (RBP)	3.88 (RBP)	4.11 (RBP)
11	3.30	3.65	3.99	4.19
12	3.37	3.72	4.07	4.28
13	3.42	3.79	4.13	4.42

**NOTE.** These nominal, *in vitro* device specifications do not take into account lesion resistance. The stent sizing should be confirmed angiographically. Do not exceed the RBP or expand the stent beyond 4.1 mm.

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**10.8 PATIENT INFORMATION:**

In addition to this Instructions for Use booklet, the ACS MULTI-LINK™ Coronary Stent System is packaged with additional patient specific information which includes:

- A patient Implant Card that includes both patient and ACS MULTI-LINK™ Stent specific information. All patients will be expected to keep this card in their possession at all times for procedure / stent identification .
- A patient Teaching Guide which includes information on Guidant Corporation, the implant procedure and the ACS MULTI-LINK™ Stent
- A Device Tracking Form (Implant and Explant) which will be completed by the Hospital staff and forwarded to Guidant Corporation for the purposes of tracking all patients who receive an ACS MULTI-LINK™ Stent, as required by Federal regulation.

## PATENTS

Manufactured under one or more of the following patents: United States, 4,323,071; 4,411,055; 4,571,240; 4,573,470; 4,581,017; 4,582,181; 4,597,755; 4,616,653; 4,619,263; 4,638,805; 4,641,654; 4,661,094; 4,664,113; 4,692,200; 4,748,982; 4,771,776; 4,771,777; 4,771,778; 4,775,371; 4,782,834; 4,790,315; 4,793,350; 4,821,722; 4,877,031; 4,892,519; 4,938,220; 4,940,062; 4,964,409; 4,976,720; 4,981,478; 4,998,917; 4,998,923; 5,002,532; 5,003,989; 5,034,001; 5,040,548; 5,042,985; 5,046,503; 5,061,273; 5,090,959; 5,135,535; 5,137,513; 5,154,725; 5,158,548; 5,159,937; 5,176,661; 5,195,971; 5,234,002; 5,242,394; 5,242,396; 5,242,399; 5,256,143; 5,279,562; 5,290,230; 5,300,025; 5,300,085; 5,316,706; 5,318,527; 5,324,259; 5,334,154; 5,342,621; 5,344,426; 5,344,426; 5,346,505; 5,348,537; 5,360,401; 5,369,401; 5,391,172; 5,409,495; 5,415,638; 5,421,955; 5,423,885; 5,437,083; 5,441,515; 5,443,458; 5,443,500; 5,456,667; 5,458,605; 5,458,615; 5,476,505; 5,507,768; RE 33,166; RE 34,564. Other U.S. patents pending. Foreign patents issued and pending.

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# Graphical Symbols for Medical Device Packaging

<b>STERILE</b>	<b>EO</b>
Sterilized with ethylene oxide gas.	
<b>LOT</b>	
Lot number	
	
Each device is for one (1) use only.	
	
Read instructions prior to use.	
	
Date of Manufacture	
	
Expires	
<b>REF</b>	
Catalog number	
<b>F</b>	
French size	

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**ACS RX MULTI-LINK™ Coronary Stent System**

**Instructions For Use**

60  
1/1

**ACS RX MULTI-LINK™ Coronary Stent System**

**ACS Draft version 3.1, revised 9/29/97**

**Information for Prescribers**

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**ACS RX MULTI-LINK™ Coronary Stent System (CSS)**  
**Information for Prescribers**

**1. DEVICE DESCRIPTION**

The ACS RX MULTI-LINK™ Coronary Stent System includes:

- A pre-mounted 316L stainless steel stent.
- An elastic membrane underneath the stent to aid in even stent expansion.
- Two radiopaque markers, located underneath the balloon, which fluoroscopically mark the ends of the stent.
- Two proximal Delivery System shaft markers (95 and 105 cm from the distal tip).
- A third shaft marker denoting the guide wire exit notch.

**Table 1. Device specifications**

Stent Diameter	Stent Length	Minimum Guiding Catheter Inner Diameter *	Stent Deployment Pressure	Rated Burst Pressure	Nominal Expanded Stent Length	Stent Free % Area
3.0 mm	15 mm	0.064 inch	6 atm	8 atm	14.6 mm	83.10 %
3.5 mm	15 mm	0.064 inch	6 atm	8 atm	14.3 mm	85.23 %
3.0 mm	25 mm	0.072 inch	7 atm	8 atm	25.1 mm	83.10 %
3.5 mm	25 mm	0.072 inch	7 atm	8 atm	24.3 mm	85.23 %

\* See individual manufacturer specifications for (Fr.) equivalent.

**2. INDICATIONS**

The ACS RX MULTI-LINK™ Coronary Stent System is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 22 mm) with a reference vessel diameter ranging from 3.0 mm to 3.5 mm and is intended to improve coronary luminal diameter (See Individualization of Treatment). Long term outcome (beyond six months) for this permanent implant is unknown at present.

**3. CONTRAINDICATIONS**

ACS RX MULTI-LINK™ Coronary Stent System is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion which prevents complete inflation of an angioplasty balloon.

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#### 4. WARNINGS

- Since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events, judicious selection of patients is necessary.
- Persons allergic to 316L stainless steel may suffer an allergic reaction to this implant.

#### 5. PRECAUTIONS

*(see also Individualization of Treatment)*

- Implantation of the stent should be performed only by physicians who have received appropriate training.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized ACS MULTI-LINK™ Stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition.

##### 5.1. *Stent Handling - Precautions*

- **For single use only.** Do not resterilize or reuse. Note product "Use Before" date.
- **Do not remove stent from its delivery balloon** as removal may damage the stent and/or lead to stent embolization.
- **Special care must be taken not to handle or in any way disrupt the stent on the balloon.** This is most important during catheter removal from packaging, placement over guide wire and advancement through hemostasis valve adapter and guiding catheter hub.
- Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

##### 5.2 *Stent Placement - Precautions*

- **Do not prepare or pre-inflate balloon prior to stent deployment** other than as directed. Use balloon purging technique described in the Instructions for Use.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by

stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

- Do not expand the stent if it is not properly positioned in the vessel. (See Stent/System Removal - Precautions)
- Placement of a stent has the potential to compromise side branch patency.
- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure as indicated on product label.** (See Balloon Inflated Diameter dimensions in Table 8). Use of pressures higher than specified on product label may result in a ruptured balloon with possible intimal damage and dissection.
- **Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgment of the stent from the balloon may occur.**
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

### 5.3 *Stent/System Removal - Precautions*

Should **unusual resistance** be felt at any time during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be removed as a single unit.

**When removing the Delivery System as a single unit:**

- **DO NOT** retract the Delivery System into the guiding catheter.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating hemostatic valve to secure the Delivery System to the guiding catheter; then remove the guiding catheter and Delivery System as a single unit.

Failure to follow these steps and/or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and/or delivery system components such as the balloon or the elastic membrane.

If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

### 5.4 *Post Implant - Precautions*

- Great care must be exercised when **crossing a newly deployed stent** with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry.
- Do not perform a **magnetic resonance imaging (MRI)** scan on patients post-stent implantation until the stent has completely endothelialized (eight weeks) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

## 6. ADVERSE EVENTS

A total of 1593 patients were enrolled in five multicenter clinical trials to evaluate the use of the ACS MULTI-LINK™ Stent for treatment of symptomatic coronary artery disease. Of these, 1073 received the ACS MULTI-LINK™ Stent and 520 received the Palmaz-Schatz Stent. These patients form the basis for the observed events reported (see Clinical Studies).

### SUMMARY OF CLINICAL TRIAL PATIENT ENROLLMENTS (n=1,593)

	ACS MULTI-LINK STENT	CONTROL STENT	PATIENT TOTALS
Randomized Clinical Trial	520	520	1,040
Restenosis Registry	201	-	201
RX Registry	202	-	202
RX HP Registry	101	-	101
Feasibility Study	49	-	49
<b>PATIENT TOTALS:</b>	<b>1,073</b>	<b>520</b>	<b>1,593</b>

Twelve patients (12/1073 or 1.1%) who received the ACS MULTI-LINK™ Stent died during the clinical studies. One of these patients died within 30 days of receiving the stent implant as a result of a transfusion related grand mal seizure<sup>1</sup>. There were 11 late deaths which occurred between 58 and 353 days after stenting. Eight late deaths were cardiac related; congestive heart failure (n=4), chronic atrial fibrillation (n=1), sustained ventricular tachycardia (n=1), biventricular heart failure (n=1), and "sudden death" (n=1). Three late deaths were not cardiac related; ruptured abdominal aortic aneurysm (n=1), metastatic liver cancer (n=1) and suicide (n=1).

<sup>1</sup>One patient death < 30 days from the RX Registry (ACS 96-003)

### 6.1 Observed Adverse Events

#### 6.1.1 Randomized Clinical Trial

In the randomized comparative clinical trial (the ASCENT trial) the incidence of thrombosis in patients stented with the ACS MULTI-LINK™ Stent was 0.6% (3/520). All of these thromboses occurred within 24 hours of stent implantation. The incidence of vascular complications requiring surgical repair after stent placement in the randomized comparative clinical trial was 1.5% (8/520). The rate for bleeding requiring transfusion was 0.8% (4/520).

Initial delivery failure occurred in 2.9% (15/520) of patients as follows: operator was unable to deliver the first stent (n=12), stent was not deployed at the lesion site (n=2), and inability to post dilate (n=1). Delivery of a second ACS MULTI-LINK™ Stent was successful in all but 1.5% (8/520) of patients.

#### 6.1.2 Rapid Exchange Registry

The incidence of thrombosis in patients stented with the ACS RX MULTI-LINK Stent was 1.5% (3/202) in the non-randomized RX registry. The incidence of vascular complications requiring surgical repair after stent placement was 2.0% (4/202), while the rate for bleeding requiring transfusion was 0.5% (1/202).

There were no initial delivery failures.

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**Table 2 - Principal Adverse Events at 6 Months**  
%, [+ 95% confidence interval], Number/Denominator

Randomized *de novo* patients and non-randomized restenosis patients, (n = 1,241)

Complication	MULTI-LINK™ DE NOVO (n=520)	Palmaž Schatz® DE NOVO (n=520)	MULTI-LINK™ RESTENOSIS (n=201)
Death Total	1.5% [0.7%, 3.0%], 8/520	3.1% [1.8%, 4.9%], 16/520	0.5% [0.0%, 2.7%], 1/201
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
30-Days	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.5% [0.7%, 3.0%], 8/520	1.9% [0.9%, 3.5%], 10/520	0.5% [0.0%, 2.7%], 1/201
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	4.6% [3.0%, 6.8%], 24/520	4.0% [1.7%, 7.7%], 8/201
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	4.0% [2.5%, 6.1%], 21/520	4.0% [1.7%, 7.7%], 8/201
Out-of-Hospital	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
CABG Total	2.5% [1.3%, 4.2%], 13/520	2.1% [1.1%, 3.8%], 11/520	1.0% [0.1%, 3.5%], 2/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.9% [0.9%, 3.5%], 10/520	1.3% [0.5%, 2.8%], 7/520	1.0% [0.1%, 3.5%], 2/201
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	1.9% [0.9%, 3.5%], 10/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.2% [0.0%, 1.1%], 1/520	1.0% [0.3%, 2.2%], 5/520	0.0% [0.0%, 1.5%], 0/201
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	1.3% [0.2%, 2.8%], 7/520	0.0% [0.0%, 1.5%], 0/201
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	3.3% [1.9%, 5.2%], 17/520	1.0% [0.1%, 3.5%], 2/201
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/201
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	3.7% [2.2%, 5.6%], 19/520	2.0% [0.5%, 5.0%], 4/201

<sup>1</sup> = One patient had two events; one in-hospital and one out-of-hospital.

**Table 3 - Principal Adverse Events at 30 days**  
%, [+ 95% confidence interval], Number/Denominator

Randomized *de novo* patients and non-randomized *de novo* registry patients, (n = 722)

Complication	MULTI-LINK™ DE NOVO (n=520)	RX MULTI-LINK™ DE NOVO (n=202)
Death Total	0.0% [0.0%, 0.6%], 0/520	0.5% [0.0%, 2.7%], 1/202
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/202
Out-of-Hospital 30 Days	0.0% [0.0%, 0.6%], 0/520	0.5% [0.0%, 2.7%], 1/202
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	0.5% [0.0%, 2.7%], 1/202
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/202
Out-of-Hospital 30 Days	0.0% [0.0%, 0.6%], 0/520	0.5% [0.0%, 2.7%], 1/202
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	2.5% [0.3%, 4.3%], 5/202
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	2.5% [0.3%, 4.3%], 5/202
Out-of-Hospital 30 Days	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/202
CABG Total	2.5% [1.3%, 4.2%], 13/520	0.0% [0.0%, 1.5%], 0/202
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/202
Out-of-Hospital 30 Days	1.9% [0.9%, 3.5%], 10/520	0.0% [0.0%, 1.5%], 0/202
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	1.5% [0.3%, 4.3%], 3/202
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	1.0% [0.1%, 3.5%], 2/202
Out-of-Hospital 30 Days	0.2% [0.0%, 1.1%], 1/520	0.5% [0.0%, 2.7%], 1/202
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	0.5% [0.0%, 2.7%], 1/202
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	2.0% [0.5%, 5.0%], 4/202
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/202
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	0.0% [0.0%, 1.5%], 0/202

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## 6.2 Potential Adverse Events

Adverse events (in alphabetical order) may be associated with the use of a coronary stent in native coronary arteries (including those listed in Table 2):

- Acute myocardial infarction
- Arrhythmias, including VF and VT
- Death
- Dissection
- Drug reactions to antiplatelet 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

## 7. CLINICAL STUDIES

A total of 1,241 patients were enrolled at 59 North American investigational sites in the multicenter ASCENT trial. Of these, 1040 patients with *de novo* native coronary artery lesions were randomized equally to receive the ACS MULTI-LINK™ Stent (n=520) and the Palmaz-Schatz Stent (n=520) in a parallel comparison, while an additional 201 primary restenosis patients were enrolled in a non-randomized arm to receive the ACS MULTI-LINK™ Stent. The primary endpoint of six month clinical target vessel failure was defined as the composite of death, myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass surgery (CABG), and percutaneous transluminal coronary angioplasty (PTCA), attributed to the target vessel. All major endpoints were adjudicated by a clinical events committee blinded to treatment assignment.

