CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 20913/S001

ADMINISTRATIVE DOCUMENTS

MAR 2 3 1999

CSO Review of Draft Labeling
NDA 20-912/S-001 and NDA 20-913/S-001

Date of Supplements: October 16, 1998

Date of Review: March 8, 1999

Applicant Name: Merck Research Laboratories

Products: Aggrastat (tirofiban) Injection, 12.5 mg/50 ml Vial (NDA 20-912)

Aggrastat (tirofiban) Injection Premixed, 25 mg/500 ml IntraVia ™ Container (NDA 20-913)

Evaluation:

These submissions provide for changes to the **CLINICAL PHARMACOLOGY** and **DOSAGE AND ADMINISTRATION** sections of the labeling and supportive data for the changes. The changes are as follows:

1. ' has been changed to "controlled' in the first sentence of the second paragraph following Table 2 in the *Clinical Trials*/**CLINICAL PHARMACOLOGY** subsection, because it is redundant.

2. The last sentence of the *Precautions*/**DOSAGE AND ADMINISTRATION** subsection has been changed from the following:

   to the following:

   Any unused solution should be discarded.

3. The first sentence in the second paragraph of the *Directions for Use*/**DOSAGE AND ADMINISTRATION** subsection has been changed from the following:

   to the following:

AGGRASTAT Injection Premixed is supplied as 500 mL of 0.9% sodium chloride containing 50 μg/mL tirofiban.

4. The following sentence has been added as the last paragraph of the *Directions for Use*/**DOSAGE AND ADMINISTRATION** subsection:

   AGGRASTAT may be administered in the same intravenous line as dopamine, lidocaine, potassium chloride, and PEPCID* (famotidine) Injection.

Medical Review

Dr. Throckmorton reviewed the proposed clinical changes and found them to be acceptable.

Pharmacology Review

Dr. Stolzenberg reviewed the proposed changes and found them to be acceptable.

Chemistry Review

In his review, dated February 17, 1999, Mr. Advani states that, in the original October 16, 1998 submission, the firm provides data to support the proposed intravenous compatibility statement. He further notes that on February 12, 1999, in response to his request for information, the sponsor also provides a description of the methods used and sample chromatograms from the compatibility studies, as well as the rationale for limiting these studies to a maximum four hour duration. In addition, the sponsor also provides references to the stability studies data that justified the elimination of the precaution to discard any unused solution after 24 hours. Finally, the sponsor also clarifies the chemical structure. I discussed the supplement and his review with Mr. Advani and he believes all of the changes made to the **DOSAGE AND ADMINISTRATION** section are acceptable.

Recommendation:

I recommend that the Division issue an approvable letter for this supplement, as set forth under 21 CFR 314.70 (b) (3). The letter should require the sponsor to submit FPL identical to the submitted draft labeling.

/S/
Colleen LoCicero, CSO

cc: orig NDA 20-912
orig NDA 20-913
HFD-110
HFD-110/LoCicero

RHPC Review of Final Printed Labeling

NDA 20-912/S-001

NDA 20-913/S-001

JUL – 9 1999

Date of submission:	May 19, 1999
Date of review:	June 24, 1999
Applicant Name:	Merck Research Laboratories
Products:	Aggrastat (tirofiban) Injection, 12.5 mg/50 ml Vial (NDA 20-912)
	Aggrastat (tirofiban) Injection Premixed, 25 mg/500 ml IntraVia ™ Container (NDA 20-913)

Evaluation:

I reviewed the submitted final printed labeling in its entirety for both applications and found the labeling to be identical in content to the October 16, 1998 submitted draft labeling, as was requested by the Agency in our March 23, 1999 approvable letter, with an exception. Changes to the **ADVERSE REACTIONS** section that were submitted on February 17, 1999 in 'Special Supplements-Changes Being Effected' and subsequently approved on June 9, 1999 are also included in the May 19, 1999 submitted final printed labeling.

Recommendation:

I recommend that the Division issue an approval letter for this submission, as set forth under 21 CFR 314.70(b)(3).

/S/

Colleen LoCicero, RHPC

cc: orig NDA 20-912
orig NDA 20-913
HFD-110
HFD-110/LoCicero
HFD-110/ABlount