

McKenna & Cuneo, L.L.P.

Attorneys at Law

Los Angeles
San Francisco
San Diego

1900 K Street, N.W. ■ Washington, D.C. 20006-1108
202-496-7500 ■ Fax: 202-496-7756
www.mckennacuneo.com

Denver
Dallas
Brussels

February 15, 2000

VIA FEDERAL EXPRESS

Ms. Cecelia Parise
Office of Generic Drugs
Food and Drug Administration
Room E-112 (HFD-600)
Metro Park North 2
7500 Standish Place
Rockville, MD 20855

Gary L. Yingling
202-496-7645
gary_yingling@mckennacuneo.com

0183 00 FEB 28 10 30

Re: **Patent Listing Abuses by the Brand Industry**
Docket No. 85N-0214 – 180-Day Generic Drug Exclusivity

Dear Ms. Parise:

As you know, on November 4, 1999, the National Pharmaceutical Alliance (“NPA”) submitted Comments to the Food and Drug Administration (“FDA”) on the proposed regulation to implement the 180-day exclusivity provisions of the Hatch-Waxman Act (64 Fed. Reg. 42873; Docket No. 85N-0214). In the Comments, NPA requested that the agency take action to curb brand industry abuses with respect to the listing of inappropriate patents in FDA’s *Approved Drug Products With Therapeutic Equivalence Evaluations* (the “Orange Book”).

For every irrelevant patent that the brand industry lists with FDA, the industry sets in motion the potential to obtain a 30-month stay against FDA approval of a competing generic drug. Since the brand industry reaps millions of dollars of profits during that 30 month period, clearly there is no incentive for them to list only material patents with FDA. Therefore, NPA implores FDA to initiate administrative, rulemaking or enforcement action to curb these abuses.

In support of our request, and in response to your inquiry, we are providing additional examples of patent listing abuses. A chart containing these examples is attached.

85N-0214

C70

McKenna & Cuneo, L.L.P.

Attorneys at Law

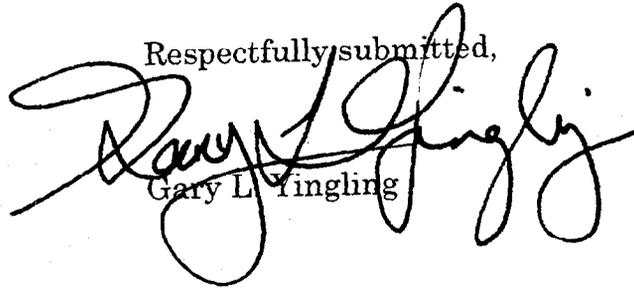
Ms. Cecelia Parise

February 15, 2000

Page 2

Thank you for your consideration of this information.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Gary L. Yingling". The signature is fluid and cursive, with the first name "Gary" being the most prominent.

Gary L. Yingling

GLY/rld

Enclosure(s)

cc: Chris Sizemore, President, NPA
FDA Dockets Management Branch

Patent Listing Abuses
By The Brand Drug Industry

2/15/2000

| Brand Drug Company | Drug | Category | Summary |
|----------------------|-----------------------------|---|---|
| Abbott | Hytrin® (terazosin) | Hydrate Method of Use Term Extension | Abbott listed a patent on the dihydrate form of the drug. Abbott also listed a patent for a new use of the product. Abbott also sued for infringement of an expired patent that was still listed, arguing in court that the patent deserved a term extension. |
| Astra Merck | Prilosec® (omeprazole) | Secondary Metabolite Method of Use Extended Release Mechanism | Astra Merck listed patents for the single isomer, perprazole (also called esomeprazole) and the salt form, sulphenamide. Astra also listed patents for several unapproved uses. Astra also listed a patent for the drug's delayed release mechanism. |
| Bayer | Adalat CC® (nifedipine) | Extended Release Mechanism | Bayer listed a patent on the drug's extended release mechanism. |
| Bristol-Myers Squibb | Desyrel® (trazadone) | Packaging | BMS listed a patent for a tablet configuration consisting of "multifractionable tablets with bisectable/trisectable structures." |
| Bristol-Myers Squibb | Duricef® (cefadroxil) | Hydrate | BMS listed patents for both the hemihydrate and monohydrate forms of the drug. |
| Bristol-Myers Squibb | Platinol AQ® (cisplatin) | Packaging | BMS listed a patent for the drug being "protected from light" via packaging in a brown bottle. |

| | | | |
|----------------------|---------------------------------|--|--|
| Bristol-Myers Squibb | Taxol® (paroxetine) | Dosage Administration | BMS listed a patent covering the dose (135-175 mg) and administration (parenteral administration over 3 hour period) for the drug. |
| Eli Lilly | Prozac® (fluoxetine) | Isomer | Eli Lilly listed a patent for the single isomer, (R)-fluoxetine. |
| Eli Lilly | Evista® (raloxifene HCl) | Method of Use Solvate Dosage Administration Formulation | Eli Lilly listed 18 patents in the Orange Book, many for unapproved uses such as treating endocrine disorders, breast cancer, prostate cancer, and lowering cholesterol. Lilly listed patents for the hemisolvate, non-solvated crystalline, ester, ether, and acid salt forms of the drug. Lilly listed patents covering the dose (range of mg) and administration (to man, woman, postmenopausal woman, etc.) of the drug. Lilly also listed patents for formulations of tablets and capsules, and formulations highlighting inactive ingredients. |
| Glaxo | Wellbutrin®/ Zyban® (bupropion) | Formulation Method of Use | Glaxo listed a patent for a membrane coated tablet that has a specific dissolution profile and that is not related to the product's hydrogel matrix tablet. Glaxo listed method-of-use patents for unapproved uses. |
| Glaxo | Zantac® (ranitidine) | Polymorph Formulation | Glaxo listed its "Form 2 crystalline" patent, along with the original "Form 1 crystalline" patent, on the Form 1 drug. Glaxo also listed a patent for a formulation improvement involving pH and ethanol. |