Eligible patients, with angina or positive functional study, were identified for elective stenting of a *de novo* native coronary artery lesion visually estimated to be between 3.0 and 3.75 mm in diameter and < 20 mm in length which would be covered by up to two 15 mm stents. These patients underwent standard balloon angioplasty after which a stent delivery system of the appropriate size was advanced and deployed. Additional non-compliant high pressure balloons with a balloon to artery ratio of 1.0-1.1:1.0 were utilized to attain optimal stent apposition.

The anticoagulation regimen administered to 98.8% of patients was aspirin 325 mg/day for at least one year and ticlopidine 250 mg bid for at least 30 days. At the discretion of the investigator, alternative therapy was allowed for non-optimal results which were defined as > 2 stents deployed, > 20% residual stenosis, any residual dissection, poor distal runoff or the presence of thrombus.

Follow-up intervals were 2, 4, and 6 weeks and 6, 9, and 12 months. The study randomization was successful as both treatment groups were demographically equivalent. All randomized patients were

included in the intent-to-treat efficacy analysis.

The ACS RX MULTI-LINK™ Stent was evaluated in a non-randomized registry of 202 patients at 18 investigational sites in the United States utilizing the same protocol criteria as the randomized trial and in addition included evaluating a 25 mm stent for lesions  $\leq$  22 mm in length.

**Table 4. Principal Effectiveness and Safety Results - Randomized Trial  
All Patients Treated (n=1040)**

**Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)**

<b>Effectiveness Measures</b>	<b>ACS MULTI-LINK</b>	<b>Palmaz-Schatz</b>	<b>Difference</b>
Device Success by QCA	97.4% [95.6%, 98.6%] (483/496)	96.8% [95.3%, 98.4%] (482/498)	0.6% [-1.5%, 2.7%]
Procedure Success by QCA	95.2% [92.9%, 96.9%] (472/496)	92.8% [90.1%, 94.9%] (462/498)	2.4% [-0.6%, 5.3%]
In-Stent % DS post procedure, mm*	8 ± 11% [-3.9%, 12%] (482/520)	10 ± 12% [-3.4%, 100%] (485/520)	-1.7%* [-3.1%, -0.2%]
In-Stent % DS at 9 month follow-up	32 ± 20% [-1.6%, 100%] (192/271)	34 ± 20% [-1.1%, 100%] (171/263)	-2.2% [-6.3%, 1.9%]
In-Stent Restenosis Rate (9 mo)	15.6% [13.5%, 25.0%] (30/192)	20.5% [14.7%, 27.3%] (35/174)	-4.5% [-12.4, 3.4%]
Target Site Revascularization Free (6 mo. K-M)	93.8% [91.4%, 96.2%]	93.3% [90.9%, 91.4%]	0.5% [-2.6%, 3.5%]
Target Vessel Failure Free (6 mo. K-M)	87.7% [84.8%, 90.6%]	86.9% [84.0%, 89.8%]	0.8% [-3.3%, 4.9%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.8% [3.1%, 7.0%] (25/520)	6.0% [4.1%, 8.4%] (31/520)	-1.2% [-3.9%, 1.6%]
Out-of-Hospital Clinical Event Rate	8.3% [6.0%, 11.0%] (43/520)	10.2% [7.7%, 13.1%] (53/520)	-1.9% [-5.4%, 1.6%]
Bleeding Complication Rate	0.8% [0.2%, 2.0%] (4/520)	1.3% [0.5%, 2.8%] (7/520)	-0.6% [-1.8%, 0.7%]
Vascular Event Rate	1.5% [0.7%, 3.0%] (8/520)	3.3% [1.9%, 5.2%] (17/520)	-1.7% [-3.6%, 0.1%]
Subacute Thrombosis Rate	0.6% [0.1%, 1.7%] (3/520)	1.9% [0.9%, 3.5%] (10/520)	-1.3% [-2.7%, 0.0%]
Survival at 30 days (K-M)*	100.0% [99.4%, 100.0%]	98.8% [97.8%, 99.8%]	1.2%* [0.2%, 2.1%]
Survival at 180 days (K-M)	99.4% [98.8%, 100.0%]	98.0% [96.8%, 99.2%]	1.3% [0.0%, 2.7%]
MACE Rate at 6 months	12.7% [10.0%, 15.0%] (66/520)	16.0% [12.9%, 19.4%] (83/520)	-3.3% [-7.5%, 1.0%]
Hospitalization Post-Intervention (days)	1.6 ± 1.6 [1.0, 18] (520/520)	1.7 ± 2.4 [1.0, 32] (520/520)	-0.01 [-0.34, 0.15]

*Device success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device alone (i.e. without the use of other types of stents or new balloon devices).*

*Procedure Success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device and any adjunctive device without death, coronary artery bypass surgery (CABG), or myocardial infarction (Q-wave or non-Q-wave) within seven days of the procedure*

*QCA = Quantitative coronary angiography*

*% DS = percent diameter stenosis by QCA.*

*Target Vessel Failure (TVF) = The composite of acute and late-term major events of death, CABG, Q-wave MI or non-Q-wave MI, and percutaneous transluminal coronary angioplasty (PTCA) attributable to the target vessel. (K-M = actuarial freedom-from TVF by Kaplan Meier survival analysis).*

*Target Site Revascularization (TSR) = Repeat PTCA or CABG to the original site of intervention. (K-M = actuarial freedom-from TSR by Kaplan Meier survival analysis).*

*MACE = Major Adverse Cardiac Event of death, Q-wave MI or non-Q-wave MI, CABG, or PTCA to the treated site.*

*In-Hospital Clinical Event = Any MACE occurring prior to hospital discharge.*

*Out of Hospital Clinical Event = Any MACE occurring from hospital discharge through up to one year of clinical follow-up.*

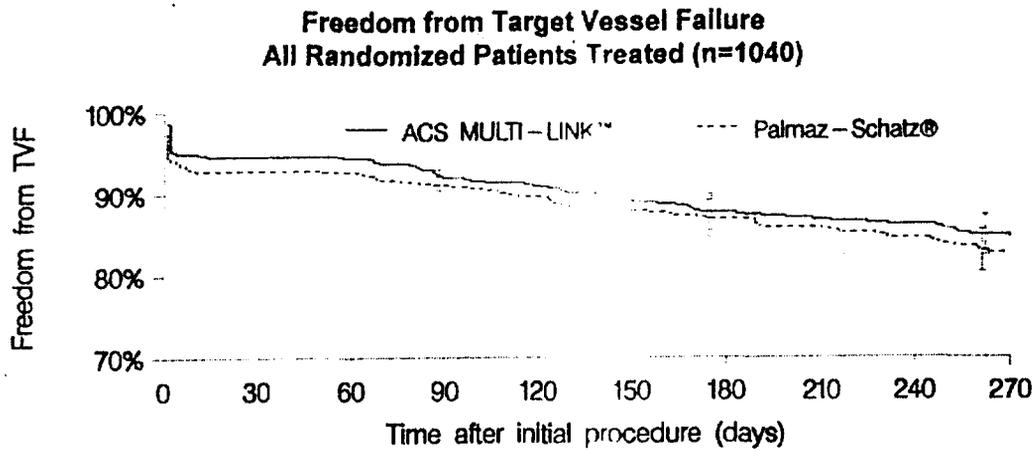
*Bleeding Complication = Blood loss necessitating a transfusion.*

*Vascular Event = Any hematoma > 5 cm, arteriovenous fistula, pseudoaneurysm, retroperitoneal bleed, peripheral nerve disorder and surgical repair.*

*Subacute Thrombosis = Any cardiac death, subacute closure requiring revascularization of the target site or total closure indicated by QCA within 30 days of the index intervention.*

*\* = difference is statistically significant, p-value < 0.05 (2-tailed) based on t-test or Chi-square analysis as appropriate.*

Figure 1. Freedom from Target Vessel Failure - All Randomized Patients



Kaplan Meier Survival Analysis - TVF free at 6 months difference [95% CI] of 0.8%[-3.3%, 4.9%]

	Time after initial procedure (days)									
	0	7	14	30	60	90	120	180	210	270
<b>ACS MULTI-LINK™</b>										
# At risk	513	492	490	490	469	455	448	418	388	295
# Events	7	26	28	28	29	40	45	62	65	74
% Survived	98.7%	95.0%	94.6%	94.6%	94.4%	92.2%	91.2%	87.7%	87.0%	84.8%
SE	0.5%	1.0%	1.0%	1.0%	1.0%	1.2%	1.3%	1.5%	1.5%	1.6%
<b>Palmaz-Schatz®</b>										
# At risk	506	484	482	482	469	458	450	424	390	298
# Events	14	36	38	38	39	47	54	68	73	84
% Survived	97.5%	93.3%	92.9%	92.9%	92.7%	91.1%	89.7%	86.9%	85.8%	83.0%
SE	0.7%	1.1%	1.1%	1.1%	1.1%	1.3%	1.3%	1.5%	1.6%	1.7%

**Tests Between Groups**

Test	Chi-Square	Deg Frdm	P-value
Log-Rank	1.37	1	0.24
Wilcoxon	1.38	1	0.24

12

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**Table 5. Principal Effectiveness and Safety Results - Restenosis Registry**

**All Patients Treated (n=721)**  
**Percent, Number/denominator, [95% confidence interval] or Mean ± SD (Number) {range}**

<b>Effectiveness Measures</b>	<b>Restenosis ACS MULTI-LINK (n=201)</b>	<b>De novo ACS MULTI-LINK (n=520)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	98.0%[94.9%, 99.4%] (193/197)	97.4% [95.6%, 98.6%] (483/496)	0.6%[-1.8%, 3.0%]
Procedure Success by QCA	94.9%[90.9%, 97.5%] (187/197)	95.2%[92.9%, 96.9%] (472/496)	0.0%[-3.7%, 3.6%]
In-Stent % DS post procedure, mm	8 ± 11% (-44%, 30%) (182/201)	8 ± 11% (-39%, 42%) (482/520)	-0.3%[-2.2%, 1.5%]
Target Site Revascularization Free (6 mo. K-M)	94.6%[91.3%, 97.9%]	93.8%[91.4%, 96.2%]	0.8%[-3.1%, 4.7%]
Target Vessel Failure Free (6 mo. K-M)	89.1%[84.6%, 93.6%]	87.7%[84.8%, 90.6%]	1.4%[-3.9%, 6.7%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.0%[1.7%, 7.7%] (8/201)	4.8%[3.1%, 7.0%] (25/520)	-0.8%[-4.1%, 2.4%]
Out-of Hospital Clinical Event Rate	7.5%[4.2%, 13.0%] (15/201)	8.3%[6.0%, 11.0%] (43/520)	-0.8%[-5.1%, 3.5%]
Bleeding Complication Rate	0.0%[0.0%, 0.5%] (0/201)	0.8% [0.2%, 2.0%] (4/520)	-0.8%[-1.5%, 0.0%]
Vascular Event Rate	1.0%[0.1%, 3.5%] (2/201)	1.5%[0.7%, 3.0%] (8/520)	-0.5%[-2.3%, 1.2%]
Subacute Thrombosis Rate	0.0%[0.0%, 0.5%] (0/201)	0.6%[0.1%, 1.7%] (3/520)	-0.6%[-1.2%, 0.1%]
Survival at 30 days (K-M)	100.0%[98.5%, 100.0%]	100.0%[99.4%, 100%]	0.0% [0.0%,0.0%]
Survival at 180 days (K-M)	99.4%[98.8%, 100.0%]	99.4%[98.8%, 100.0%]	0.0% [0.0%,0.0%]
MACE Rate at 6 months	10.4%[6.6%, 15.5%] (21/201)	12.7%[10.0%, 15.9%] (66/520)	-2.2%[-7.4%, 2.9%]
Hospitalization Post-Intervention (days)*	1.3±0.7[1.0, 5.0] (201/201)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.30*[-0.53,-0.08]

Refer to Table 4 footnotes for definitions.

