CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-473

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-473

Bayer Corporation
Attention: Andrew Verderame
400 Morgan Lane
West Haven, CT 06516-4175

Dear Mr. Verderame:

Please refer to your new drug application (NDA) dated March 4, 2002, received March 5, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CIPRO® XR (ciprofloxacin extended-release tablets), 500 mg.

We acknowledge receipt of your submissions dated:

April 9, 2002	May 9, 2002	November 21, 2002
April 11, 2002	June 28, 2002	November 22, 2002
April 12, 2002	July 12, 2002	November 26, 2002 (4)
April 22, 2002	July 18, 2002 (3)	December 4, 2002 (2)
April 23, 2002	August 7, 2002	December 6, 2002 (4)
May 6, 2002	September 10, 2002	December 12, 2002 (2)
May 7, 2002	September 20, 2002	
May 8, 2002	November 15, 2002 (2)	

This new drug application provides for the use of CIPRO® XR (ciprofloxacin extended-release tablets) for uncomplicated urinary tract infections (acute cystitis).

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and patient package insert submitted December 12, 2002) and submitted labeling (immediate container and carton labels submitted September 20, 2002). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-473**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated December 12, 2002. These commitments are listed below.

1. Provide confirmative evidence of CIPRO XR efficacy in treating uncomplicated urinary tract infections caused by *S. saprophyticus.*

Protocol Submission:	July 1, 2003
Study Start:	October 1, 2003
Final Report Submission:	December 31, 2004

2. Provide an annual update on CIPRO XR usage patterns for the first two years of product availability; with the submission dates being no later than February 28, 2004 and February 28, 2005 respectively.

Submit any clinical protocols for these studies to your IND for this product. Submit any nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected 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."**

The text in italics below addresses the application of FDA's Pediatric Rule at 21 CFR 314.55 to this NDA. The Pediatric Rule has been challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. The government has not yet decided whether to seek a stay of the court's order. In addition, the government has not yet decided whether to appeal the decision; an appeal must be filed within 60 days. **Therefore, this letter contains a description of the pediatric studies that would be required under the Pediatric Rule, if the Pediatric Rule remained in effect and/or were upheld on appeal.** Please be aware that whether or not these pediatric studies will be required will depend upon the resolution of the litigation. FDA will notify you as soon as possible as to whether this application will be subject to the requirements of the Pediatric Rule as described below. In any event, we hope you will decide to conduct these pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens must contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (21 CFR 314.55).

Based on information submitted, we conclude the following:

For uncomplicated urinary tract infections (acute cystitis) caused by Escherichia coli, Proteus mirabilis, Enterococcus faecalis, or Staphylococcus saprophyticus.

- *We are deferring submission of pediatric studies for pediatric patients ages 0-16 years until December 31, 2008.*

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. 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 insert directly to:

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

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Jouhayna Saliba, 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 Evaluation IV
Center for Drug Evaluation and Research

Enclosure

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
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APPEARS THIS WAY
ON ORIGINAL