Cordis Corporation
14201 N.W. 60th Avenue
Miami Lakes FL 33014

July 7, 2003

Dear Colleague:

Subacute Thrombosis in Association with CYPHER™ Coronary Stents – What is Known?
Since the introduction of the CYPHER™ Sirolimus-eluting Coronary Stent in the United States on April 24, 2003, it is estimated that over 50,000 patients have received a CYPHER™ Stent. We have received adverse event reports of stent thrombosis occurring at the time of implantation or within a few days of implantation. Some centers have reported multiple events.

Thrombosis is a rare complication of any coronary stenting procedure. In completed and ongoing clinical trials of the CYPHER™ Stent inside and outside of the U.S., the rate of stent thrombosis appears to have been similar to that of a bare metal stent. We are carefully reviewing the adverse event reports received from U.S. centers to try to determine if the thrombosis rate in current clinical experience differs from the rate in clinical studies completed pre-approval.

As part of our previous commitments, we are undertaking a post-marketing registry in the U.S., which will be started in July 2003, to help assess the experience with actual clinical use of the CYPHER™ Stent. Cordis Corporation, in cooperation with FDA, will continue to monitor the information that is received and promptly inform you about any new findings.

Based on the reports so far, factors impacting the rate of thrombosis may include failure to achieve adequate stent apposition (due to under-deployment) or suboptimal use of antiplatelet medication. In addition, Cordis Corporation has become aware that some interventionalists have been over-expanding smaller stents for use in larger diameter vessels. Overexpansion of stents beyond their intended diameter may negatively affect performance and is not advisable. Due to the extremely high demand for the CYPHER™ Stent, Cordis Corporation concentrated its manufacturing efforts on the 2.5 mm and 3.0 mm diameter CYPHER™ Stents to serve the patient populations with the greatest perceived potential benefit. We have recently started to introduce the 3.5 mm CYPHER™ Stents.

What You Should Do

1. Follow the Instructions for Use

To help ensure that your experience is similar to that observed in pre-approval clinical trials, we strongly advise you to use the product in accordance with the Indications for Use and procedures contained in the package insert. Please take particular note of the following:

- *Select the appropriate stent size*
  We recommend that the stent size match the reference vessel diameter as closely as possible. The 2.5 mm and 3.0 mm diameter CYPHER™ Stents are based on a 6-cell design; the 3.5 mm diameter CYPHER™ Stent is based on a 7-cell design. Use of a CYPHER™ Stent in a vessel larger than the nominal stent diameter could adversely affect the stent's performance. We recommend that you NOT use the smaller stents for larger vessels.

- *Select appropriate patients*
  The CYPHER™ Stent is indicated for improving coronary luminal diameter in patients with symptomatic ischemic disease due to discrete de novo lesions of lengths ≤ 30 mm in native coronary arteries with reference vessel diameters of ≥ 2.5 mm to ≤ 3.5 mm. The CYPHER™ Stent is NOT indicated for the treatment of restenosis, nor has it been adequately evaluated for use in acute myocardial infarction, saphenous vein graft lesions, or bifurcation lesions. The safety and effectiveness of the CYPHER™ Stent have not been established for these situations.

- *Use an adequate antiplatelet regimen*
  In certain in vitro laboratory settings, sirolimus has been shown to potentiate the effect of some platelet agonists. While the clinical significance of the effect is unknown, it is advis able to be sure the patient is receiving a fully effective antiplatelet regimen, including an ade quate pre-medication period or optimal loading dose. Administration of continued antiplatelet therapy for three (3) months post-stenting is considered critical.

- *Use the proper technique for stent deployment*
  - Be sure that the stent is fully deployed and in contact with the vessel wall. Poor stent apposition due to under-deployment is a factor that can increase the thrombosis risk for any coronary stent.
  - Predilate the lesion with a PTCA catheter. The CYPHER™ Stent is not approved for direct stenting. The longitudinal length of pre-dilatation by the PTCA balloon should be limited to avoid creating a region of vessel injury that is outside the boundaries of the CYPHER™ Stent upon deployment.

2. Report Your Experience

In most product development programs, rare side effects are difficult to detect, and their risks for special populations are difficult to assess. Therefore, as a matter of course, it is important for you to report any product complaints and adverse events directly to Cordis by:

- **Telephone to Customer Service at** 1-800-327-7714

Further, you should follow the reporting procedures established by your facility in accordance with the Safe Medical Devices Act of 1990 (SMDA), which requires hospitals and other user facilities to reports deaths and serious injuries associated with the use of medical devices. You may also report adverse events directly to FDA/MedWatch by:

- **Telephone** at 1-800-FDA-1088 (1-800-332-1088)
- **Fax** at 1-800-FDA-0178 (1-800-332-0178)
- **Online** at www.fda.gov/MedWatch
- **Mail** postage paid MedWatch form

For more information, visit the MedWatch website at **www.fda.gov/MedWatch.**

Please feel free to contact Cordis Corporation for any questions you may have on the subject matter of this letter. We, in cooperation with FDA, will continue to keep you updated with the latest information.

Sincerely,

Dennis Donohoe, M.D.
Vice President, Therapeutics and Clinical Research
Cordis Corporation