**Table 6. Principal Effectiveness and Safety Results - ACS RX MULTI-LINK™ Registry**  
**ACS RX Registry patients and ACS Randomized patients, (n=722)**  
**Percent, [95% confidence interval] (Number/denominator) or mean ± SD [range] (Number)**

<b>Effectiveness Measures</b>	<b>RX ACS MULTI-LINK (n=202)</b>	<b>De novo ACS MULTI-LINK (n=520)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	100.0%[96.8%, 100.0%] (91/91)	97.4% [95.6%, 98.6%] (483/496)	2.6%[1.2%, 4.0%]
Procedure Success by QCA	96.7%[93.6, 98.9%] (88/91)	95.2%[92.9%, 96.9%] (472/496)	1.5%[-2.6%, 5.7%]
In-Stent % DS post procedure, mm	7 ± 10% (-21%, 29%) (87/202)	8 ± 11% (-39%, 42%) (482/520)	-0.8%[-3.2%, 1.6%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	3.0%[1.1%, 6.4%] (6/202)	4.8%[3.1%, 7.0%] (25/520)	-1.8%[-4.8%, 1.1%]
Out-of Hospital Clinical Event Rate (30 days)	0.5%[0.0%, 2.7%] (1/202)	0.2%[0.0%, 1.1%] (1/520)	0.3%[-0.7%, 1.3%]
Bleeding Complication Rate	0.5%[0.0%, 2.7%] (1/201)	0.8% [0.2%, 2.0%] (4/520)	-0.3%[-1.5%, 1.0%]
Vascular Event Rate	2.0%[0.5%, 5.0%] (4/202)	1.5%[0.7%, 3.0%] (8/520)	0.4%[-1.8%, 2.6%]
Subacute Thrombosis Rate	1.5%[0.3%, 4.3%] (3/202)	0.6%[0.1%, 1.7%] (3/520)	0.9%[-0.9%, 2.7%]
Survival at 30 days (K-M)	99.5%[98.7%, 100%] (200/202)	100.0%[99.4%, 100.0%] (520/520)	-0.5% [-1.5%, 0.5%]
MACE Rate at 30 days	3.5%[1.4%, 7.0%] (21/202)	5.0%[3.3%, 7.2%] (26/520)	-1.5%[-4.7%, 1.6%]
Hospitalization Post-Intervention (days)*	1.3±1.2[1.0, 5.0] (200/202)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.30*[-0.53,-0.08]

Refer to Table 4 footnotes for definitions.

**Table 7. Principal Effectiveness and Safety Results -  
ACS RX MULTI-LINK™ 25 mm vs. ACS MULTI-LINK™ 2x15 mm Registry (n=166)<sup>1</sup>  
Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)**

<b>Effectiveness Measures</b>	<b>RX ACS MULTI-LINK 25mm Stent (n=92)</b>	<b>De novo ACS MULTI-LINK 2 x 15m Stent (n=74)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	100%[92%, 100%] (36/36)	97.1%[90.1%, 99.7%] (68/70)	2.9%[-1.0%, 6.8%]
Procedure Success by QCA	97.2%[85.5%, 99.9%] (35/36)	95.7%[88.0%, 99.1%] (67/70)	1.5%[-5.7%, 8.7%]
In-Stent % DS post procedure, mm	7 ± 9% (-9%, 29%) (36/92)	10 ± 12% (-19%, 37%) (67/74)	-2.2%[-6.8%, 2.4%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	2.2%[0.3%, 7.6%] (2/92)	4.1%[0.8%, 11.4%] (3/74)	-1.9%[-7.3%, 3.5%]
Out-of Hospital Clinical Event Rate (30 days)	0.0%[0.0%, 3.2%] (0/92)	1.4%[0.0%, 7.3%] (1/74)	-1.4%[-4.0%, 1.3%]
Bleeding Complication Rate	0.0% [0.0%, 3.2%] (0/92)	0.0% [0.0%, 4.0%] (0/74)	0.0%[0.0%, 0.0%]
Vascular Event Rate	3.3%[0.7%, 9.2%] (3/92)	1.4%[0.0%, 7.3%] (1/74)	1.9%[-2.6%, 6.4%]
Subacute Thrombosis Rate	0.0%[0.0%, 3.2%] (0/92)	1.4%[0.0%, 7.3%] (1/74)	-1.4%[-4.0%, 1.3%]
Survival at 30 days (K-M)	100.0% [96.8%, 100.0%]	100.0% [99.4%, 100%]	0.0%[0.0%, 0.0%]
MACE Rate at 30 days	2.2% [0.3%, 7.6%] (2/92)	5.4% [1.5%, 13.3%] (4/74)	-3.2%[-9.2%, 2.7%]
Hospitalization Post-Intervention (days)*	1.06±0.41 [0.0, 4.0] (90/92)	1.64±1.59 [1.0, 11.0] (74/74)	-0.58*[-0.92, -0.24]

<sup>1</sup> = Subset analysis: 2 x 15 mm patients from Randomized Trial and 25 mm patients from RX Registry.

Refer to Table 4 footnotes for definitions

## 8. INDIVIDUALIZATION OF TREATMENT

The risks and benefits described above should be considered for each patient before use of the ACS RX MULTI-LINK™ CSS. Patient selection factors to be assessed should include a judgment regarding risk of antiplatelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

Premorbid conditions that increase the risk of a poor initial result or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed. The relationship of baseline and procedural variables to TVF was examined. The only statistically significant predictor of TVF was post-procedural Minimum Lumen Diameter (MLD), that is, TVF was less likely with larger MLD's.

Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3 mm, intra-procedural thrombus, or poor distal runoff and/or dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of a thrombus or dissection should be considered a marker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation.

### 8.1 Use in Special Populations

The safety and effectiveness of the ACS MULTI-LINK™ Stent have not been established in:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameter < 3 mm.
- Patients with lesions located in the left main coronary artery, ostial lesions or lesions located at a bifurcation.
- Patients with diffuse disease or poor outflow distal to the identified lesions.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with more than two overlapping stents due to risk of thrombosis and restenosis.
- Patients for longer than six months.

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters to treat in-stent stenosis has not been established.

## 9. HOW SUPPLIED

**STERILE.** This device is sterilized with ethylene oxide. Non-pyrogenic. Do not use if the package is opened or damaged.

**CONTENTS.** One (1) ACS MULTI-LINK™ Coronary Stent System

**STORAGE.** Store in a cool, dry, dark place.

## 10. OPERATOR'S MANUAL

### 10.1 INSPECTION PRIOR TO USE

Prior to using the ACS RX MULTI-LINK™ Coronary Stent System, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is centered on the balloon or located between the radiopaque balloon markers. Do not use if any defects are noted.

### 10.2 MATERIALS REQUIRED

Quantity	Material
	Appropriate guiding catheter(s)
2 - 3	10-20 cc syringes
1,000 u /500 cc	Heparinized Normal Saline (HepNS)
1	0.014 inch X 175 cm guide wire
1	Rotating hemostatic valve with 0.096 inch minimum inner diameter
	60% contrast diluted 1:1 with normal saline
1	Inflation device
1	Three-way stopcock
1	Torque device

### 10.3 PREPARATION

#### Guide Wire Lumen Flush

Step	Action
1.	Remove protective cover from tip.
2.	Flush guide wire lumen with HepNS until fluid exits guide wire exit notch.

#### Balloon Preparation

Step	Action
1.	Prepare inflation device / syringe with diluted contrast medium.
2.	Attach inflation device / syringe to stopcock; attach to inflation port.
3.	With tip down, orient Delivery System vertically.
4.	Open stopcock to Delivery System; pull negative for 30 seconds; release to neutral for contrast fill.
5.	Close stopcock to Delivery System; purge inflation device / syringe of all air.
6.	Repeat steps 3 through 5 until all air is expelled.  NOTE. If air is seen in shaft, repeat Balloon Preparation steps 3 through 6 to prevent uneven stent expansion.
7.	If a syringe was used, attach a prepared inflation device to stopcock.
8.	Open stopcock to Delivery System.
9.	Leave on neutral.

### 10.4 DELIVERY PROCEDURE

Step	Action
1.	Prepare vascular access site according to standard practice.
2.	Predilate lesion with PTCA catheter.
3.	Maintain neutral pressure on inflation device. Open rotating hemostatic valve as widely as possible.
4.	Backload Delivery System onto proximal portion of guide wire while maintaining guide wire position across target lesion.
5.	Advance Delivery System over guide wire to target lesion. Utilize radiopaque balloon markers to position stent across lesion; perform angiography to confirm stent position.  NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be <b>removed as a single unit</b> . See Stent/System Removal - Precautions section for specific Delivery system removal instructions.
6.	Tighten rotating hemostatic valve. Stent is now ready to be deployed.

**10.5 DEPLOYMENT PROCEDURE**

Step	Action
1.	<p><b>CAUTION.</b> Refer to Table 6 for <i>in vitro</i> stent outer diameter, deployment pressure, and RBP.</p> <p>Deploy stent slowly by pressurizing Delivery System in 2 atm increments, every 5 seconds, until stent is completely expanded. Maintain pressure for 30 seconds. <b>Do not exceed RBP or expand stent beyond 4.1 mm.</b></p>
2.	Deflate balloon by pulling negative on inflation device for 30 seconds.

**10.6 REMOVAL PROCEDURE**

Step	Action
1.	Ensure balloon is fully deflated.
2.	Fully open rotating hemostatic valve.
3.	<p>While maintaining guide wire position and negative pressure on inflation device, withdraw Delivery System.</p> <p>NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be <b>removed as a single unit</b>. See Stent/System Removal - Precautions section for specific Delivery system removal instructions.</p> <p>NOTE. If elastic membrane has stretched beyond distal tip post-stent implantation, it does not indicate any problem.</p>
4.	Tighten rotating hemostatic valve.
5.	<p>Repeat angiography to assess stented area.</p> <p>If necessary, post dilate within stent using PTCA catheter. Balloon inflations should incorporate balloon size closely matching vessel.</p>
6.	Final stent diameter should match reference vessel. <b>ASSURE STENT IS NOT UNDERDILATED.</b>

**10.7 IN VITRO INFORMATION**

**Table 8. Stent Outer Diameters for the ACS RX MULTI-LINK™ CSS.**  
Deployment pressures are highlighted and rated burst pressures (RBP) are marked.

Inflation Pressure (atm)	Stent Diameter (mm)	
	3.0	3.5
4	1.90	2.16
5	2.99	3.13
6	3.09 (15mm)	3.53 (15mm)
7	3.16 (25mm)	3.60 (25mm)
8	3.24 (RBP)	3.68 (RBP)
9	3.31	3.75
10	3.38	3.83
11	3.44	3.88
12	3.50	3.93
13	3.56	3.99
14	3.62	4.05

**NOTE.** These nominal, *in vitro* device specifications do not take into account lesion resistance. The stent sizing should be confirmed angiographically. Do not exceed the RBP or expand the stent beyond 4.1 mm.

**10.8 PATIENT INFORMATION:**

In addition to this Instructions for Use booklet, the ACS RX MULTI-LINK™ Coronary Stent System is packaged with additional patient specific information which include:

- A patient Implant Card that includes both patient and ACS MULTI-LINK™ Stent specific information. All patients will be expected to keep this card in their possession at all times for procedure / stent identification .
- A patient Teaching Guide which includes information on Guidant Corporation, the implant procedure and the ACS MULTI-LINK™ Stent
- A Device Tracking Form (Implant and Explant) which will be completed by the Hospital staff and forwarded to Guidant Corporation for the purposes of tracking all patients who receive an ACS MULTI-LINK™ Stent, as required by Federal regulation.

PATENTS

Manufactured under one or more of the following patents: United States, 4,323,071; 4,411,055; 4,571,240; 4,573,470; 4,581,017; 4,582,181; 4,597,755; 4,616,653; 4,619,263; 4,638,805; 4,641,654; 4,661,094; 4,664,113; 4,692,200; 4,748,982; 4,771,776; 4,771,777; 4,771,778; 4,775,371; 4,782,834; 4,790,315; 4,793,350; 4,821,722; 4,877,031; 4,892,519; 4,938,220; 4,940,062; 4,964,409; 4,976,720; 4,981,478; 4,998,917; 4,998,923; 5,002,532; 5,003,989; 5,034,001; 5,040,548; 5,042,985; 5,046,503; 5,061,273; 5,090,959; 5,135,535; 5,137,513; 5,154,725; 5,158,548; 5,159,937; 5,176,661; 5,195,971; 5,234,002; 5,242,394; 5,242,396; 5,242,399; 5,256,143; 5,279,562; 5,290,230; 5,300,025; 5,300,085; 5,316,706; 5,318,527; 5,324,259; 5,334,154; 5,342,621; 5,344,426; 5,344,426; 5,346,505; 5,348,537; 5,360,401; 5,369,401; 5,391,172; 5,409,495; 5,415,638; 5,421,955; 5,423,885; 5,437,083; 5,441,515; 5,443,458; 5,443,500; 5,456,667; 5,458,605; 5,458,615; 5,476,505; 5,507,768; RE 33,166; RE 34,564. Other U.S. patents pending. Foreign patents issued and pending.

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## Graphical Symbols for Medical Device Packaging

<b>STERILE</b>	<b>EO</b>
Sterilized with ethylene oxide gas.	
<b>LOT</b>	
Lot number	
	
Each device is for one (1) use only.	
	
Read instructions prior to use.	
	
Date of Manufacture	
	
Expires	
<b>REF</b>	
Catalog number	
<b>F</b>	
French size	

19 82

**ACS RX MULTI-LINK™ HP Coronary Stent System**

**Instructions For Use**

83  
60

# ACS RX MULTI-LINK HP™ Coronary Stent System

ACS Draft version, revised 9/29/97

Information for Prescribers

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**ACS RX MULTI-LINK HP™ Coronary Stent System (CSS)**  
**Information for Prescribers**

**1. DEVICE DESCRIPTION**

The ACS RX MULTI-LINK HP™ Coronary Stent System includes:

- A pre-mounted 316L stainless steel stent.
- An elastic membrane underneath the stent to aid in even stent expansion.
- Two radiopaque markers, located underneath the balloon, which fluoroscopically mark the ends of the stent.
- Two proximal Delivery System shaft markers, ( 95 and 105 cm from the distal tip).
- A third shaft marker denoting the guide wire exit notch

The ACS RX MULTI-LINK HP™ Coronary Stent System can be reinflated up to the rated burst pressure (RBP), without moving the placement of the balloon within the stent, to optimize stent apposition .

