DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 14-214/S-058

Sanofi Aventis U.S. LLC
Attention: Debra Kolb (Mailstop 55A-430A)
Specialist, US RAMP
55 Corporate Drive
Bridgewater, NJ 08807

Dear Ms. Kolb:

Please refer to your supplemental new drug application dated October 22, 2008, received October 23, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NegGram® (nalidixic acid) Caplets.

This "Prior Approval" supplemental new drug application provides for the following changes to the package insert (additions are noted by underline and deletions are noted by ~~strikethrough~~).

1. In the **PRECAUTIONS/General** subsection of the package insert, the first paragraph is modified as follows:

   Blood counts and renal and liver function tests should be performed periodically if treatment is continued for more than two weeks. NegGram should be used with caution in patients with liver disease, epilepsy, or severe cerebral arteriosclerosis. (See **WARNINGS**.) ~~While c~~Caution should be used in patients with ~~severe~~ renal ~~failure~~ insufficiency~~, therapeutic concentrations of NegGram in the urine, without increased toxicity due to drug accumulation in the blood, have been observed in patients on full dosage with creatinine clearances as low as 2 mL/minute to 8 mL/minute.~~(See **DOSAGE AND ADMINISTRATION**.)

2. In the **DOSAGE AND ADMINISTRATION,** a new subsection titled **Renal Insufficiency** is added as follows:

   Renal Insufficiency.
   The normal dosage of nalidixic acid may be employed in patients with plasma creatinine of less than 300 µmol/L (creatinine clearance more than 20 mL/minute). Dosage should be halved in patients with plasma creatinine of more than 300 µmol/L (creatinine clearance 20 mL/minute or less).

We completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text, submitted on October 22, 2008.

The final printed labeling (FPL) must be identical to the enclosed labeling package insert.

As soon as possible, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling for the package insert. Upon receipt, we will transmit this version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions, "**SPL for approved NDA 14-214/S-058**."

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
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Sherry Spriggs, Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure Package Insert

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

/s/

Renata Albrecht

3/28/2009 11:02:52 AM