| | | | |
|------------------------------|---|----------------------------------|---|
| Hoechst Marion Roussel | Cardizem CD® (diltiazem) | Extended Release Mechanism | HMR listed a patent for the extended release mechanism. |
| Hoechst Marion Roussel | Seldane® (terfenadine) | Secondary Metabolite | HMR listed a patent for the fexofenadine metabolite (marketed as Allegra®), as well as the original compound, terfenadine. |
| Merck | Sinemet CR® (carbidopa/ levodopa) | Extended Release Mechanism | Merck listed a patent on the drug's extended release mechanism. |
| Merck | Pepcid® (famotidine) | Dosage Administration | Merck listed a patent covering the dose (10 mg) and administration (30 minutes prior to food consumption). |
| Novartis | Aredia® (pamidronate) | Hydrate | Novartis listed a patent on the disodium pentahydrate form of the drug. |
| Novartis | SandImmune® (cyclosporine) | Formulation | Novartis listed a patent for its newer microemulsion formulation, marketed as Neoral®. |
| Pfizer | Enablex® | Method of Use | Pfizer listed method-of-use patents for unapproved uses. |
| Pfizer | Procardia XL® (nifedipine) | Extended Release Mechanism | Pfizer listed a patent on the extended release mechanism. |
| Pharmacia & Upjohn | Glynase® (glyburide) | Formulation | P&U listed a patent for a "formulation improvement" involving the inactive ingredient, spray-dried lactose. |
| Pharmacia & Upjohn | Xanax® (alprazolam) | Packaging | P&U listed a patent for the tablet configuration consisting of a rectangle with three notches. |
| Schering | Claritin® (loratidine) | Secondary Metabolite | Schering listed a patent for the desloratidine metabolite, as well as the parent compound, loratidine. |

| | | | |
|--------------------------|----------------------------|------------------------------------|---|
| SmithKline Beecham | Paxil® (paroxetine) | Hydrate | SKB listed patents on both the hemihydrate and anhydrous forms of the drug. |
| Tap Pharma- ceuticals | Lupron Depot® | Formulation | Tap listed a patent for the drug delivery system. |
| Warner Lambert | Neurontin® (gabapentin) | Hydrate Method of Action | W-L listed a patent on the older monohydrate form of the compound, which was not contained in Neurontin®. W-L also listed a patent for a 3-day titration schedule for the drug. |
| Zeneca | Diprivan® (propofol) | Formulation | Zeneca listed a patent for a formulation improvement using the inactive ingredient, EDTA. |

From: ANNE G. PICCIANO (202)496-7689
MCKENNA & CUNEO
1900 K STREET, N.W.

SHIPPER'S FEDEX ACCOUNT #



WASHINGTON, DC, 20006

To: Dockets Management Branch (202)496-7568
Food and Drug Administration
Room 1061, HFA-305
5630 Fishers Lane
Rockville, MD, 20852

SHIP DATE: 17FEB00
WEIGHT: 1 LBS

Ref: 171950010



DELIVERY ADDRESS
TRK # 7908 1231 3870 FORM 0201

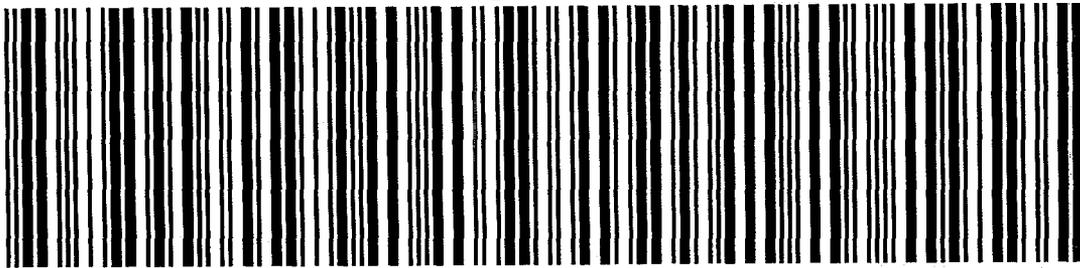
PRIORITY OVERNIGHT

FRI
AA

Deliver by:
18FEB00

20852-MD-US

IAD
19 EDGA



Shipping Label

Schedule Courier

Find a Dropoff Location

Shipping History

Shipment Complete

Cancel Shipment

1. Use the "Print" feature from your browser to send this page to your laser printer.
2. Fold the printed page along the horizontal line.
3. Place label in air waybill pouch and affix it to your shipment so that the barcode portion of the label can be read and scanned.
4. To print a receipt of your shipment, please click on "Shipping History."

Ship a New Package

Ship Inside U.S.

Ship Outside U.S.

Ship to Same Recipient

Use of this system constitutes your agreement to the service conditions in the current FedEx service Guide, available upon request.

FedEx will not be responsible for any claim in excess of \$100 per package, whether the result of loss, damage, delay, non-delivery, misdelivery, or misinformation, unless you declare a higher value, pay an additional charge, document your actual loss and file a timely claim. Limitations found in the current FedEx Service Guide apply. Your right to recover from FedEx for any loss, including intrinsic value of the package, loss of sales, income interest, profit, attorney's fees, costs, and other forms of damage whether direct, incidental, consequential, or special is limited to the greater of \$100 or the authorized declared value. Recovery cannot exceed actual documented loss. Maximum for items of extraordinary value is \$500, e.g. jewelry, precious metals, negotiable instruments and other items listed in our Service Guide. Written claims must be filed within strict time limits, see current FedEx Service Guide.