**Table 1. Device specifications**

Stent Diameter	Stent Length	Minimum Guiding Catheter Inner Diameter *	Stent Deployment Pressure	Rated Burst Pressure	Nominal Expanded Stent Length	Stent Free % Area
3.0 mm	15 mm	0.064 inch	11 atm	16 atm	14.6 mm	83.10 %
3.5 mm	15 mm	0.064 inch	11 atm	16 atm	14.3 mm	85.23 %
3.75 mm	15 mm	0.064 inch	11 atm	16 atm	14.0 mm	85.96 %

\* See individual manufacturer specifications for (Fr.) equivalent

**2. INDICATIONS**

The ACS RX MULTI-LINK HP™ Coronary Stent System is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 20 mm) with a reference vessel diameter ranging from 3.0 mm to 3.75 mm and is intended to improve coronary luminal diameter (See Individualization of Treatment). Long term outcome (beyond six months) for this permanent implant is unknown at present

**3. CONTRAINDICATIONS**

ACS RX MULTI-LINK HP™ Coronary Stent System is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion which prevents complete inflation of an angioplasty balloon.

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#### 4. WARNINGS

- Since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events, judicious selection of patients is necessary.
- Persons allergic to 316L stainless steel may suffer an allergic reaction to this implant.

#### 5. PRECAUTIONS

*(see also Individualization of Treatment)*

- Implantation of the stent should be performed only by physicians who have received appropriate training.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized ACS MULTI-LINK™ Stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition.

##### 5.1. *Stent Handling - Precautions*

- **For single use only. Do not resterilize or reuse. Note product "Use Before" date.**
- **Do not remove stent from its delivery balloon as removal may damage the stent and/or lead to stent embolization.**
- **Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during catheter removal from packaging, placement over guide wire and advancement through hemostasis valve adapter and guiding catheter hub.**
- **Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.**
- **Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.**

##### 5.2 *Stent Placement - Precautions*

- **Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use balloon purging technique described in the Instructions for Use.**
- **Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).**
- **When treating multiple lesions, the distal lesion should be initially stented, followed by**

stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

- Do not expand the stent if it is not properly positioned in the vessel. (See Stent/System Removal - Precautions)
- Placement of a stent has the potential to compromise side branch patency.
- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure as indicated on product label.** (See Balloon Inflated Diameter dimensions in Table 7). Use of pressures higher than specified on product label may result in a ruptured balloon with possible intimal damage and dissection.
- **Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgment of the stent from the balloon may occur.**
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

### 5.3 *Stent/System Removal - Precautions*

Should **unusual resistance** be felt at any time during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be removed as a single unit.

**When removing the Delivery System as a single unit:**

- **DO NOT** retract the Delivery System into the guiding catheter.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating hemostatic valve to secure the Delivery System to the guiding catheter; then remove the guiding catheter and Delivery System as a **single unit**.

Failure to follow these steps and/or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and/or delivery system components such as the balloon or the elastic membrane.

If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

### 5.4 *Post Implant - Precautions*

- Great care must be exercised when **crossing a newly deployed stent** with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry.
- **Do not perform a magnetic resonance imaging (MRI) scan on patients post-stent implantation until the stent has completely endothelialized (eight weeks) to minimize the potential for migration.** The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

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## 6. ADVERSE EVENTS

A total of 1593 patients were enrolled in five multicenter clinical trials to evaluate the use of the ACS MULTI-LINK™ Stent for treatment of symptomatic coronary artery disease. Of these, 1073 received the ACS MULTI-LINK™ Stent and 520 received the Palmaz-Schatz Stent. These patients form the basis for the observed events reported (see Clinical Studies).

### SUMMARY OF CLINICAL TRIAL PATIENT ENROLLMENTS (n=1,593)

	ACS MULTI-LINK STENT	CONTROL STENT	PATIENT TOTALS
Randomized Clinical Trial	520	520	1,040
Restenosis Registry	201	-	201
RX Registry	202	-	202
RX HP Registry	101	-	101
Feasibility Study	49	-	49
<b>PATIENT TOTALS:</b>	<b>1,073</b>	<b>520</b>	<b>1,593</b>

Twelve patients (12/1073 or 1.1%) who received the ACS MULTI-LINK™ Stent died during the clinical studies. One of these patients died within 30 days of receiving the stent implant as a result of a transfusion related grand mal seizure<sup>1</sup>. There were 11 late deaths which occurred between 58 and 353 days after stenting. Eight late deaths were cardiac related; congestive heart failure (n=4), chronic atrial fibrillation (n=1), sustained ventricular tachycardia (n=1), biventricular heart failure (n=1), and "sudden death" (n=1). Three late deaths were not cardiac related; ruptured abdominal aortic aneurysm (n=1), metastatic liver cancer (n=1) and suicide (n=1).

<sup>1</sup>One patient death < 30 days from the RX Registry

### 6.1 Observed Adverse Events

#### 6.1.1 Randomized Clinical Trial

In the randomized comparative clinical trial, the incidence of thrombosis in patients stented with the ACS MULTI-LINK™ Stent was 0.6% (3/520). All of these thromboses occurred within 24 hours of stent implantation. The incidence of vascular complications requiring surgical repair after stent placement in the randomized comparative clinical trial was 1.5% (8/520). The rates for bleeding requiring transfusion were 0.8% (4/520). Initial delivery failure occurred in 2.9% (15/520) of patients as follows: operator was unable to deliver the first stent (n=12), stent was not deployed at the lesion site (n=2), and inability to post dilate (n=1). Delivery of a second ACS MULTI-LINK™ Stent was successful in all but 1.5% (8/520) of patients.

#### 6.1.2 Rapid Exchange High Pressure Registry

The incidence of thrombosis in patients stented with the ACS RX MULTI-LINK HP™ Stent was 0% (0/101) in the non-randomized RX HP Registry. The incidence of vascular complications requiring surgical repair after stent placement was 3.0% (3/101), while the rate of bleeding requiring transfusion was 0% (0/101).

Delivery failure occurred in 2% (2/101) of patients as follows: inability to deliver a second stent (n=1),

inability to deliver the first stent (n=1), although delivery of a second stent was successful. Stent delivery was eventually successful in all but 1.0% (1/101) of patients

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**Table 2 - Principal Adverse Events at 6 Months**

%, [+ 95% confidence interval], Number/Denominator

Randomized *de novo* patients and non-randomized restenosis patients, (n = 1,241)

Complication	MULTI-LINK™ DE NOVO (n=520)	PalmaZ Schatz® DE NOVO (n=520)	MULTI-LINK™ RESTENOSIS (n=201)
Death Total	1.5% [0.7%, 3.0%], 8/520	3.1% [1.8%, 4.9%], 16/520	0.5% [0.0%, 2.7%], 1/201
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
30-Days	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.5% [0.7%, 3.0%], 8/520	1.9% [0.9%, 3.5%], 10/520	0.5% [0.0%, 2.7%], 1/201
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	4.6% [3.0%, 6.8%], 24/520	4.0% [1.7%, 7.7%], 8/201
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	4.0% [2.5%, 6.1%], 21/520	4.0% [1.7%, 7.7%], 8/201
Out-of-Hospital	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
CABG Total	2.5% [1.3%, 4.2%], 13/520	2.1% [1.1%, 3.8%], 11/520	1.0% [0.1%, 3.5%], 2/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.9% [0.9%, 3.5%], 10/520	1.3% [0.5%, 2.8%], 7/520	1.0% [0.1%, 3.5%], 2/201
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	1.9% [0.9%, 3.5%], 10/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.2% [0.0%, 1.1%], 1/520	1.0% [0.3%, 2.2%], 5/520	0.0% [0.0%, 1.5%], 0/201
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	1.3% [0.2%, 2.8%], 7/520	0.0% [0.0%, 1.5%], 0/201
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	3.3% [1.9%, 5.2%], 17/520	1.0% [0.1%, 3.5%], 2/201
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/201
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	3.7% [2.2%, 5.6%], 19/520	2.0% [0.5%, 5.0%], 4/201

<sup>1</sup> = One patients had two events; one in-hospital and one out-of-hospital.

**Table 3 - Principal Adverse Events at 30 days**

%, [+ 95% confidence interval], Number/Denominator

Randomized *de novo* patients and non-randomized *de novo* registry patients, (n = 621)

Complication	MULTI-LINK™ DE NOVO (n=520)	RX MULTI-LINK™ HP DE NOVO (n=101)
Death Total	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Out-of-Hospital 30 Days	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
Out-of-Hospital 30 Days	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	2.0% [0.2%, 7.0%], 2/101
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	2.0% [0.2%, 7.0%], 2/101
Out-of-Hospital 30 Days	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
CABG Total	2.5% [1.3%, 4.2%], 13/520	1.0% [0.0%, 5.4%], 1/101
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	1.0% [0.0%, 5.4%], 1/101
Out-of-Hospital 30 Days	1.9% [0.9%, 3.5%], 10/520	0.0% [0.0%, 2.9%], 0/101
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	0.0% [0.0%, 2.9%], 0/101
Out-of-Hospital 30 Days	0.2% [0.0%, 1.1%], 1/520	0.0% [0.0%, 2.9%], 0/101
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 2.9%], 0/101
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	0.0% [0.0%, 2.9%], 0/101
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	1.0% [0.0%, 5.4%], 1/101

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## 6.2 Potential Adverse Events

Adverse events (in alphabetical order) may be associated with the use of a coronary stent in native coronary arteries (including those listed in Table 2):

- Acute myocardial infarction
- Arrhythmias, including VF and VT
- Death
- Dissection
- Drug reactions to antiplatelet 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

## 7. CLINICAL STUDIES

A total of 1,241 patients were enrolled at 59 North American investigational sites in the multicenter ASCENT trial. Of these, 1040 patients with *de novo* native coronary artery lesions were randomized equally to receive the ACS MULTI-LINK™ Stent (n=520) and the Palmaz-Schatz Stent (n=520) in a parallel comparison, while an additional 201 primary restenosis patients were enrolled in a non-randomized arm to receive the ACS MULTI-LINK™ Stent. The primary endpoint of six month clinical target vessel failure was defined as the composite of death, myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass surgery (CABG), and percutaneous transluminal coronary angioplasty (PTCA), attributed to the target vessel. All major endpoints were adjudicated by a clinical events committee blinded to treatment assignment.

Eligible patients, with angina or positive functional study, were identified for elective stenting of a *de novo* native coronary artery lesion visually estimated to be between 3.0 and 3.75 mm in diameter and < 20 mm in length which would be covered by up to two 15 mm stents. These patients underwent standard balloon angioplasty after which a stent delivery system of the appropriate size was advanced and deployed. Additional non-compliant high pressure balloons with a balloon to artery ratio of 1.0-1.1:1.0 were utilized to attain optimal stent apposition.

The anticoagulation regimen administered to 98.8% of patients was aspirin 325 mg/day for at least one year and ticlopidine 250 mg bid for at least 30 days. At the discretion of the investigator, alternative therapy was allowed for non-optimal results which were defined as > 2 stents deployed, > 20% residual stenosis, any residual dissection, poor distal runoff or the presence of thrombus.

Follow-up intervals were 2, 4, and 6 weeks and 6, 9, and 12 months. The study randomization was successful as both treatment groups were demographically equivalent. All randomized patients were included in the intent-to-treat efficacy analysis.

The ACS RX MULTI-LINK™ HP Stent was evaluated in a non-randomized registry of 101 patients at 11 investigational sites in the United States utilizing the same protocol criteria as the randomized trial and allowing for post-dilatation with the delivery system balloon at up to 16 atm.

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**Table 4. Principal Effectiveness and Safety Results - Randomized Trial**

**All Patients Treated (n=1040)**  
**Percent, [95% confidence interval] (Number/denominator) or mean ± SD [range] (Number)**

Effectiveness Measures	ACS MULTI-LINK (n=520)	Palmaz-Schatz (n=520)	Difference
Device Success by QCA	97.4% [95.6%, 98.6%] (483/496)	96.8% [95.3%, 98.4%] (482/498)	0.6% [-1.5%, 2.7%]
Procedure Success by QCA	95.2% [92.9%, 96.9%] (472/496)	92.8% [90.1%, 94.9%] (462/498)	2.4% [-0.6%, 5.3%]
In-Stent % DS post procedure, mm*	8 ± 11% [-39%, 42%] (482/520)	10 ± 12% [-34%, 100%] (485/520)	-1.7%* [-3.1%, -0.2%]
In-Stent % DS at 9 month follow-up	32 ± 20% [-16%, 100%] (192/271)	34 ± 20% [-11%, 100%] (171/263)	-2.2% [-6.3%, 1.9%]
In-Stent Restenosis Rate (9 mo)	15.6% [13.5%, 15.0%] (30/192)	20.5% [14.7%, 27.3%] (35/174)	-4.5% [-12.4, 3.4%]
Target Site Revascularization Free (6 mo. K-M)	93.8% [91.4%, 96.2%]	93.3% [90.9%, 91.4%]	0.5% [-2.6%, 3.5%]
Target Vessel Failure Free (6 mo. K-M)	87.7% [84.8%, 90.6%]	86.9% [84.0, 89.8%]	0.8% [-3.3%, 4.9%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.8% [3.1%, 7.0%] (25/520)	6.0% [4.1%, 8.4%] (31/520)	-1.2% [-3.9%, 1.6%]
Out-of Hospital Clinical Event Rate	8.3% [6.0%, 11.0%] (43/520)	10.2% [7.7%, 13.1%] (53/520)	-1.9% [-5.4%, 1.6%]
Bleeding Complication Rate	0.8% [0.2%, 2.0%] (4/520)	1.3% [0.5%, 2.8%] (7/520)	-0.6% [-1.8%, 0.7%]
Vascular Event Rate	1.5% [0.7%, 3.0%] (8/520)	3.3% [1.9%, 5.2%] (17/520)	-1.7% [-3.6%, 0.1%]
Subacute Thrombosis Rate	0.6% [0.1%, 1.7%] (3/520)	1.9% [0.9%, 3.5%] (10/520)	-1.3% [-2.7%, 0.0%]
Survival at 30 days* (K-M)	100.0% [99.4%, 100.0%]	98.8% [97.8%, 99.8%]	1.2%* [-0.2%, -2.1%]
Survival at 180 days (K-M)	99.4% [98.8%, 100.0%]	98.0% [96.8%, 99.2%]	1.3% [0.0%, 2.7%]
MACE Rate at 6 months	12.7% [10.0%, 15.9%] (66/520)	16.0% [12.9%, 19.4%] (83/520)	-3.3% [-7.5%, 1.0%]
Hospitalization Post-Intervention (days)	1.6 ± 1.6 [1.0, 18] (520/520)	1.7 ± 2.4 [1.0, 32] (520/520)	-0.01 [-0.34, 0.15]

