DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-537/S-070
NDA 19-847/S-044
NDA 19-857/S-051
NDA 20-780/S-028
NDA 21-473/S-025

Bayer Pharmaceuticals Corporation
Attention: Janet Herrington, Ph.D.
Deputy Director, Regulatory Affairs
P.O. Box 1000
Montville, New Jersey 07045-1000

Dear Dr. Herrington:

We have received your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Drug Product Name	**NDA Number**	**Supplement number**	**Date of supplement**	**Date of receipt**
CIPRO® (ciprofloxacin hydrochloride) Tablets	19-537	S-070	November 3, 2008	November 3, 2008
CIPRO® IV (ciprofloxacin) 1% Solution in Vials	19-847	S-044	November 3, 2008	November 14, 2008
CIPRO® IV (ciprofloxacin) 0.2 % Solution in 5% Dextrose	19-857	S-051	November 3, 2008	November 14, 2008
CIPRO® (ciprofloxacin) Oral Suspension	20-780	S-028	November 3, 2008	November 14, 2008
CIPRO® XR (ciprofloxacin extended-release tablets)	21-473	S-025	November 3, 2008	November 14, 2008

We acknowledge receipt of your submissions dated February 19, 2009 and March 27, 2009.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) for an approved drug if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since Cipro® was approved on October 22, 1987, we have become aware of additional information about the risk of tendon-related adverse events as described in our July 7, 2008 letter. This

information was not available when Cipro® was granted marketing authorization. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA notified you in our July 7, 2008, letter that the development of a Medication Guide was required as provided for under 21 CFR Part 208. In response, you converted your previously approved patient package insert to a Medication Guide and revised it to include the new safety information. Pursuant to 21 CFR Part 208, FDA has determined that Cipro® poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Cipro®. FDA has determined that Cipro® is a product that has serious risk(s) (relative to benefits) of which patients should be made aware because information concerning the risk(s) could affect patients' decisions to use, or continue to use Cipro®. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Cipro®.

Your proposed REMS, submitted on November 3, 2008 and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your February 19, 2009 and March 27, 2009 submissions.

Your assessment of the REMS should include an evaluation of:

a. Patients' understanding of the serious risks of Cipro®
b. A report on periodic assessments of the distribution and dispending of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 19-537, NDA 19-847, NDA 19-857, NDA 20-780, and
NDA 21-473 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 19-537, NDA 19-847, NDA 19-857,
NDA 20-780, and NDA 21-473
PROPOSED REMS MODIFICATION
< other supplement identification > [if included]
<REMS ASSESSMENT> [if included]

If you do not submit electronically, please send 5 copies of submissions containing REMS assessments or proposed modifications of the REMS.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, 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 (text for the package insert, Medication Guide). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 19-537/S-070, NDA 19-847/S-044, NDA 19-857/S-051, NDA 20-780/S-028, and NDA 21-473/S-025."**

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

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 Hyun Son, Pharm.D., Acting Safety Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, M.D., MPH
Deputy Director for Safety
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: REMS
Medication Guide

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

/s/

Ozlem Belen

4/27/2009 02:59:00 PM