DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-839/S-033

Sanofi-Aventis Inc.
Attention: Mr. John Cook
300 Somerset Corporate Boulevard
P.O. Box 6977
Bridgewater, NJ, 08807

Dear Mr. Cook:

Please refer to your supplemental new drug application dated August 4, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plavix (clopidogrel bisulfate) 75 mg Tablets.

This supplemental new drug application provides the following changes to the **ADVERSE REACTIONS: Postmarketing Experience** section of the package insert:

Under the **ADVERSE REACTION; Post-marketing Experience** section, the following terms:

serum sickness
acute liver failure
interstitial pneumonitis
toxic epidermal necrolysis
stomatitis

were added based on your post-marketing safety surveillance database. The entire section was changed from:

- *Body as a whole:*
  - hypersensitivity reactions, anaphylactoid reactions
- *Central and Peripheral Nervous System disorders:*
  - confusion, hallucinations, taste disorders
- *Hepato-biliary disorders:*
  - abnormal liver function test, hepatitis (non-infectious)
- *Platelet, Bleeding and Clotting disorders:*
  - cases of bleeding with fatal outcome (especially intracranial, gastrointestinal and retroperitoneal hemorrhage)
  - agranulocytosis, aplastic anemia/pancytopenia, thrombotic thrombocytopenic purpura (TTP) – some cases with fatal outcome- (see **WARNINGS)**.
  - conjunctival, ocular and retinal bleeding
- *Respiratory, thoracic and mediastinal disorders:*
  - bronchospasm
- *Skin and subcutaneous tissue disorders:*

- angioedema, erythema multiforme, Stevens-Johnson syndrome, lichen planus

- *Renal and urinary disorders:*
  - glomerulopathy, increased creatinine levels
- *Vascular disorders:*
  - vasculitis, hypotension
- *Gastrointestinal disorders:*
  - colitis (including ulcerative or lymphocytic colitis), pancreatitis
- *Musculoskeletal, connective tissue and bone disorders:*
  - myalgia

To read as follows (the proposed added changes are identified by underline):

• *Body as a whole:*
- hypersensitivity reactions, anaphylactoid reactions, serum sickness
• *Central and Peripheral Nervous System disorders:*
- confusion, hallucinations, taste disorders
• *Hepato-biliary system disorders:*
- abnormal liver function test, hepatitis (non-infectious), acute liver failure
• *Platelet, Bleeding and Clotting disorders:*
- cases of bleeding with fatal outcome (especially intracranial, gastrointestinal and retroperitoneal hemorrhage)
- agranulocytosis, aplastic anemia/pancytopenia, thrombotic thrombocytopenic purpura (TTP) - some cases with fatal outcome – (see **WARNINGS**.)
- conjunctival, ocular and retinal bleeding
• *Respiratory, thoracic and mediastinal disorders:*
- bronchospasm, interstitial pneumonitis
• *Skin and subcutaneous tissue disorders:*
- angioedema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, lichen planus
• *Renal and urinary disorders:*
- glomerulopathy, increased creatinine levels
• *Vascular disorders:*
- vasculitis, hypotension
• *Gastrointestinal disorders:*
- colitis (including ulcerative or lymphocytic colitis) , pancreatitis, stomatitis
• *Musculoskeletal, connective tissue and bone disorders:*
- myalgia"

We have completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on August 4, 2005.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410

FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Meg Pease-Fye, M.S.
Regulatory Project Manager
(301) 796-1130

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: approved labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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