*Device success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device alone (i.e. without the use of other types of stents or new balloon devices).*

*Procedure Success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device and any adjunctive device without death, coronary artery bypass surgery (CABG), or myocardial infarction (Q-wave or non-Q-wave) within seven days of the procedure.*

*QCA = Quantitative coronary angiography*

*% DS = percent diameter stenosis by QCA.*

*Target Vessel Failure (TVF) = The composite of acute and late-term major events of death, CABG, Q-wave MI or non-Q-wave MI, and percutaneous transluminal coronary angioplasty (PTCA) attributable to the target vessel. (K-M =actuarial freedom-from TVF by Kaplan Meier survival analysis).*

*Target Site Revascularization (TSR) = Repeat PTCA or CABG to the original site of intervention. (K-M = actuarial freedom-from TSR by Kaplan Meier survival analysis).*

*MACE = Major Adverse Cardiac Event of death, Q-wave MI or non-Q-wave MI, CABG, or PTCA to the treated site.*

*In-Hospital Clinical Event = Any MACE occurring prior to hospital discharge.*

*Out of Hospital Clinical Event = Any MACE occurring from hospital discharge through up to one year of clinical follow-up.*

*Bleeding Complication = Blood loss necessitating a transfusion.*

*Vascular Event = Any hematoma > 5 cm, arteriovenous fistula, pseudoaneurysm, retroperitoneal bleed, peripheral nerve disorder and surgical repair.*

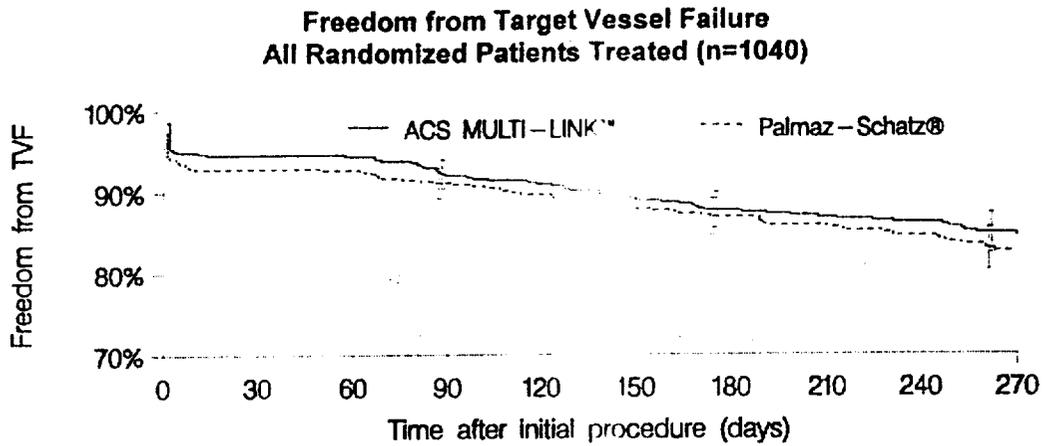
*Subacute Thrombosis = Any cardiac death, subacute closure requiring revascularization of the target site or total closure indicated by QCA within 30 days of the index intervention.*

*\* = difference is statistically significant, p-value < 0.05 (2-tailed) based on t-test or Chi-square analysis as appropriate.*

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**Figure 1. Freedom from Target Vessel Failure - All Randomized Patients**



Kaplan Meier Survival Analysis - TVF free at 6 months difference [95% CI] 0.4%[-3.8%, 4.6%]

	Time after initial procedure (days)									
	0	7	14	30	60	90	120	180	210	270
<b>ACS MULTI-LINK™</b>										
# At risk	513	492	490	490	469	455	448	418	388	295
# Events	7	26	28	28	29	40	45	62	65	74
% Survived	98.7%	95.0%	94.6%	94.6%	94.4%	92.2%	91.2%	87.7%	87.0%	84.8%
SE	0.5%	1.0%	1.0%	1.0%	1.0%	1.2%	1.3%	1.5%	1.5%	1.6%
<b>Palmaz-Schatz®</b>										
# At risk	506	484	482	482	469	458	450	424	390	298
# Events	14	36	38	38	39	47	54	68	73	84
% Survived	97.5%	93.3%	92.9%	92.9%	92.7%	91.1%	89.7%	86.9%	85.8%	83.0%
SE	0.7%	1.1%	1.1%	1.1%	1.1%	1.3%	1.3%	1.5%	1.6%	1.7%

**Tests Between Groups**

Test	Chi-Square	Deg Frdm	P-value
Log-Rank	1.37	1	0.24
Wilcoxon	1.38	1	0.24

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**Table 5. Principal Effectiveness and Safety Results - Restenosis Registry**  
**Percent, Number/denominator, [95% confidence interval] or Mean ± SD (Number) {range}**  
**All Patients Treated (n=721)**

<b>Effectiveness Measures</b>	<b>Restenosis ACS MULTI-LINK (n=520)</b>	<b>De novo ACS MULTI-LINK (n=520)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	98.0%[94.9%, 99.4%] (193/197)	97.4% [95.6%, 98.6%] (483/496)	0.6%[-1.8%, 3.0%]
Procedure Success by QCA	94.9%[90.9%, 97.5%] (187/197)	95.2%[92.9%, 96.9%] (472/496)	0.0%[-3.7%, 3.6%]
In-Stent % DS post procedure, mm	8 ± 11% (-44% - 40%) (182/201)	8 ± 11% (-39%, 42%) (482/520)	-0.3%[-2.2%, 1.5%]
Target Site Revascularization Free (6 mo. K-M)	94.6% [91.3%, 97.9%]	93.8% [91.4%, 96.2%]	0.8%[-3.1%, 4.7%]
Target Vessel Failure Free (6 mo. K-M)	89.1% [84.6%, 93.6%]	87.7% [84.8%, 90.6%]	1.4%[-3.9%, 6.7%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.0%[1.7%, 7.7%] (8/201)	4.8%[3.1%, 7.0%] (25/520)	-0.8%[-4.1%, 2.4%]
Out-of Hospital Clinical Event Rate	7.5%[4.2%, 11.0%] (15/201)	8.3%[6.0%, 11.0%] (43/520)	-0.8%[-5.1%, 3.5%]
Bleeding Complication Rate	0.0%[0.0%, 1.5%] (0/201)	0.8% [0.2%, 2.0%] (4/520)	-0.8%[-1.5%, 0.0%]
Vascular Event Rate	1.0%[0.1%, 1.9%] (2/201)	1.5%[0.7%, 3.0%] (8/520)	-0.5%[-2.3%, 1.2%]
Subacute Thrombosis Rate	0.0%[0.0%, 1.5%] (0/201)	0.6%[0.1%, 1.7%] (3/520)	-0.6%[-1.2%, 0.1%]
Survival at 30 days (K-M)	100% [98.5%, 100%]	100% [99.4%, 100%]	0.0% [0.0%, 0.0%]
Survival at 180 days (K-M)	99.4% [98.8%, 100%]	99.4% [98.8%, 100%]	0.0% [0.0%, 0.0%]
MACE Rate at 6 months	10.4%[6.6%, 15.5%] (21/201)	12.7%[10.0%, 15.9%] (66/520)	-2.2%[-7.4%, 2.9%]
Hospitalization Post-Intervention (days)*	1.3±0.7[1.0, 5.0] (201/201)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.30*[-0.53,-0.08]

**Refer to Table 4 footnotes for definitions.**

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71

**Table 6. Principal Effectiveness and Safety Results - ACS RX MULTI-LINK HP™ CSS Registry**  
 Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)  
 All Patients Treated (n=621)

<b>Effectiveness Measures</b>	<i>De novo</i> <b>ACS RX MULTI-LINK HP (n=101)</b>	<i>De novo</i> <b>ACS MULTI-LINK (n=520)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	98.0%[93.0%, 99.8%] (99/101)	97.4% [95.6%, 98.6%] (483/496)	-0.2%[-3.2%, 2.8%]
Procedure Success by QCA	98.0%[93.0%, 99.8%] (99/101)	95.2%[92.9%, 96.9%] (482/496)	3.1%[-0.4%, 6.5%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	2.0%[0.2%, 7.0%] (2/101)	4.8%[3.1%, 7.0%] (25/520)	-2.8%[-6.1%, 0.5%]
Out-of-Hospital Clinical Event Rate (30 days)	0.0%[0.0%, 2.6%] (0/101)	0.2%[0.0%, 1.1%] (1/520)	0.2%[-0.6%, 0.2%]
Bleeding Complication Rate	0.0%[0.0%, 2.6%] (0/101)	0.8% [0.2%, 2.0%] (4/520)	-0.8%[-1.5%, 0.0%]
Vascular Event Rate	3.0%[0.6%, 8.4%] (3/101)	1.5%[0.7%, 3.0%] (8/520)	1.4%[-2.0%, 4.9%]
Subacute Thrombosis Rate	0.0%[0.0%, 2.6%] (0/101)	0.6%[0.1%, 1.7%] (3/520)	-0.4%[-1.2%, 0.1%]
Survival at 30 days (K-M)	100.0% [97.1%, 100%]	100% [99.4%, 100%]	0.0% [-0.0%, 0.0%]
MACE Rate at 30 days	2.0%[0.2%, 7.1%] (2/101)	5.0%[3.3%, 7.2%] (26/520)	-3.0%[-6.3%, 0.3%]
Hospitalization Post-Intervention (days)*	1.3±1.6 [1.0, 5.0] (101/101)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.33*[-0.34,-0.31]

Refer to table 4 footnotes for definitions

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## 8. INDIVIDUALIZATION OF TREATMENT

The risks and benefits described above should be considered for each patient before use of the ACS MULTI-LINK™ CSS. Patient selection factors to be assessed should include a judgment regarding risk of antiplatelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

Premorbid conditions that increase the risk of a poor initial result or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed. The relationship of baseline and procedural variables to TVF was examined. The only statistically significant predictor of TVF was post-procedural Minimum Lumen Diameter (MLD), that is, TVF was less likely with larger MLD's.

Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3 mm, intra-procedural thrombus, or poor distal runoff and/or dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of a thrombus or dissection should be considered a marker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation.

### 8.1 Use in Special Populations

The safety and effectiveness of the ACS MULTI-LINK™ Stent have not been established in:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameter < 3 mm.
- Patients with lesions located in the left main coronary artery, ostial lesions or lesions located at a bifurcation.
- Patients with diffuse disease or poor outflow distal to the identified lesions.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with more than two overlapping stents due to risk of thrombosis and restenosis.
- Patients for longer than six months.

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters to treat in-stent stenosis has not been established.

## 9. HOW SUPPLIED

**STERILE.** This device is sterilized with ethylene oxide. Non-pyrogenic. Do not use if the package is opened or damaged.

**CONTENTS.** One (1) ACS MULTI-LINK™ Coronary Stent System

**STORAGE.** Store in a cool, dry, dark place.

**10. OPERATOR'S MANUAL**

**10.1 INSPECTION PRIOR TO USE**

Prior to using the ACS RX MULTI-LINK HP™ Coronary Stent System, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is centered on the balloon or located between the radiopaque balloon markers. Do not use if any defects are noted.

**10.2 MATERIALS REQUIRED**

Quantity	Material
	Appropriate guiding catheter(s)
2 - 3	10-20 cc syringes
1,000 u /500 cc	Heparinized Normal Saline (HepNS)
1	0.014 inch X 175 cm guide wire
1	Rotating hemostatic valve with 0.096 inch minimum inner diameter
	60% contrast diluted 1:1 with normal saline
1	Inflation device
1	Three-way stopcock
1	Torque device

**10.3 PREPARATION**

**Guide Wire Lumen Flush**

Step	Action
1.	Remove protective cover from tip.
2.	Flush guide wire lumen with HepNS until fluid exits guide wire exit notch.

**Balloon Preparation**

Step	Action
1.	Prepare inflation device / syringe with diluted contrast medium.
2.	Attach inflation device / syringe to stopcock; attach to inflation port.
3.	With tip down, orient Delivery System vertically.
4.	Open stopcock to Delivery System: pull negative for 30 seconds; release to neutral for contrast fill.
5.	Close stopcock to Delivery System; purge inflation device / syringe of all air.
6.	Repeat steps 3 through 6 until all air is expelled.
	NOTE: If air is seen in shaft, repeat Balloon Preparation steps 3 through 6 to prevent uneven stent expansion.
7.	If a syringe was used, attach a prepared inflation device to stopcock.
8.	Open stopcock to Delivery System
9.	Leave on neutral.

