APPLICATION NUMBER:

19-537 / S-049
20-780 / S-013
19-847 / S-027
19-857 / S-031

APPROVAL LETTER
NDA 19-537/S-049  
NDA 19-857/S-031  
NDA 19-847/S-027  
NDA 20-780/S-013

Bayer Pharmaceuticals Corporation  
Attention: Mr. Andrew Verderame  
Director, Regulatory Affairs  
400 Morgan Lane  
West Haven, CT 06516

Dear Mr. Verderame:

Please refer to your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

<table>
<thead>
<tr>
<th>Name of Drug Product</th>
<th>NDA Number</th>
<th>Supplement Number</th>
<th>Date of Supplement</th>
<th>Date of Receipt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cipro\textsuperscript{®} (ciprofloxacin hydrochloride) Tablets, 100 mg, 250 mg, 500 mg and 750 mg</td>
<td>19-537</td>
<td>S-049</td>
<td>09-23-03</td>
<td>09-25-03</td>
</tr>
<tr>
<td>Cipro\textsuperscript{®} IV (ciprofloxacin) 0.2% Solution in 5% Dextrose, 200 mg and 400 mg</td>
<td>19-857</td>
<td>S-031</td>
<td>09-24-03</td>
<td>09-29-03</td>
</tr>
<tr>
<td>Cipro\textsuperscript{®} IV (ciprofloxacin) 1% Solution Vials, 200 mg, 400 mg and 1200 mg</td>
<td>19-847</td>
<td>S-027</td>
<td>09-24-03</td>
<td>09-29-03</td>
</tr>
<tr>
<td>Cipro\textsuperscript{®} (ciprofloxacin) Oral Suspension, 5% and 10%</td>
<td>20-780</td>
<td>S-013</td>
<td>09-24-03</td>
<td>09-29-03</td>
</tr>
</tbody>
</table>

We acknowledge receipt of your submissions dated:

January 26, 2004  March 12, 2004  March 19, 2004  
January 30, 2004  March 17, 2004  March 24, 2004  
February 12, 2004  March 18, 2004 (2)  March 25, 2004

These supplemental new drug applications provide for the use of Cipro\textsuperscript{®} (ciprofloxacin) for the treatment of complicated urinary tract infections and pyelonephritis for pediatric patients (1 to 17 years of age) with the following information to be included in the INDICATIONS AND USAGE section of the final printed labeling.

**Complicated Urinary Tract Infections and Pyelonephritis due to Escherichia coli.**

NOTE: Although effective in clinical trials, ciprofloxacin is not a drug of first choice in the pediatric population due to an increased incidence of adverse events compared to controls, including events related to joints and/or surrounding tissues. (See WARNINGS, PRECAUTIONS, Pediatric Use, ADVERSE REACTIONS and CLINICAL STUDIES.)
summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled “Postmarketing Study Protocol”, “Postmarketing Study Final Report”, or “Postmarketing Study Correspondence.”

In addition, submit three copies of the introductory promotional materials that you propose to use for these products for the newly approved pediatric indications 4 weeks prior to distribution. We remind you of your agreement during our March 23, 2004 teleconference to include the complete text from the INDICATIONS AND USAGE section of the labeling in all promotional materials and advertisements for the pediatric complicated urinary tract infections and pyelonephritis indications, including the NOTE regarding efficacy, safety and preclinical information. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Special Pathogen and Immunologic Drug Products and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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 reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Yon Yu, Pharm D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

(See appended electronic signature page)

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluations IV
Center for Drug Evaluations and Research
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
3/25/04 04:14:08 PM