



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Public Health Service

MAY 14 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

WARNING LETTER

VIA FEDERAL EXPRESS  
VIA FACSIMILE

Ronald W. Dollens  
President and Chief Executive Officer  
Guidant Corporation  
111 Monument Circle 29<sup>th</sup> Floor  
P.O. Box 44906  
Indianapolis, Indiana 46244

Dear Mr. Dollens:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration has reviewed some of the promotional materials pertaining to Guidant's ACS Rx Multi-Link™ Coronary Stent System. The stent is a device within the meaning of section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). It was approved for marketing pursuant to the approval of a premarket approval application, designated P970020. The device is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 20mm) 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 is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* and restenotic native coronary artery lesions (length < 22mm) with a reference vessel diameter ranging from 3.0 mm to 3.5 mm and is intended to improve coronary luminal diameter.

The system was approved as a restricted device. The sale, distribution and use of the device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Act under the authority of section 515(d)(1)(B)(ii) of the Act. The device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the labeling must specify the requirements that apply to the training of practitioners who may use the device as approved in the approval order and insofar as the sale and distribution of the device must not violate sections 502(q) and (r) of the Act.

The promotional materials that we reviewed consist of the November and December 1997 issues of "ACS Multi-Link Stent™ Newsletter," a brochure entitled, "Restenosis. All Stents are NOT Created Equal" and a document called, "Stenting in 1998." As discussed

below, these materials present misleading and inappropriate statements about, and comparisons involving, Guidant's RX Multi-Link stent.

The November 11 newsletter contains a statement that "the Instructions for Use state a minimum deployment pressure of 6 ATM and 7 ATM for the 15mm and 25mm, respectively. The preceptors have compiled a significant amount of experience and recommend using 8ATM to 10 ATM routinely to ensure full apposition of the stent to the vessel wall." It also says "Deploy the stent at least 8 ATM and up to 10 ATM." However, the approved labeling contains a chart at item 10.7 that indicates that the deployment pressure should be 6 or 7 ATM and that the rated burst pressure will be exceeded after 8 ATM. The explicit advice to deploy the stent at between 8 and 10 ATM is a change affecting the safety of the device and requires the submission of a PMA supplement, as provided by the agency's regulations at 21 CFR 814.39. That regulation requires that after FDA approval of a PMA, an applicant shall submit to the agency for review and approval a PMA supplement for changes affecting the safety or effectiveness of a device, unless the change is of a type for which FDA has provided an alternate submission.

The December issue includes a discussion of "What happens if my vessel turns out to be less than 3.0mm?" However, the approved labeling contains a statement that the product is indicated for use in patients . . . with "a reference vessel diameter ranging from 3.0 mm to 3.5 mm . . ." The labeling includes a statement that "The safety and effectiveness of the ACS MULTI-LINK™ Stent have not been established in patients with coronary artery reference vessel diameter <3 mm." The explicit reference to use in a diameter outside the range included in the product's approved indications for use has changed the intended use for the product.

FDA's regulations at 21 CFR 801.4 provide that the intended use of a device refers to the objective intent of the persons responsible for the labeling of a device. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. The objective intent may be shown by, for example, labeling claims, advertising matter or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised.

Guidant's Multi-Link stent is misbranded within the meaning of section 502(a) of the Act because the promotional materials contain information that is inconsistent with the approved labeling for the product and in direct contradiction to it. It is misbranded within the meaning of 502(o) of the Act because no notice or other information respecting it was submitted to FDA as required by section 510(k) of the Act.

The product is adulterated within the meaning of section 501(f)(1)(B) of the Act because it is a class III device without an approved application for premarket approval in effect as required by section 515(a) of the Act and without an approved investigational device exemption in effect as required by 520(g) of the Act. As noted above, FDA's regulations

at 21 CFR 814.39 require that for a device with an approved premarket approval application, changes that affect the safety or effectiveness of the device require the submission of a supplemental application. The changes that you have made in the labeling affect the safety and effectiveness of your device.

This letter is not intended to be an all-inclusive list of deficiencies associated with your device. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter may also be reflected in other promotional and advertising materials used by your firm. You are responsible for investigating and reviewing all materials to ensure compliance with applicable regulations.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by FDA without further notice. These actions include, but are not limited to, seizure, injunction and/or civil money penalties.

Please notify this office in writing, within 15 working days of your receipt of this letter, of the specific steps you have taken to correct the noted violations. Your response should include steps being taken to address any misleading information currently in the marketplace that has resulted from your marketing campaign and steps you plan to prevent similar violations in the future. If corrective action cannot be completed within 15 working days, please state the reason for the delay and the time within which the corrections will be completed.

In addition to the claims that we have cited above, we have some concerns about the comparative claims that you have made between your device and the AVE Micro II stent. Your document, "Stenting in 1998," compares your product with the AVE Micro II stent. The charts that you present as data in your promotional brochure are misleading. The results of the studies are not the results of head-to-head studies so the comparisons are not appropriate. Your package insert states that the clinical studies conducted to evaluate the use of the ACS Multi-Link Stent for treatment of symptomatic coronary artery disease included patients who received the ACS Multi-Link Stent and patients who received the Palmaz-Schatz balloon-expandable Stent. There were no studies that directly compared the use of the ACS Multi-Link stent with the use of the AVE stent, a comparison which you do make in your charts. It is not clear that any of the stents with which you compare your product were ever tested in head to head studies against your company's device.

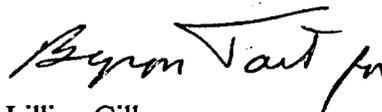
Further, neither the studies of AVE nor those of Guidant had as their primary endpoint an angiographic measure. We have been advised by CDRH's Office of Device Evaluation that for both AVE and Guidant clinical trials, the primary endpoint variables were the Target Vessel Revascularization and the Target Vessel Failure at six months, and that the difference in these rates for both trials was not statistically significant. The performances of the two stents were similar. Thus, your comparisons are misleading. This means that the chart, in your brochure, "Restenosis. All Stents are NOT Created Equal," referring to angiographic restenosis rate may present a very biased sample and not support your

comparison. Further, the angiographic follow-up in the trials you used was obtained from a subset of patients that does not represent a significant percentage of the trial participants.

While these last two items do not pose clear violations of the Act, please respond to these issues as well. Your response to this letter should be sent to Deborah Wolf, Regulatory Counsel, Promotion and Advertising Policy Staff (HFZ-302), Office of Compliance, Center for Devices and Radiological Health, 2098 Gaither Road, Rockville, Maryland 20850.

A copy of this letter is being sent to FDA's Detroit District Office. Please send a copy of your response to the Director, Detroit District Office, Food and Drug Administration (HFR-MW140), 1560 E. Jefferson Avenue, Detroit, Michigan 48207-3179.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Lillian Gill". The signature is written in a cursive style with a large, sweeping initial "L".

Lillian Gill  
Director  
Office of Compliance  
Center for Devices and  
Radiological Health