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#### 10.4 DELIVERY PROCEDURE

Step	Action
1.	Prepare vascular access site according to standard practice.
2.	Predilate lesion with PTCA catheter.
3.	Maintain neutral pressure on inflation device. Open rotating hemostatic valve as widely as possible.
4.	Backload Delivery System onto proximal portion of guide wire while maintaining guide wire position across target lesion.
5.	Advance Delivery System over guide wire to target lesion. Utilize radiopaque balloon markers to position stent across lesion; perform angiography to confirm stent position. NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent deployment, the entire system should be removed as a <b>single unit</b> . See Stent/System Removal - Precautions section for specific Delivery system removal instructions.
6.	Tighten rotating hemostatic valve. Stent is now ready to be deployed.

#### 10.5 DEPLOYMENT PROCEDURE

Step	Action
1.	<b>CAUTION.</b> Refer to Table 5 for <i>in vitro</i> stent outer diameter, deployment pressure, and RBP. Deploy stent slowly by pressurizing Delivery System in 2 atm increments, every 5 seconds, until stent is completely expanded. Maintain pressure for 30 seconds. <b>Do not exceed RBP or expand stent beyond 4.1 mm.</b> If necessary, without moving balloon within stent, the Delivery System can be reinflated to optimize stent apposition. <b>Do not exceed RBP or expand stent beyond 4.1 mm.</b>
2.	Deflate balloon by pulling negative on inflation device for 30 seconds.

#### 10.6 REMOVAL PROCEDURE

Step	Action
1.	Ensure balloon is fully deflated.
2.	Fully open rotating hemostatic valve
3.	While maintaining guide wire position and negative pressure on inflation device, withdraw Delivery System. NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be removed as a <b>single unit</b> . See Stent/System Removal - Precautions section for specific Delivery system removal instructions. NOTE. If elastic membrane has stretched beyond distal tip post-stent implantation, it does not indicate any problem.
4.	Tighten rotating hemostatic valve.
5.	Repeat angiography to assess stented area. If necessary, post dilate within stent using PTCA catheter. Balloon inflations should incorporate balloon size closely matching vessel.
6.	Final stent diameter should match reference vessel. <b>ASSURE STENT IS NOT UNDERDILATED.</b>

10.7 **IN VITRO INFORMATION**

**Table 7. Stent Outer Diameters for the ACS MULTI-LINK HP™ Coronary Stent System**  
Deployment pressures are highlighted and rated burst pressures (RBP) are marked.

Inflation Pressure (atm)	Stent Diameter(mm)		
	3.0	3.5	3.75
8	2.98	3.33	3.54
9	3.00	3.35	3.57
10	3.02	3.38	3.64
11	3.06	3.44	3.76
12	3.12	3.54	3.85
13	3.20	3.61	3.90
14	3.25	3.66	3.95
15	3.28	3.71	3.99
16	3.31 (RBP)	3.73 (RBP)	4.03 (RBP)
17	3.33	3.75	4.06
18	3.36	3.78	4.09

NOTE. These nominal, *in vitro* device specifications do not take into account lesion resistance. The stent sizing should be confirmed angiographically. Do not exceed the RBP or expand the stent beyond 4.1 mm.

10.8 **PATIENT INFORMATION:**

In addition to this Instructions for Use booklet, the ACS RX MULTI-LINK HP™ Coronary Stent System is packaged with additional patient specific information which include:

- A patient Implant Card that includes both patient and ACS MULTI-LINK™ Stent specific information. All patients will be expected to keep this card in their possession at all times for procedure / stent identification .
- A patient Teaching Guide which includes information on Guidant Corporation, the implant procedure and the ACS MULTI-LINK™ Stent
- A Device Tracking Form (Implant and Explant) which will be completed by the Hospital staff and forwarded to Guidant Corporation for the purposes of tracking all patients who receive an ACS MULTI-LINK™ Stent, as required by Federal regulation.

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## PATENTS

Manufactured under one or more of the following patents: United States, 4,323,071; 4,411,055; 4,571,240; 4,573,470; 4,581,017; 4,582,181; 4,597,755; 4,616,653; 4,619,263; 4,638,805; 4,641,654; 4,661,094; 4,664,113; 4,692,200; 4,748,982; 4,771,776; 4,771,777; 4,771,778; 4,775,371; 4,782,834; 4,790,315; 4,793,350; 4,821,722; 4,877,031; 4,892,519; 4,938,220; 4,940,062; 4,964,409; 4,976,720; 4,981,478; 4,998,917; 4,998,923; 5,002,532; 5,003,989; 5,034,001; 5,040,548; 5,042,985; 5,046,503; 5,061,273; 5,090,959; 5,135,535; 5,137,513; 5,154,725; 5,158,548; 5,159,937; 5,176,661; 5,195,971; 5,234,002; 5,242,394; 5,242,396; 5,242,399; 5,256,143; 5,279,562; 5,290,230; 5,300,025; 5,300,085; 5,316,706; 5,318,527; 5,324,259; 5,334,154; 5,342,621; 5,344,426; 5,344,426; 5,346,505; 5,348,537; 5,360,401; 5,369,401; 5,391,172; 5,409,495; 5,415,638; 5,421,955; 5,423,885; 5,437,083; 5,441,515; 5,443,458; 5,443,500; 5,456,667; 5,458,605; 5,458,615; 5,476,505; 5,507,768; RE 33,166; RE 34,564. Other U.S. patents pending. Foreign patents issued and pending.

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# Graphical Symbols for Medical Device Packaging

<b>STERILE</b>	<b>EO</b>
Sterilized with ethylene oxide gas.	
<b>LOT</b>	
Lot number	
	
Each device is for one (1) use only.	
	
Read instructions prior to use.	
	
Date of Manufacture	
	
Expires	
<b>REF</b>	
Catalog number	
<b>F</b>	
French size	

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**ACS OTW MULTI-LINK™ HP Coronary Stent System**

**Instructions For Use**

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# ACS OTW MULTI-LINK HP™ Coronary Stent System

ACS Draft version, revised 9/29/97

Information for Prescribers

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**ACS OTW MULTI-LINK HP™ Coronary Stent System (CSS)**  
**Information for Prescribers**

**1. DEVICE DESCRIPTION**

The ACS OTW MULTI-LINK HP™ Coronary Stent System includes:

- A pre-mounted 316L stainless steel stent.
- An elastic membrane underneath the stent to aid in even stent expansion.
- Two radiopaque markers, located underneath the balloon, which fluoroscopically mark the ends of the stent.
- Two proximal Delivery System shaft markers, (95 and 105 cm from the distal tip).

The ACS OTW MULTI-LINK HP™ Coronary Stent System can be reinflated up to the rated burst pressure (RBP), without moving the placement of the balloon within the stent, to optimize stent apposition

**Table 1. Device specifications**

Stent Diameter	Stent Length	Minimum Guiding Catheter Inner Diameter *	Stent Deployment Pressure	Rated Burst Pressure	Nominal Expanded Stent Length	Stent Free % Area
3.0 mm	15 mm	0.064 inch	11 atm	16 atm	14.6 mm	83.10 %
3.5 mm	15 mm	0.064 inch	11 atm	16 atm	14.3 mm	85.23 %
3.75 mm	15 mm	0.064 inch	11 atm	16 atm	14.0 mm	85.96 %

\* See individual manufacturer specifications for (Fr.) equivalent.

**2. INDICATIONS**

The ACS OTW MULTI-LINK HP™ Coronary Stent System is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 20 mm) with a reference vessel diameter ranging from 3.0 mm to 3.75 mm and is intended to improve coronary luminal diameter (See Individualization of Treatment). Long term outcome (beyond six months) for this permanent implant is unknown at present

**3. CONTRAINDICATIONS**

ACS OTW MULTI-LINK™ Coronary Stent System is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion which prevents complete inflation of an angioplasty balloon.

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#### 4. WARNINGS

- Since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events, judicious selection of patients is necessary.
- Persons allergic to 316L stainless steel may suffer an allergic reaction to this implant.

#### 5. PRECAUTIONS

*(see also Individualization of Treatment)*

- Implantation of the stent should be performed only by physicians who have received appropriate training.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized ACS MULTI-LINK™ Stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition.

##### 5.1. *Stent Handling - Precautions*

- **For single use only.** Do not resterilize or reuse. Note product "Use Before" date.
- **Do not remove stent from its delivery balloon** as removal may damage the stent and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during catheter removal from packaging, placement over guide wire and advancement through hemostasis valve adapter and guiding catheter hub.
- Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

##### 5.2 *Stent Placement - Precautions*

- **Do not prepare or pre-inflate balloon prior to stent deployment** other than as directed. Use balloon purging technique described in the Instructions for Use.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by

stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

- Do not expand the stent if it is not properly positioned in the vessel. (See Stent/System Removal - Precautions)
- Placement of a stent has the potential to compromise side branch patency.
- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure as indicated on product label.** (See Balloon Inflated Diameter dimensions in Table 7). Use of pressures higher than specified on product label may result in a ruptured balloon with possible intimal damage and dissection.
- **Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgment of the stent from the balloon may occur.**
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

### 5.3 *Stent/System Removal - Precautions*

Should **unusual resistance be felt at any time** during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be removed as a **single unit**.

**When removing the Delivery System as a single unit:**

- DO NOT retract the Delivery System into the guiding catheter.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating hemostatic valve to secure the Delivery System to the guiding catheter; then remove the guiding catheter and Delivery System as a **single unit**.

Failure to follow these steps and/or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and/or delivery system components such as the balloon or the elastic membrane.

If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

### 5.4 *Post Implant - Precautions*

- Great care must be exercised when **crossing a newly deployed stent** with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry.
- Do not perform a **magnetic resonance imaging (MRI)** scan on patients post-stent implantation until the stent has completely endothelialized (eight weeks) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

## 6. ADVERSE EVENTS

A total of 1593 patients were enrolled in five multicenter clinical trials to evaluate the use of the ACS MULTI-LINK™ Stent for treatment of symptomatic coronary artery disease. Of these, 1073 received the ACS MULTI-LINK™ Stent and 520 received the Palmaz-Schatz Stent. These patients form the basis for the observed events reported (see Clinical Studies).

### SUMMARY OF CLINICAL TRIAL PATIENT ENROLLMENTS (n=1,593)

	ACS MULTI-LINK STENT	CONTROL STENT	PATIENT TOTALS
Randomized Clinical Trial	520	520	1,040
Restenosis Registry	201	-	201
RX Registry	202	-	202
RX HP Registry	101	-	101
Feasibility Study	49	-	49
<b>PATIENT TOTALS:</b>	<b>1,073</b>	<b>520</b>	<b>1,593</b>

Twelve patients (12/1073 or 1.1%) who received the ACS MULTI-LINK™ Stent died during the clinical studies. One of these patients died within 30 days of receiving the stent implant as a result of a transfusion related grand mal seizure<sup>1</sup>. There were 11 late deaths which occurred between 58 and 353 days after stenting. Eight late deaths were cardiac related; congestive heart failure (n=4), chronic atrial fibrillation (n=1), sustained ventricular tachycardia (n=1), biventricular heart failure (n=1), and "sudden death" (n=1). Three late deaths were not cardiac related; ruptured abdominal aortic aneurysm (n=1), metastatic liver cancer (n=1) and suicide (n=1).

<sup>1</sup>One patient death < 30 days from the RX Registry (ACS 96-003)

### 6.1 Observed Adverse Events

#### 6.1.1 Randomized Clinical Trial

In the randomized comparative clinical trial (the ASCENT trial), the incidence of thrombosis in patients stented with the ACS MULTI-LINK™ Stent was 0.6% (3/520). All of these thromboses occurred within 24 hours of stent implantation. The incidence of vascular complications requiring surgical repair after stent placement in the randomized comparative clinical trial was 1.5% (8/520). The rate for bleeding requiring transfusion was 0.8% (4/520).

Initial delivery failure occurred in 2.9% (15/520) of patients as follows: operator was unable to deliver the first stent (n=12), stent was not deployed at the lesion site (n=2), inability to post dilate (n=1), and one balloon noted to be damaged before attempted delivery (n=1). Delivery of a second ACS MULTI-LINK™ Stent was successful in all but 1.5% (8/520) of patients.

#### 6.1.2 Rapid Exchange High Pressure Registry

The incidence of thrombosis in patients stented with the ACS RX MULTI-LINK HP™ Stent was 0% (0/101) in the non-randomized RX HP Registry. The incidence of vascular complications requiring surgical repair after stent placement was 3.0% (3/101) while the rate of bleeding requiring transfusion was 0% (0/101).

Delivery failure occurred in 2% (2/101) of patients as follows: inability to deliver a second stent (n=1), inability to deliver the first stent (n=1), although delivery of a second stent was successful. Stent delivery was eventually successful in all but 1.0% (1/101) of patients

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**Table 2 - Principal Adverse Events at 6 Months**

%, [+ 95% confidence interval], Number/Denominator

Randomized *de novo* patients and non-randomized restenosis patients, (n = 1,241)

Complication	MULTI-LINK™ DE NOVO (n=520)	Palmaz Schatz® DE NOVO (n=520)	MULTI-LINK™ RESTENOSIS (n=201)
Death Total	1.5% [0.7%, 3.0%], 8/520	3.1% [1.8%, 4.9%], 16/520	0.5% [0.0%, 2.7%], 1/201
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
30-Days	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.5% [0.7%, 3.0%], 8/520	1.9% [0.9%, 3.5%], 10/520	0.5% [0.0%, 2.7%], 1/201
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.0% [0.0%, 0.6%], 0/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	4.6% [3.0%, 6.8%], 24/520	4.0% [1.7%, 7.7%], 8/201
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	4.0% [2.5%, 6.1%], 21/520	4.0% [1.7%, 7.7%], 8/201
Out-of-Hospital	0.6% [0.1%, 1.7%], 3/520	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 1.5%], 0/201
CABG Total	2.5% [1.3%, 4.2%], 13/520	2.1% [1.1%, 3.8%], 11/520	1.0% [0.1%, 3.5%], 2/201
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	1.9% [0.9%, 3.5%], 10/520	1.3% [0.5%, 2.8%], 7/520	1.0% [0.1%, 3.5%], 2/201
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	1.9% [0.9%, 3.5%], 10/520 <sup>1</sup>	0.0% [0.0%, 1.5%], 0/201
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	1.2% [0.4%, 2.5%], 6/520	0.0% [0.0%, 1.5%], 0/201
Out-of-Hospital	0.2% [0.0%, 1.1%], 1/520	1.0% [0.3%, 2.2%], 5/520	0.0% [0.0%, 1.5%], 0/201
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	1.3% [0.2%, 2.8%], 7/520	0.0% [0.0%, 1.5%], 0/201
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	3.3% [1.9%, 5.2%], 17/520	1.0% [0.1%, 3.5%], 2/201
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 1.5%], 0/201
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	3.7% [2.2%, 5.6%], 19/520	2.0% [0.5%, 5.0%], 4/201

<sup>1</sup> = One patient had two events; one in-hospital and one out-of-hospital.

