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March 30, 2000

John M. Treacy, Director
Advisors and Consultants Staff
Room 1093
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

Subject: **NDA 20-807/S-004**
Refludan® [lepirudin (rDNA) for injection]

Briefing Document for Cardiovascular and Renal Drugs Advisory Committee Meeting May 2, 2000

Dear Mr. Treacy,

Quintiles, Inc., as the US agent for Aventis Pharmaceuticals, Inc. (formerly Hoechst Marion Roussel) has been authorized to communicate with the FDA regarding the above referenced NDA supplement.

In accordance with the December 1999 draft guideline on the public disclosure of materials provided to advisory committees in connection with open advisory committee meetings, we are submitting the Sponsor's final Briefing Document which is prepared for the May 2, 2000 meeting of the Cardiovascular and Renal Drugs Advisory Committee on Refludan for acute coronary syndromes. This submission consists of one volume in duplicate that is **fully releasable** plus 23 desk copies for distribution to the Advisory Committee and Gastrointestinal and Coagulation Drug Products Division

This document was prepared to consistently reflect the data that was submitted in the original efficacy supplement. At the same time it contains some additional analyses and text changes to make the document more complete (shaded areas). Our aim has been to make the briefing document as clear and comprehensive as possible. We thus sought and received constructive comments and suggestions from internal and external advisors and experts. The additional analyses and text changes are responses to the questions and suggestions they raised and are based on the original data (no new data has been presented) and comparisons to the literature. We believe the current document more fully and thoroughly addresses the same questions other readers would raise.

Prior to the finalization of the Briefing Document, draft copies were submitted, March 13, 2000, to the Division of Gastrointestinal and Coagulation Drug Products for review and comments. As requested by the Division at the end of their review, we would like to bring to the attention of the

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advisory committee members the fact that the Division did not review the additional analyses and accompanying text in time for inclusion in their Briefing Document. To be consistent and logically follow the information discussed in the Sponsor's Briefing Document, some of the additional analyses are planned in the Sponsor's presentation on May 2, 2000.

Please contact me if you have any questions regarding this submission.

Sincerely,

Philip R. Kastner

Philip R. Kastner, Ph.D. – (816) 767-6685
Regulatory and Technical Services
Quintiles, Inc.
10245 Hickman Mills Drive
Kansas City, MO 64137-1418

cc: Two archival plus twenty-three desk copies to John M. Treacy

FDA Cardiovascular and Renal Drugs Advisory Committee
May 2, 2000

Briefing Document Concerning

Refludan® (lepirudin)

in

Acute Coronary Syndromes:

Unstable Angina and Acute Myocardial Infarction without Persistent ST Elevation

30 March 2000