# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

*APPLICATION NUMBER:*

# 19-537 / S-045

*Trade Name:* **Cipro**

*Generic Name:* **Ciprofloxacin**

*Sponsor:* **Bayer Corporation**

*Approval Date:* **December 10, 2002**

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# 19-537 / S-045

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## Reviews / Information Included in this NDA Review.

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| Summary Review | |
| Officer/Employee List | |
| Office Director Memo | |
| Cross Discipline Team Leader Review | |
| Medical Review(s) | |
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*APPLICATION NUMBER:*

# 19-537 / S-045

# APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-537/S-045

Bayer Corporation Pharmaceutical Division
Attention: Andrew S. Verderame
Director, Regulatory Affairs
400 Morgan Lane
West Haven CT 06516

Dear Mr. Verderame:

Please refer to your supplemental new drug application dated July 3, 2002, received July 5, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cipro (ciprofloxacin hydrochloride) Tablets, 100 mg, 250 mg, 500 mg, and 750 mg.

This "Changes Being Effected in 30 days" supplemental new drug application supplemental new drug application provides for Bayer [redacted] as an alternate drug substance manufacturing facility.

We have completed the review of this supplemental application, and it is approved.

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, call Jouhayna Saliba, Regulatory Project Manager, at (301) 827-2331.

Sincerely,

*{See appended electronic signature page}*

Norman R. Schmuff, Ph.D.
Chemistry Team Leader for the
Division of Special Pathogen and Immunologic Drug Products, (HFD-590)
DNDC III, Office of New Drug Chemistry
Center for Drug Evaluation 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/

Norman Schmuff
12/10/02 07:10:17 AM

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# 19-537 / S-045

# CHEMISTRY REVIEW(S)

| SUPPLEMENTAL NDA CHEMIST'S REVIEW | DUE DATE 1/5/03 | 1. ORGANIZATION HFD-590 | 2. NDA NUMBER 19-537 |
|---|---|---|---|

**3. NAME AND ADDRESS OF APPLICANT**
Bayer Corporation Pharmaceutical Division
ATTN: Andrew S. Verderame
400 Morgan Lane
West Haven, CT 06516

**4. TYPE OF SUPPLEMENT**
PAS

**5. DOCUMENT(S)**

| NUMBERS | DATED | RECEIVED |
|---|---|---|
| SCM-045 | 7/3/02 | 7/5/02 |

**6. NAME OF DRUG**
Cipro Tablets

**7. NONPROPRIETARY NAME**
ciprofloxacin hydrochloride tablets

**8. SUPPLEMENT PROVIDES FOR:**
Alternate manufacturing site for ciprofloxacin hydrochloride.

**9. AMENDMENTS/DATES**
N/A

**10. PHARMACOLOGICAL CATEGORY**
Antibacterial

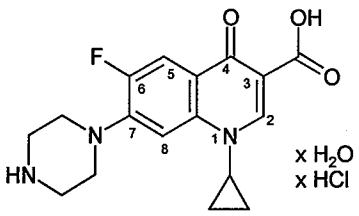
**11. HOW DISPENSED**
|X| Rx | | OTC

**12. RELATED IND/NDA/DMF(s)**
N/A

**13. DOSAGE FORM(S)**
tablets

**14. POTENCY (CIES)**
100 mg, 250 mg, 500 mg, 750 mg

**15. CHEMICAL NAME AND STRUCTURE**




3-quinoline carboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-, monohydrochloride, monohydrate

**16. MEMORANDA**
N/A

**17. COMMENTS**
This supplemental application provides for Bayer [redacted] as an alternate manufacturing facility for the ciprofloxacin hydrochloride drug substance. CMC information pertaining to this change was submitted in the July 3, 2002 amendment to the DMF [redacted] (ciprofloxacin hydrochloride drug substance). EER was submitted for this application and it was found acceptable on August 5, 2002. See review notes for further details.

**18. CONCLUSIONS AND RECOMMENDATIONS**
This supplement is recommended for approval.

**19. REVIEWER**

| NAME | SIGNATURE | DATE OF DRAFT REVIEW |
|---|---|---|
| Dorota Matecka | *[signed electronically in DFS]* | 12/6/02 |

**20. CONCURRENCE:** HFD-590/NSchmuff *[signed electronically in DFS]*

| DFS CC LIST | | L | Dorota Matecka | | L | Med: | | | PharmTox |
|---|---|---|---|---|---|---|---|---|---|
| L = Action Letter | R | L | NSchmuff | R | L | PM | | | Micro |
| R = Review | | | | | | Biopharm | | | |

**REVIEW NOTES**

This supplemental application provides for Bayer [redacted] as an alternate manufacturing facility for the ciprofloxacin hydrochloride drug substance. The currently approved manufacturing facility for the drug substance is Bayer facility in [redacted]

The applicant stated that all aspects of the ciprofloxacin hydrochloride manufacture used at the proposed facility would be the same as the currently approved for the [redacted] acility. The detailed CMC information pertaining to this change was submitted in the July 3, 2002 amendment to the DMF [redacted] ld by Bayer for ciprofloxacin hydrochloride drug substance). This amendment was reviewed and found acceptable (see ! [redacted] for further details).

In addition, the applicant committed to place the first batch of Cipro tablets manufactured using the drug substance produced at the [redacted] facility on long term stability and report the results in the NDA annual reports.

EER was submitted for this application and it was found acceptable on August 5, 2002. The copy of the acceptable EER is attached.

03-DEC-2002 FDA CDER EES Page 1 of 1

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application : NDA 19537/045
Org Code : 590
Priority : 1P

Sponsor: BAYER
400 MORGAN LANE
WEST HAVEN, CT 065164175

Stamp Date : 05-JUL-2002
PDUFA Date : 05-JAN-2003
Action Goal :
District Goal: 01-DEC-2002

Brand Name : CIPRO
Estab. Name:
Generic Name: CIPROFLOXACIN HYDROCHLORIDE
Dosage Form: (TABLET)
Strength : 100 MG, 250 MG, 500 MG,

| FDA Contacts: | | | |
|---|---|---|---|
| J. SALIBA | Project Manager (HFD-590) | 301-827-2387 |
| D. MATECKA | Review Chemist (HFD-590) | 301-827-2398 |
| N. SCHMUFF | Team Leader (HFD-590) | 301-827-2425 |

Overall Recommendation: ACCEPTABLE on 05-AUG-2002by J. D AMBROGIO(HFD-324) 301-827-0062

Establishment : [redacted] FEI : 3002806462

DMF No: [redacted] AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile : CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 05-AUG-02
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

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

/s/
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Dorota Matecka
12/9/02 07:10:44 PM
CHEMIST

Norman Schmuff
12/10/02 07:06:43 AM
CHEMIST