**Table 3 - Principal Adverse Events at 30 days**

%, [+ 95% confidence interval], Number/Denominator

Randomized *de novo* patients and non-randomized *de novo* registry patients, (n = 621)

Complication	MULTI-LINK™ DE NOVO (n=520)	RX MULTI-LINK™ HP DE NOVO (n=101)
Death Total	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Early (In-Hospital)	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Out-of-Hospital 30 Days	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Q-Wave MI	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
Out-of-Hospital 30 Days	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Non-Q-Wave Total	4.0% [2.5%, 6.1%], 21/520	2.0% [0.2%, 7.0%], 2/101
Early (In-Hospital)	3.5% [2.1%, 5.4%], 18/520	2.0% [0.2%, 7.0%], 2/101
Out-of-Hospital 30 Days	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
CABG Total	2.5% [1.3%, 4.2%], 13/520	1.0% [0.0%, 5.4%], 1/101
Early (In-Hospital)	0.6% [0.1%, 1.7%], 3/520	1.0% [0.0%, 5.4%], 1/101
Out-of-Hospital 30 Days	1.9% [0.9%, 3.5%], 10/520	0.0% [0.0%, 2.9%], 0/101
Stent Thrombosis Total	0.6% [0.1%, 1.7%], 3/520	0.0% [0.0%, 2.9%], 0/101
Early (In-Hospital)	0.4% [0.0%, 1.4%], 2/520	0.0% [0.0%, 2.9%], 0/101
Out-of-Hospital 30 Days	0.2% [0.0%, 1.1%], 1/520	0.0% [0.0%, 2.9%], 0/101
Bleeding Complications	0.8% [0.2%, 2.0%], 4/520	0.0% [0.0%, 2.9%], 0/101
Vascular Complications	1.5% [0.7%, 3.0%], 8/520	0.0% [0.0%, 2.9%], 0/101
Cerebrovascular accident	0.0% [0.0%, 0.6%], 0/520	0.0% [0.0%, 2.9%], 0/101
Stent Delivery Failure	1.5% [0.7%, 3.0%], 8/520	1.0% [0.0%, 5.4%], 1/101

## 6.2 Potential Adverse Events

Adverse events (in alphabetical order) may be associated with the use of a coronary stent in native coronary arteries (including those listed in Table 2):

- Acute myocardial infarction
- Arrhythmias, including VF and VT
- Death
- Dissection
- Drug reactions to antiplatelet 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

## 7. CLINICAL STUDIES

A total of 1,241 patients were enrolled at 59 North American investigational sites in the multicenter ASCENT trial. Of these, 1040 patients with *de novo* native coronary artery lesions were randomized equally to receive the ACS MULTI-LINK™ Stent (n=520) and the Palmaz-Schatz Stent (n=520) in a parallel comparison, while an additional 201 primary restenosis patients were enrolled in a non-randomized arm to receive the ACS MULTI-LINK™ Stent. The primary endpoint of six month clinical target vessel failure was defined as the composite of death, myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass surgery (CABG), and percutaneous transluminal coronary angioplasty (PTCA), attributed to the target vessel. All major endpoints were adjudicated by a clinical events committee blinded to treatment assignment.

Eligible patients, with angina or positive functional study, were identified for elective stenting of a *de novo* native coronary artery lesion visually estimated to be between 3.0 and 3.75 mm in diameter and < 20 mm in length which would be covered by up to two 15 mm stents. These patients underwent standard balloon angioplasty after which a stent delivery system of the appropriate size was advanced and deployed. Additional non-compliant high pressure balloons with a balloon to artery ratio of 1.0-1.1:1.0 were utilized to attain optimal stent apposition.

The anticoagulation regimen administered to 98.8% of patients was aspirin 325 mg/day for at least one year and ticlopidine 250 mg bid for at least 30 days. At the discretion of the investigator, alternative therapy was allowed for non-optimal results which were defined as > 2 stents deployed, > 20% residual stenosis, any residual dissection, poor distal runoff or the presence of thrombus.

Follow-up intervals were 2, 4, and 6 weeks and 6, 9, and 12 months. The study randomization was successful as both treatment groups were demographically equivalent. All randomized patients were included in the intent-to-treat efficacy analysis.

The ACS RX MULTI-LINK™ HP Stent, which has the identical distal end as the ACS OTW MULTI-LINK™ CSS, was evaluated in a non-randomized registry of 101 patients at 11 investigational sites in the United States utilizing the same protocol criteria as the randomized trial and allowing for post-dilatation with the delivery system balloon at up to 16 atm.

**Table 4. Principal Effectiveness and Safety Results - Randomized Trial**

**All Patients Treated (n=1040)**  
**Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)**

Effectiveness Measures	ACS MULTI-LINK (n=520)	Palmaz-Schatz (n=520)	Difference
Device Success by QCA	97.4% [95.6%, 98.6%] (483/496)	96.8% [95.3%, 98.4%] (482/498)	0.6% [-1.5%, 2.7%]
Procedure Success by QCA	95.2% [92.9%, 96.9%] (472/496)	92.8% [90.1%, 94.9%] (462/498)	2.4% [-0.6%, 5.3%]
In-Stent % DS post procedure, mm*	8 ± 11% [-39%, 32%] (482/520)	10 ± 12% [-34%, 100%] (485/520)	-1.7%* [-3.1%, -0.2%]
In-Stent % DS at 9 month follow-up	32 ± 20% [-16%, 100%] (192/271)	34 ± 20% [-11%, 100%] (171/263)	-2.2% [-6.3%, 1.9%]
In-Stent Restenosis Rate (9 mo)	15.6% [13.5%, 18.0%] (30/192)	20.5% [14.7%, 27.3%] (35/174)	-4.5% [-12.4, 3.4%]
Target Site Revascularization Free (6 mo. K-M)	93.8% [91.4%, 96.2%]	93.3% [90.9%, 91.4%]	0.5% [-2.6%, 3.5%]
Target Vessel Failure Free (6 mo. K-M)	87.7% [84.8%, 90.6%]	86.9% [84.0%, 89.8%]	0.8% [-3.3%, 4.9%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.8% [3.1%, 7.0%] (25/520)	6.0% [4.1%, 8.4%] (31/520)	-1.2% [-3.9%, 1.6%]
Out-of Hospital Clinical Event Rate	8.3% [6.0%, 11.0%] (43/520)	10.2% [7.7%, 13.1%] (53/520)	-1.9% [-5.4%, 1.6%]
Bleeding Complication Rate	0.8% [0.2%, 1.0%] (4/520)	1.3% [0.5%, 2.8%] (7/520)	-0.6% [-1.8%, 0.7%]
Vascular Event Rate	1.5% [0.7%, 2.9%] (8/520)	3.3% [1.9%, 5.2%] (17/520)	-1.7% [-3.6%, 0.1%]
Subacute Thrombosis Rate	0.6% [0.1%, 1.7%] (3/520)	1.9% [0.9%, 3.5%] (10/520)	-1.3% [-2.7%, 0.0%]
Survival at 30 days (K-M) *	100.0% [99.4%, 100.0%]	98.8% [97.8%, 99.8%]	1.2%* [0.2%, 2.1%]
Survival at 180 days (K-M)	99.4% [98.8%, 100.0%]	98.0% [96.8%, 99.2%]	1.3% [0.0%, 2.7%]
MACE Rate at 6 months	12.7% [10.0%, 15.9%] (66/520)	16.0% [12.9%, 19.4%] (83/520)	-3.3% [-7.5%, 1.0%]
Hospitalization Post-Intervention (days)	1.6 ± 1.6 [1.0, 18] (520/520)	1.7 ± 2.4 [1.0, 32] (520/520)	-0.01 [-0.34, 0.15]

*Device success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device alone (i.e. without the use of other types of stents or new balloon devices).*

*Procedure Success = Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device and any adjunctive device without death, coronary artery bypass surgery (CABG), or myocardial infarction (Q-wave or non-Q-wave) within seven days of the procedure.*

*QCA = Quantitative coronary angiography*

*% DS = percent diameter stenosis by QCA.*

*Target Vessel Failure (TVF) = The composite of acute and late-term major events of death, CABG, Q-wave MI or non-Q-wave MI, and percutaneous transluminal coronary angioplasty (PTCA) attributable to the target vessel. (K-M = actuarial freedom-from TVF by Kaplan Meier survival analysis).*

*Target Site Revascularization (TSR) = Repeat PTCA or CABG to the original site of intervention. (K-M = actuarial freedom-from TSR by Kaplan Meier survival analysis).*

*MACE = Major Adverse Cardiac Event of death, Q-wave MI or non-Q-wave MI, CABG, or PTCA to the treated site.*

*In-Hospital Clinical Event = Any MACE occurring prior to hospital discharge.*

*Out of Hospital Clinical Event = Any MACE occurring from hospital discharge through up to one year of clinical follow-up.*

*Bleeding Complication = Blood loss necessitating a transfusion.*

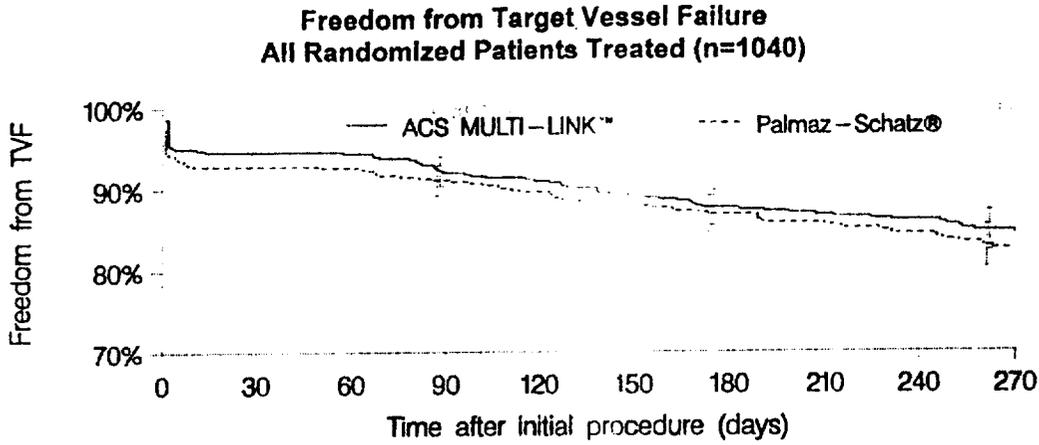
*Vascular Event = Any hematoma > 5 cm, arteriovenous fistula, pseudoaneurysm, retroperitoneal bleed, peripheral nerve disorder and surgical repair.*

*Subacute Thrombosis = Any cardiac death, subacute closure requiring revascularization of the target site or total closure indicated by QCA within 30 days of the index intervention.*

*\* = difference is statistically significant, p-value < 0.05 (2-tailed) based on t-test or Chi-square analysis as appropriate.*

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**Figure 1. Freedom from Target Vessel Failure - All Randomized Patients**



Kaplan Meier Survival Analysis - TVF free at 6 months difference [95% CI] 0.4%[-3.8%, 4.6%]

	Time after initial procedure (days)									
	0	7	14	30	60	90	120	180	210	270
<b>ACS MULTI-LINK™</b>										
# At risk	513	492	490	490	469	455	448	418	388	295
# Events	7	26	28	28	29	40	45	62	65	74
% Survived	98.7%	95.0%	94.6%	94.6%	94.4%	92.2%	91.2%	87.7%	87.0%	84.8%
SE	0.5%	1.0%	1.0%	1.0%	1.0%	1.2%	1.3%	1.5%	1.5%	1.6%
<b>Palmaz-Schatz®</b>										
# At risk	506	484	482	482	469	458	450	424	390	298
# Events	14	36	38	38	39	47	54	68	73	84
% Survived	97.5%	93.3%	92.9%	92.9%	92.7%	91.1%	89.7%	86.9%	85.8%	83.0%
SE	0.7%	1.1%	1.1%	1.1%	1.1%	1.3%	1.3%	1.5%	1.6%	1.7%

**Tests Between Groups**

Test	Chi-Square	Deg Frdm	P-value
Log-Rank	1.37	1	0.24
Wilcoxon	1.38	1	0.24

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**Table 5. Principal Effectiveness and Safety Results - Restenosis Registry**

**All Patients Treated (n=721)**  
**Percent, Number/denominator, [95% confidence interval] or Mean ± SD (Number) (range)**

