DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-847/S-032
NDA 19-857/S-038

Bayer Pharmaceuticals Corporation
Attention: Ms. Janet Herrington
Deputy Director
400 Morgan Lane
West Haven, CT 06516-4175

Dear Ms. Herrington:

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

NDA #	Drug Product	Supplement Number	Letter Date	Receipt Date
19-847	Cipro® (ciprofloxacin) IV 1% Solution in Vials, 200 mg, 400 mg	S-032	December 22, 2004	December 23, 2004
19-857	Cipro® (ciprofloxacin) IV 0.2 % Solution in 5% Dextrose in Flexible Containers, 200 mg, 400 mg	S-038	December 22, 2004	December 23, 2004

We acknowledge receipt of your submissions dated February 18, 2005.

These "Changes Being Effected" supplemental new drug applications provide for the following revisions to the package insert (additions are double underlined and deletions are ~~struck out~~):

1. **ADVERSE REACTIONS**

- The SKIN/HYPERSENSITIVITY statement under the **Adverse Reactions in Adult Patients** subsection was revised to read:

SKIN/HYPERSENSITIVITY: allergic reactions, anaphylactic reactions including life-threatening anaphylactic shock, erythema multiforme/Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal necrolysis, vasculitis, angioedema, edema of the lips, face, neck, conjunctivae, hands or lower extremities, purpura, fever, chills, flushing, pruritus, urticaria, cutaneous candidiasis, vesicles, increased perspiration, hyperpigmentation, erythema

nodosum, thrombophlebitis, burning, paresthesia, erythema, swelling, photosensitivity (See **WARNINGS**.)

- "Lyell's Syndrome" was added to the list of **Post-Marketing Adverse Events** to read:

Agitation, agranulocytosis, albuminuria, anosmia, candiduria, cholesterol elevation (serum), confusion, constipation, delirium, dyspepsia, dysphagia, erythema multiforme, exfoliative dermatitis, fixed eruption, flatulence, glucose elevation (blood), hemolytic anemia, hepatic failure, hepatic necrosis, hyperesthesia, hypertonia, hypesthesia, hypotension (postural), jaundice, marrow depression (life threatening), methemoglobinemia, moniliasis (oral, gastrointestinal, vaginal), myalgia, myasthenia, myasthenia gravis (possible exacerbation), myoclonus, nystagmus, pancreatitis, pancytopenia (life threatening or fatal outcome), peripheral neuropathy, phenytoin alteration (serum), potassium elevation (serum), prothrombin time prolongation or decrease, pseudomembranous colitis (The onset of pseudomembranous colitis symptoms may occur during or after antimicrobial treatment.), psychosis (toxic), renal calculi, serum sickness like reaction, Stevens-Johnson syndrome, taste loss, tendonitis, tendon rupture, torsade de pointes, toxic epidermal necrolysis (Lyell's Syndrome), triglyceride elevation (serum), twitching, vaginal candidiasis, and vasculitis. (See **PRECAUTIONS**.)

2. OVERDOSAGE

- The first paragraph in this section was revised to read:

In the event of acute overdosage, the patient should be carefully observed and given supportive treatment, including monitoring of renal function. Adequate hydration must be maintained. Only a small amount of ciprofloxacin (< 10%) is removed from the body after hemodialysis or peritoneal dialysis.

3. HOW SUPPLIED

- This section was revised to read:

CIPRO I.V. (ciprofloxacin) is available as a clear, colorless to slightly yellowish solution. CIPRO I.V. is available in 200 mg and 400 mg strengths. The concentrate is supplied in vials while the premixed solution is supplied in latex-free flexible containers as follows:

VIAL: manufactured ~~by Bayer HealthCare LLC and Hollister-Stier, Spokane, WA 99220.~~for Bayer Pharmaceuticals Corporation by Bayer HealthCare LLC, Shawnee, Kansas.

SIZE	STRENGTH	NDC NUMBER
20 mL	200 mg, 1%	~~0026-8562-20~~ 0085-1763-03
40 mL	400 mg, 1%	~~0026-8564-64~~ 0085-1731-01

FLEXIBLE CONTAINER: manufactured for Bayer Pharmaceuticals Corporation by ~~Abbott Laboratories~~ Hospira, Inc., North Chicago, IL 60064.

SIZE	STRENGTH	NDC NUMBER
100 mL 5% Dextrose	200 mg, 0.2%	~~0026-8552-36~~0085-1755-02
200 mL 5% Dextrose	400 mg, 0.2%	~~0026-8554-63~~0085-1741-02

FLEXIBLE CONTAINER: manufactured for Bayer Pharmaceuticals Corporation by Baxter Healthcare Corporation, Deerfield, IL 60015.

SIZE	STRENGTH	NDC NUMBER
100 mL 5% Dextrose	200 mg, 0.2%	~~0026-8527-36~~0085-1781-01
200 mL 5% Dextrose	400 mg, 0.2%	~~0026-8527-63~~0085-1762-01

STORAGE

Vial: Store between 5 – 30ºC (41 – 86ºF).
Flexible Container: Store between 5 – 25ºC (41 – 77ºF).
Protect from light, avoid excessive heat, protect from freezing.
CIPRO I.V. (ciprofloxacin) is also available in a 120 mL Pharmacy Bulk Package.
Ciprofloxacin is also available as CIPRO (ciprofloxacin HCl) Tablets ~~100 mg,~~ 250, 500, and 750 mg and CIPRO (ciprofloxacin*) 5% and 10% Oral Suspension.
Does not comply with USP with regards to "loss on drying" and "residue on ignition".

4. The company signature was revised to read:

Bayer HealthCare

Bayer Pharmaceuticals Corporation
400 Morgan Lane
West Haven, CT 06516

Distributed by:

Schering-Plough

Schering Corporation
Kenilworth, NJ 07033

CIPRO is a registered trademark of Bayer Aktiengesellschaft and is used under license by Schering Corporation.

Rx Only
~~08724752, R.6~~ 08918506, R.0 ~~4/04~~ 11/04 ©2004BayerPharmaceuticalsCorporation ~~12318~~ 12566

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Abbott Number To Come

We completed our review of these applications, as amended, and they are approved effective on the date of this letter.

If you issue a letter communicating important information about these drug products (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to each 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 the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Robin Anderson, R.N., M.B.A, Labeling Reviewer, 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

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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