<b>Effectiveness Measures</b>	<b>Restenosis ACS MULTI-LINK (n=201)</b>	<b>De novo ACS MULTI-LINK (n=520)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	98.0% [94.9%, 99.4%] (193/197)	97.4% [95.6%, 98.6%] (483/496)	0.6% [-1.8%, 3.0%]
Procedure Success by QCA	94.9% [90.9%, 97.5%] (187/197)	95.2% [92.9%, 96.9%] (472/496)	0.0% [-3.7%, 3.6%]
In-Stent % DS post procedure, mm	8 ± 11% (-44%, 30%) (182/201)	8 ± 11% (-39%, 42%) (482/520)	-0.3% [-2.2%, 1.5%]
Target Site Revascularization Free (6 mo. K-M)	94.6% [91.3%, 97.9%]	93.8% [91.4%, 96.2%]	0.8% [-3.1%, 4.7%]
Target Vessel Failure (6 mo. K-M)	89.1% [84.6%, 93.6%]	87.7% [84.8%, 90.6%]	1.4% [-3.9%, 6.7%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	4.0% [1.7%, 7.0%] (8/201)	4.8% [3.1%, 7.0%] (25/520)	-0.8% [-4.1%, 2.4%]
Out-of Hospital Clinical Event Rate	7.5% [4.2%, 10.0%] (15/201)	8.3% [6.0%, 11.0%] (43/520)	-0.8% [-5.1%, 3.5%]
Bleeding Complication Rate	0.0% [0.0%, 1.5%] (0/201)	0.8% [0.2%, 2.0%] (4/520)	-0.8% [-1.5%, 0.0%]
Vascular Event Rate	1.0% [0.1%, 2.5%] (2/201)	1.5% [0.7%, 3.0%] (8/520)	-0.5% [-2.3%, 1.2%]
Subacute Thrombosis Rate	0.0% [0.0%, 1.5%] (0/201)	0.6% [0.1%, 1.7%] (3/520)	-0.6% [-1.2%, 0.1%]
Survival at 30 days (K-M)	100% [98.5%, 100%]	100% [99.4%, 100%]	0.0% [0.0%, 0.0%]
Survival at 180 days (K-M)	99.4% [98.8%, 100%]	99.4% [98.8%, 100%]	0.0% [0.0%, 0.0%]
MACE Rate at 6 months	10.4% [6.6%, 15.5%] (21/201)	12.7% [10.0%, 15.9%] (66/520)	-2.2% [-7.4%, 2.9%]
Hospitalization Post-Intervention (days)*	1.3 ± 0.7 [1.0, 5.0] (201/201)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.30* [-0.53, -0.08]

Refer to Table 4 footnotes for definitions.

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**Table 6. Principal Effectiveness and Safety Results - ACS RX MULTI-LINK HP™ CSS Registry**

**All Patients Treated (n=621)**

**Percent, [95% confidence interval] (Number/denominator) or mean ± SD {range} (Number)**

<b>Effectiveness Measures</b>	<b><i>De novo</i> ACS RX MULTI-LINK HP (n=101)</b>	<b><i>De novo</i> ACS MULTI-LINK (n=520)</b>	<b>Difference (95% CI's)</b>
Device Success by QCA	98.0%[93.0%, 99.8%] (99/101)	97.4% [95.6%, 98.6%] (483/496)	-0.2%[-3.2%, 2.8%]
Procedure Success by QCA	98.0%[93.0%, 99.8%] (99/101)	95.2%[92.9%, 96.9%] (482/496)	3.1%[-0.4%, 6.5%]
<b>Safety Measures</b>			
In-Hospital Clinical Event Rate	2.0%[0.2%, 7.0%] (2/101)	4.8%[3.1%, 7.0%] (25/520)	-2.8%[-6.1%, 0.5%]
Out-of Hospital Clinical Event Rate (30 days)	0.0%[0.0%, 2.9%] (0/101)	0.2%[0.0%, 1.1%] (1/520)	0.2%[-0.6%, 0.2%]
Bleeding Complication Rate	0.0%[0.0%, 2.9%] (0/101)	0.8% [0.2%, 2.0%] (4/520)	-0.8%[-1.5%, 0.0%]
Vascular Event Rate	3.0%[0.6%, 8.4%] (3/101)	1.5%[0.7%, 3.0%] (8/520)	1.4%[-2.0%, 4.9%]
Subacute Thrombosis Rate	0.0%[0.0%, 2.9%] (0/101)	0.6%[0.1%, 1.7%] (3/520)	-0.4%[-1.2%, 0.1%]
Survival at 30 days (K-M)	100% [97.1%, 100%]	100% [99.4%, 100%]	0.0% [-0.0%,0.0%]
MACE Rate at 30 days	2.0%[0.2%, 7.0%] (2/101)	5.0%[3.3%, 7.2%] (26/520)	-3.0%[-6.3%, 0.3%]
Hospitalization Post-Intervention (days)*	1.3±1.6 [1.0, 5.0] (101/101)	1.6 ± 1.6 [1.0, 18] (520/520)	-0.33*[-0.34,-0.31]

Refer to Table 4 footnotes for definitions

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## 8. INDIVIDUALIZATION OF TREATMENT

The risks and benefits described above should be considered for each patient before use of the ACS MULTI-LINK™ CSS. Patient selection factors to be assessed should include a judgment regarding risk of antiplatelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

Premorbid conditions that increase the risk of a poor initial result or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed. The relationship of baseline and procedural variables to TVF was examined. The only statistically significant predictor of TVF was post-procedural Minimum Lumen Diameter (MLD), that is, TVF was less likely with larger MLD's.

Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3 mm, intra-procedural thrombus, or poor distal runoff and/or dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of a thrombus or dissection should be considered a marker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation.

### 8.1 Use in Special Populations

The safety and effectiveness of the ACS MULTI-LINK™ Stent have not been established in:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameter < 3 mm.
- Patients with lesions located in the left main coronary artery, ostial lesions or lesions located at a bifurcation.
- Patients with diffuse disease or poor outflow distal to the identified lesions.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with more than two overlapping stents due to risk of thrombosis and restenosis.
- Patients for longer than six months.

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters to treat in-stent stenosis has not been established.

## 9. HOW SUPPLIED

**STERILE.** This device is sterilized with ethylene oxide. Non-pyrogenic. Do not use if the package is opened or damaged.

**CONTENTS.** One (1) ACS MULTI-LINK™ Coronary Stent System

**STORAGE.** Store in a cool, dry, dark place.

## 10. OPERATOR'S MANUAL

### 10.1 INSPECTION PRIOR TO USE

Prior to using the ACS OTW MULTI-LINK HP™ Coronary Stent System, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is centered on the balloon or located between the radiopaque balloon markers. Do not use if any defects are noted.

### 10.2 MATERIALS REQUIRED

Quantity	Material
	Appropriate guiding catheter(s)
2 - 3	10-20 cc syringes
1,000 u /500 cc	Heparinized Normal Saline (HepNS)
1	0.014 inch X 175 cm extendable or 0.014 inch X 300 cm guide wire
1	Rotating hemostatic valve with 0.096 inch minimum inner diameter
	60% contrast diluted 1:1 with normal saline
1	Inflation device
1	Three-way stopcock
1	Torque device
1	Guide wire introducer

### 10.3 PREPARATION

#### Guide Wire Lumen Flush

Step	Action
1.	Remove protective cover from tip.
2.	Attach syringe with HepNS to guide wire port.
3.	Flush until fluid exits distal tip.

#### Balloon Preparation

Step	Action
1.	Prepare inflation device / syringe with diluted contrast medium.
2.	Attach inflation device / syringe to stopcock; attach to inflation port.
3.	With tip down, orient Delivery System vertically.
4.	Open stopcock to Delivery System: pull negative for 30 seconds; release to neutral for contrast fill.
5.	Close stopcock to Delivery System: purge inflation device / syringe of all air.
6.	Repeat steps 3 through 5 until all air is expelled.
	NOTE. If air is seen in shaft, repeat Balloon Preparation steps 3 through 6 to prevent uneven stent expansion.
7.	If a syringe was used, attach prepared inflation device to stopcock.
8.	Open stopcock to Delivery System.
9.	Leave on neutral.

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10.4 **DELIVERY PROCEDURE**

Step	Action
1.	Prepare vascular access site according to standard practice.
2.	Predilate lesion with PTCA catheter.
3.	Prepare guide wire for extension.
4.	Maintain neutral pressure on inflation device. Open rotating hemostatic valve as widely as possible.
5.	Backload Delivery System onto proximal portion of guide wire while maintaining guide wire position across target lesion.
6.	Advance Delivery System over guide wire to target lesion. Utilize radiopaque balloon markers to position stent across lesion; perform angiography to confirm stent position. NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be removed as a <b>single unit</b> . See Stent/System Removal - Precautions section for specific Delivery system removal instructions.
7.	Tighten rotating hemostatic valve. Stent is now ready to be deployed.

10.5 **DEPLOYMENT PROCEDURE**

Step	Action
1.	<b>CAUTION.</b> Refer to Table 5 for <i>in vitro</i> stent outer diameter, deployment pressure, and RBP. Deploy stent slowly by pressurizing Delivery System in 2 atm increments, every 5 seconds, until stent is completely expanded. Maintain pressure for 30 seconds. <b>Do not exceed RBP or expand stent beyond 4.1 mm.</b> NOTE. If necessary, without moving balloon within stent, the Delivery System can be reinflated to optimize stent apposition. <b>Do not exceed RBP or expand stent beyond 4.1 mm.</b>
2.	Deflate balloon by pulling negative on inflation device for 30 seconds.

10.6 **REMOVAL PROCEDURE**

Step	Action
1.	Ensure balloon is fully deflated.
2.	Fully open rotating hemostatic valve
3.	While maintaining guide wire position and negative pressure on inflation device, withdraw Delivery System.  NOTE. Should <b>unusual resistance</b> be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be removed as a <b>single unit</b> . See Stent/System Removal - Precautions section for specific Delivery system removal instructions.  NOTE. If elastic membrane has stretched beyond distal tip post-stent implantation, it does not indicate any problem.
4.	Tighten rotating hemostatic valve.
5.	Repeat angiography to assess stented area.  If necessary, post dilate within stent using PTCA catheter. Balloon inflations should incorporate balloon size closely matching vessel.
6.	Final stent diameter should match reference vessel. <b>ASSURE STENT IS NOT UNDERDILATED.</b>

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**10.7 IN VITRO INFORMATION**

**Table 7. Stent Outer Diameters for the ACS OTW MULTI-LINK HP™ CSS.**  
Deployment pressures are highlighted and rated burst pressures (RBP) are marked.

Inflation Pressure (atm)	Stent Diameter (mm)		
	3.0	3.5	3.75
8	2.98	3.33	3.54
9	3.00	3.35	3.57
10	3.02	3.38	3.64
11	3.06	3.44	3.76
12	3.12	3.54	3.85
13	3.20	3.61	3.90
14	3.25	3.66	3.95
15	3.28	3.71	3.99
16	3.31 (RBP)	3.73 (RBP)	4.03 (RBP)
17	3.33	3.75	4.06
18	3.36	3.78	4.09

**NOTE.** These nominal, *in vitro* device specifications do not take into account lesion resistance. The stent sizing should be confirmed angiographically. Do not exceed the RBP or expand the stent beyond 4.1 mm.

**10.8 PATIENT INFORMATION:**

In addition to this Instructions for Use booklet, the ACS OTW MULTI-LINK HP™ Coronary Stent System is packaged with additional patient specific information which include:

- A patient Implant Card that includes both patient and ACS MULTI-LINK™ Stent specific information. All patients will be expected to keep this card in their possession at all times for procedure / stent identification .
- A patient Teaching Guide which includes information on Guidant Corporation, the implant procedure and the ACS MULTI-LINK™ Stent
- A Device Tracking Form (Implant and Explant) which will be completed by the Hospital staff and forwarded to Guidant Corporation for the purposes of tracking all patients who receive an ACS MULTI-LINK™ Stent, as required by Federal regulation.

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PATENTS

Manufactured under one or more of the following patents: United States, 4,323,071; 4,411,055; 4,571,240; 4,573,470; 4,581,017; 4,582,181; 4,597,755; 4,616,653; 4,619,263; 4,638,805; 4,641,654; 4,661,094; 4,664,113; 4,692,200; 4,748,982; 4,771,776; 4,771,777; 4,771,778; 4,775,371; 4,782,834; 4,790,315; 4,793,350; 4,821,722; 4,877,031; 4,892,519; 4,938,220; 4,940,062; 4,964,409; 4,976,720; 4,981,478; 4,998,917; 4,998,923; 5,002,532; 5,003,989; 5,034,001; 5,040,548; 5,042,985; 5,046,503; 5,061,273; 5,090,959; 5,135,535; 5,137,513; 5,154,725; 5,158,548; 5,159,937; 5,176,661; 5,195,971; 5,234,002; 5,242,394; 5,242,396; 5,242,399; 5,256,143; 5,279,562; 5,290,230; 5,300,025; 5,300,085; 5,316,706; 5,318,527; 5,324,259; 5,334,154; 5,342,621; 5,344,426; 5,344,426; 5,346,505; 5,348,537; 5,360,401; 5,369,401; 5,391,172; 5,409,495; 5,415,638; 5,421,955; 5,423,885; 5,437,083; 5,441,515; 5,443,458; 5,443,500; 5,456,667; 5,458,605; 5,458,615; 5,476,505; 5,507,768; RE 33,166; RE 34,564. Other U.S. patents pending. Foreign patents issued and pending.

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# Graphical Symbols for Medical Device Packaging

<b>STERILE</b>	<b>EO</b>
Sterilized with ethylene oxide gas.	
<b>LOT</b>	
Lot number	
	
Each device is for one (1) use only.	
	
Read instructions prior to use.	
	
Date of Manufacture	
	
Expires	
<b>REF</b>	
Catalog number	
<b>F</b>	
French size	

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